URO ONCO PATH | International Congress on Frontiers in Urologic Oncology and Uropathology

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International Congress on Frontiers in

Urologic Oncology and Uropathology

10th-12th January 2025 | Bhubaneswar, Odisha

Update for Practicing Pathologists and Uro-oncologists

Kalinga Institute of Medical Sciences

Organised By

IAIO International Association for Integrated Oncology | GUPS Genitourinary Pathology Society | KIMS Bhubaneswar | AIIMS Bhubaneshwar | MEU India

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International Congress on Frontiers in Urologic Oncology and Uropathology

Welcome !

International Congress on Frontiers in Urologic Oncology and Uropathology-2025, Bhubaneswar, India

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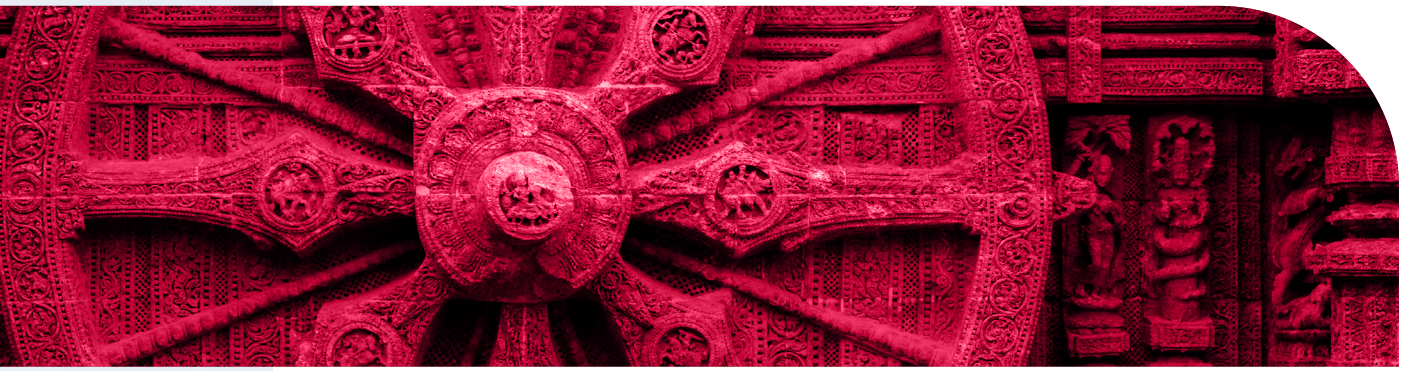
INTERNATIONAL ASSOCIATION FOR INTEGRATED ONCOLOGY



Preface

This book presents the proceedings of the International Congress on Frontiers in Urologic Oncology and Uropathology, held from 10th to 12th January 2025 in Bhubaneswar, India, with the theme "Update for Practicing Pathologists and Uro-oncologists." After a thorough peer review of the submitted abstracts, over 50 abstracts were selected for inclusion in the conference proceedings. We extend our heartfelt thanks to all the participants for their valuable contributions to both the conference and these proceedings.

We are deeply thankful to the reviewers for their time and effort in evaluating the abstracts and ensuring the quality of this compilation. Finally, we would like to thank everyone involved in the coordination of the International Congress on Frontiers in Urologic Oncology and Uropathology, whose dedication and invaluable time made the proceedings a grand success.

The success of the International Congress on Frontiers in Urologic Oncology and Uropathology is a result of the collaborative efforts of a committed group of individuals, and everyone involved should take pride in this remarkable accomplishment.

Remembering A Legacy...

Dr. Ondrej Hes

1968-2022

"A Champion is one who is remembered, a legend is one who is never forgotten"

As a sense of loss prevails us, the world will always remember Dr. Ondrej Hes as a giant intellectual, a champion, a legend renowned in the field of genitourinary pathology, moreover, an outstanding teacher and an exemplary mentor. Besides all the numerous traits that can be ascribed, the most striking of them all was his simplicity, humility and straightforwardness.

Dr. Ondrej, or Ondra, as he was known by those close, was a world-renowned genitourinary pathologist with over 400 publications, especially for his pioneering and innovative work in the field of renal tumors. His research was greatly implemental towards various GUPS consensus papers, LOTR, papillary renal tumors, eosinophilic and oncocytic renal tumors among the many. The legend was always on the lookout to find families for many of the "orphan" renal tumors, notably "LOT." During my brief interaction with him, Dr. Ondrej was always so obliging, accommodative and an enthusiastic educator. He never turned down any questions from junior students, eager to train in genitourinary pathology, and was always encouraging, inspiring, promising and courteous as a senior author in various multi-institutional collaborations. The warmth and modesty with which he interacted with his students was endearing. His legacy will continue to live as an inspiration to all his colleagues, friends and students globally.

Dr. Ondrej Hes will always be remembered as an esteemed pillar in the field of genitourinary pathology, a true academician and scholar, an admired teacher and mentor, who touched the lives of countless pathologists, who continue to look up to him and revere him for his unsurmountable knowledge, dedication and passion.

A legend unmatchable, a teacher unparalleled, a human inimitable....

A Heartfelt Tribute from the entire GUPS family !

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Welcome Address

Dr. Sambit K. Mohanty

Organizing Secretary

Dear Esteemed Delegates,

It is with great honor and enthusiasm that I extend a warm welcome to each of you at the International Congress on Frontiers in Urologic Oncology and Uropathology. This congress is a testament to the power of collaboration and shared vision in advancing medical knowledge and improving patient care.

As organizing secretary, I am delighted by the incredible breadth of expertise that this congress brings together. The program has been designed to cover cutting-edge research, groundbreaking innovations, and multidisciplinary approaches in urologic oncology and uropathology. Each session is crafted to foster critical discussions and inspire transformative ideas.It is a privilege to host this event at KIMS, Bhubaneswar, an institution synonymous with academic brilliance and clinical excellence.

KIMS, Bhubaneswar, renowned for its state-of-the-art infrastructure and commitment to academic excellence, serves as the perfect backdrop for this prestigious gathering. Over the next few days, I urge you to engage actively in discussions, challenge existing paradigms, and contribute your unique perspectives to the collective pool of knowledge.

This event is not just about knowledge sharing—it is about building a community of professionals dedicated to advancing healthcare. I encourage you to use this platform to forge new collaborations, challenge conventions, and inspire the next generation of medical breakthroughs.

I look forward to dynamic interactions and the impactful outcomes that this congress promises. Thank you for joining us in this shared mission to advance our field and improve the lives of our patients.

Best wishes,

Dr. Sambit K. Mohanty

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Dr. Sourav K. Mishra

Organizing Secretary

Dear Esteemed Participants,

It is my distinct privilege to welcome you to the International Congress on Frontiers in Urologic Oncology and Uropathology. This congress represents a remarkable confluence of clinical expertise, research innovation, and the collective passion to push the boundaries of modern medicine.

As organizing secretary, I am particularly excited about the program's focus on translational research and multidisciplinary approaches, which aim to bridge the gap between clinical practice and cutting-edge science. From expert plenary talks to case-based discussions, this congress is designed to foster meaningful conversations that lead to impactful outcomes.

Beyond the academic sessions, KIMS, Bhubaneswar offers an environment that encourages professional networking and collaboration. I urge you to take full advantage of this gathering to connect with like-minded professionals, share your ideas, and establish relationships that will endure beyond the congress.

Let us use this opportunity not only to advance our field but also to reaffirm our shared commitment to improving the lives of patients worldwide. I look forward to witnessing the incredible exchanges and breakthroughs this congress will inspire.

Sincerely,

Dr. Sourav K. Mishra

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Dr. Ranjana Giri

Organizing Secretary

Dear Esteemed Colleagues,

Welcome to this extraordinary gathering of experts at the International Congress on Frontiers in Urologic Oncology and Uropathology. It is truly an honor to serve as organizing secretary for an event that brings together such a diverse and accomplished group of professionals dedicated to advancing science and improving patient care.This congress is a celebration of our shared commitment to advancing medical knowledge and improving patient outcomes in some of the most challenging domains of healthcare.

As a professional deeply involved in the interplay between research and clinical practice, I believe this congress provides an invaluable opportunity to bridge gaps, challenge assumptions, and build consensus on the future of urologic oncology and uropathology. The sessions have been meticulously planned to address cutting-edge developments, from the integration of AI in diagnostics to the evolving landscape of targeted therapies.

Our venue, KIMS, Bhubaneswar, stands as a testament to innovation and excellence, and I am confident it will inspire the same spirit in our discussions. I encourage each of you to actively engage in the proceedings, share your valuable insights, and explore collaborative opportunities.

Let us make these three days not just a scientific milestone but also a transformative experience for our field. Together, we have the potential to set new benchmarks in research, education, and clinical care.

Kind regards,

Dr. Ranjana Giri

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Dr. Anandi Lobo

Academic Chair, Organizing Committee

Dear Colleagues and Friends,

It is an absolute pleasure to welcome you all to the International Congress on Frontiers in Urologic Oncology and Uropathology. As a pathologist, I am thrilled to be part of this incredible gathering of minds, which brings together clinicians, pathologists and researchers, all united by a shared purpose – to deepen our understanding of urologic malignancies and their management through collaboration and innovation.

Pathology often serves as the foundation of effective cancer care. This congress is more than just a meeting – it is an opportunity for us to share insights, learn from one another, and bridge the gap between clinical and diagnostic perspectives in urologic oncology. I am excited about the collaborative conversations that will unfold over the next few days. This congress will serve as a testament to the power of teamwork in overcoming challenges and exploring new frontiers in oncology.

Thank you for being here and for your commitment to advancing patient care. Let's make these three days a truly enriching and memorable experience! Welcome, and I look forward to engaging with all of you.

Warm regards,

Dr. Anandi Lobo

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Dr. Urmila Senapati

Patron

Esteemed Guests,

Welcome to an event that embodies our dedication to progress in urologic oncology and uropathology. It is a privilege to be among such esteemed colleagues, all committed to advancing our understanding and treatment of urologic diseases. This congress provides a platform for collaboration and innovation.

The knowledge shared and relationships built during this event will have a profound impact on our field. Let us work together to explore new horizons and improve patient care.

Warm regards,

Dr. Urmila Senapati

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Dr. Rajal B. Shah

Chief Patron

Dear Delegate,

On behalf of the Genitourinary Pathology Society (GUPS), I welcome you to the first ever "International Congress on Frontiers in Urologic Oncology and Uropathology" bringing together world-renowned oncologists, pathologists, and urologists to this beautiful temple city Bhuvneshwar, Odissa, India. I could not have dreamed of a better auspicious place, the abode of Lord of Lord Sri Jagannath. We are proud to collaborate with local organizations KIMS and AIIMS and the International Association of Integrated Oncology (IAO) and believe that this collaboration will foster a fruitful exchange of knowledge and insights among pathologists, urologists, and oncologists, ultimately advancing the field of urologic oncopathology.

Genitourinary Pathology Society (GUPS) (www.gupathsociety.org) is an international not-for-profit organization founded in 2018 with a vision to advance the care of patients with urologic diseases through improvements in the subspecialty of urological pathology by enhancing best practices, research, and education. GUPS today represents over 800 members from more than 53 countries on 6 continents. The organization serves its educational mission through a variety of offerings, including Case of the Week (COW), a high-yield urological pathology digital case collection that members can access and learn from all over the world using a virtual microscope-type setup, quarterly webinars, educational outreach programs in partnership with local and international bodies and chapters and annual companion meeting with the United States and Canadian Academy of Pathology (USCAP), a premier academic pathology organization. GUPS also regularly publishes high-impact white papers and practice guidelines which have influenced and shaped the new WHO classification of GU tumors.

I would like to personally thank Dr. Sambit Mohanty, Dr. Sourav Kumar Mishra, Dr. Anandi Lobo, Dr. Ranjana Giri, and many others who have spent countless hours making sure that the event becomes a grand success! I also extend my thanks to the international faculty, specifically those traveling from long distances, who have been gracious in sharing their time and knowledge. Finally, I invite you to enjoy three days of this academic feast that is sure to delight our intellect and senses. I look forward to making new friends and learning from many of you!

Thank you !

Dr. Rajal B. Shah

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Dr. Achyuta Samanta

Chief Patron & Guest of Honor

Namaskar and Warm Greetings!

It is an absolute honor to welcome you all to the *International Congress on Frontiers in Urologic Oncology and Uropathology*, held in the culturally rich and spiritually inspiring temple city of Bhubaneswar. This conference brings together luminaries in the fields of urology, oncology, and pathology to exchange ideas, share breakthroughs, and advance global healthcare outcomes.

At KIIT and KISS, we have always strived to foster innovation, collaboration, and inclusivity in education and research. This event aligns seamlessly with our vision to bridge knowledge and transform lives, emphasizing the role of multidisciplinary approaches in addressing pressing medical challenges.

As a testament to its international stature, this event brings together 17 renowned international speakers who will share cutting-edge research, clinical advancements, and innovative perspectives. Such global participation underscores the conference's importance in driving progress in urologic oncology and uropathology.

I am confident that this Congress, with its distinguished speakers, eminent researchers, and vibrant discussions, will create lasting collaborations and inspire novel solutions for improving patient care worldwide.

Thank you for joining us in this endeavor to make a difference. Wishing you a fruitful and memorable experience!

With warm regards,

Dr. Achyuta Samanta

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Dr. Ashutosh Biswas

Chief Patron & Chief Guest

Respected Delegates, Esteemed Guests, and Colleagues,

It is with immense pride and pleasure that I extend my warmest welcome to the International Congress on Frontiers in Urologic Oncology and Uropathology. This conference symbolizes our collective commitment to advancing medical science and fostering meaningful collaborations.

At AIIMS Bhubaneswar, we remain committed to fostering an environment of research, learning, and patient-centered care. This Congress represents a unique opportunity to unite the brightest minds across disciplines, working collectively to address the ever-evolving challenges in genitourinary oncology and uropathology.

I am delighted to note that this congress features over 100 distinguished national speakers who will offer valuable insights into the rapidly evolving fields of urologic oncology and uropathology.This platform not only fosters academic collaboration but also inspires innovation and critical thinking, enabling us to push the boundaries of healthcare delivery.

As we engage in meaningful dialogues over the next three days, let us also celebrate the spirit of collaboration and the shared commitment to advancing healthcare outcomes for communities worldwide. I look forward to the thought-provoking exchanges and innovative ideas this Congress will bring forth.

Wishing you a stimulating and impactful experience.

Sincerely,

Dr. Ashutosh Biswas

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Dr. Mahul B. Amin

Chief Patron

Dear Delegates and Friends,

It is with great enthusiasm and heartfelt warmth that I welcome you to the *International Congress on Frontiers in Urologic Oncology and Uropathology*. This remarkable gathering brings together an exceptional assembly of experts, educators, and innovators, united by a shared goal of advancing the science and practice of urologic oncology.

Bhubaneswar, known for its cultural richness and serene beauty, provides the perfect backdrop for this convergence of minds. Over the next three days, we will explore the latest advancements, exchange pioneering ideas, and address the challenges that lie at the crossroads of urology, oncology, and pathology.

This Congress represents not just an academic exchange, but a movement toward bridging gaps, breaking silos, and building global collaborations to improve outcomes for patients everywhere.

Let us take this opportunity to inspire one another, exchange ideas, and collectively pave the way for a brighter future in healthcare.

Warm regards,

Dr. Mahul B. Amin

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Dr. C. B. K. Mohanty

Patron

Dear Attendees,

Welcome to this extraordinary assembly of professionals dedicated to the advancement of urologic oncology and uropathology. It is an honor to convene with experts who are passionate about pushing the boundaries of medical science. This congress offers a unique platform for collaboration and innovation.

As we engage in these enriching discussions, I encourage you to share your insights, challenge assumptions, and build lasting relationships. Together, we can make significant strides in improving patient outcomes and advancing our field.

Best wishes,

Dr. C. B. K. Mohanty

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Dr. R. C. Das

Patron

Dear Participants,

I extend a warm welcome to all of you attending the International Congress on Frontiers in Urologic Oncology and Uropathology. This event exemplifies our collective dedication to exploring new frontiers in medical science. It is an opportunity to come together, share our expertise, and inspire one another.

The collaborative spirit of this congress will undoubtedly lead to significant breakthroughs. Let us embrace this opportunity to learn, innovate, and make a lasting impact on urologic oncology and uropathology.

Sincerely,

Dr. R. C. Das

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Dr. Deepak Rautray

Patron

Dear Delegates,

Welcome to this prestigious assembly of experts in urology and pathology. It is an honor to host such a distinguished group of professionals committed to advancing our field. This congress is a platform to share knowledge, discuss innovative research, and collaborate on strategies to improve patient care.

Our time together will be both productive and inspiring. Let us take full advantage of this opportunity to learn, foster collaborations, and drive the future of urologic oncology and uropathology.

Kind regards,

Dr. Deepak Rautray

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Dr. T. S. Ganesan

Patron

Dear Participants,

It is with great enthusiasm that I welcome you to this transformative congress. This event stands as a testament to our shared commitment to excellence in urologic oncology and uropathology.

Over the next few days, let us engage in vibrant discussions, share pioneering ideas, and build connections that inspire progress. Together, we can redefine the future of patient care and strengthen the foundation of our field.

Sincerely,

Dr. T. S. Ganesan

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Dr. Surendra N. Senapati

Patron

Dear Colleagues,

It is with great excitement that I welcome you to this significant international congress. Our gathering is a testament to our collective commitment to advancing urologic oncology and uropathology. Over the next few days, we will engage in thought-provoking discussions, share cutting-edge research, and build lasting relationships.

I am confident that this congress will be a catalyst for innovation and progress. Let us work together to explore new horizons and improve patient care.

Warm regards,

Dr. Surendra N. Senapati

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Dr. Dilip K. Parida

Patron

Esteemed Delegates,

It is a great honor to welcome you to this congress. Our gathering is a reflection of our shared commitment to improving patient care through research and collaboration. The next few days will be filled with enriching discussions, groundbreaking presentations, and opportunities to forge new partnerships.

I am confident that the insights and knowledge gained from this congress will have a lasting impact on our field. Let us work together to drive innovation and make meaningful contributions to urologic oncology and uropathology.

Sincerely,

Dr. Dilip K. Parida

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Dr. Prasanta R. Mohapatra

Patron

Dear Colleagues and Friends,

Welcome to the International Congress on Frontiers in Urologic Oncology and Uropathology. This conference is a unique opportunity to engage with leading experts and advance our understanding and treatment of urologic diseases. I am honored to be part of this gathering of esteemed professionals.

As we share our knowledge and experiences, I am confident that we will inspire each other and drive significant progress. Let us collaborate, innovate, and work towards a brighter future for urologic oncology and uropathology.

Warm regards,

Dr. Prasanta R. Mohapatra

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Dr. Susama Patra

Organizing Chairperson

Dear Delegates,

It is my profound honor to welcome you to the International Congress on Frontiers in Urologic Oncology and Uropathology at the prestigious KIMS, Bhubaneswar. As a platform designed to unite medical professionals, researchers, and thought leaders, this congress offers an unparalleled opportunity to explore breakthroughs in urologic oncology and pathology.

The next three days promise to be a journey of discovery, enriched by dynamic keynote sessions, in-depth panel discussions, and the sharing of pioneering research. I invite you to immerse yourselves in this academic experience, build collaborative bridges, and push the boundaries of innovation in patient care.

Your presence reaffirms our collective commitment to improving healthcare outcomes. Let us use this opportunity to exchange ideas, strengthen professional networks, and inspire new directions in medical science.

Best wishes & Warm regards,

Dr. Susama Patra

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Dr. Dipti Rani Samanta

Organizing Chairperson

Dear Delegates,

Welcome to the International Congress on Frontiers in Urologic Oncology and Uropathology. This congress represents a unique blend of scientific rigor and professional camaraderie, designed to foster innovative thinking and multidisciplinary collaboration.

I am confident that the discussions and research shared at this congress will leave an indelible impact on our field. Let us embrace this opportunity to not only exchange knowledge but also to inspire the next generation of medical advancements.

Through the sessions, and discussions, I am certain that we will uncover insights that will help us push the boundaries of urology and oncology. Thank you for contributing to this extraordinary platform. Together, let us strive to set new benchmarks in patient care.

Sincerely,

Dr. Dipti Rani Samanta

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Dr. Ranjan Mohapatra

Organizing Chairperson

Dear Friends and Colleagues,

It is a great honor to welcome you to this pivotal congress, hosted in the vibrant city of Bhubaneswar. As we gather at KIMS, a center of excellence in healthcare and education, I am reminded of the transformative power of collaboration and knowledge sharing.

This congress is an opportunity to not only share cutting-edge research but also to redefine the future of urologic oncology and uropathology. Let us engage wholeheartedly, challenge existing paradigms, and forge partnerships that will inspire breakthroughs in patient care.

Warm regards,

Dr. Ranjan Mohapatra

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Dr. Subodh Das

Organizing Chairperson

Dear Participants,

It is with great pride that I welcome you to this highly anticipated congress. This event is a platform for us to come together as a global community, driven by a common goal—to push the boundaries of what is possible in urologic oncology and uropathology.

With a program featuring trailblazing research, expert speakers, and vibrant discussions, this congress promises to set new standards in urologic oncology and pathology. Let us work together to unlock innovations that will redefine our field.

Over the next few days, I look forward to engaging discussions, groundbreaking research presentations, and the camaraderie of colleagues committed to excellence in patient care. Together, we will shape the future of our field.

Warm regards,

Dr. Subodh Das

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Dr. Saroj K. Das Majumdar

Organizing Chairperson

Dear Esteemed Delegates,

On behalf of the organizing team, it is my honor to welcome you to this extraordinary congress. With KIMS, Bhubaneswar as our host, we have the perfect setting to exchange ideas, explore innovations, and celebrate the progress we have achieved in urologic oncology and uropathology.This congress represents not just a sharing of knowledge but a celebration of our collective passion for advancing medical science.

The sessions and discussions ahead promise to be both enriching and inspiring. Let us take full advantage of this platform to exchange knowledge, foster collaborations, and drive impactful innovations in patient care.I am certain that our time together will yield meaningful contributions to the field and beyond.

Warm regards,

Dr. Saroj K. Das Majumdar

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Dr. Ghanashyam Biswas

President,
International Association for Integrated Oncology

Dear Friends and Colleagues,

A heartfelt welcome to the International Congress on Frontiers in Urologic Oncology and Uropathology! As President of the International Association for Integrated Oncology (IAIO), My team is thrilled to join hands with such a distinguished group of professionals, all driven by a shared passion for advancing the frontiers of oncology.

IAIO is more than an association—it is a growing family dedicated to bridging gaps in oncology education, research and care. With a vision of fostering collaboration and innovation, we aim to empower professionals and improve cancer care today in India and worldwide tomorrow.

I hope this congress for three days from 10th to 12th January 2025 in the temple city of the Bhubaneswar, Odisha, India inspires new ideas, strengthens connections, and paves the way for meaningful progress. Let's make these three days a remarkable experience of learning and camaraderie.

With warm regards,

Prof. (Dr). Ghanashyam Biswas

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Dr. Sushil Kumar Giri

President,
Odisha Society of Oncology (OSO)

Dear Friends and Colleagues,

With great pleasure and pride, I welcome you to the International Congress on Frontiers in Urologic Oncology and Uropathology. This event promises to be a cornerstone in advancing our understanding of urologic cancers.

As President of the Odisha Society of Oncology (OSO), I am deeply honored to be part of this extraordinary gathering of brilliant minds. OSO has always been committed to fostering collaboration and innovation in oncology in general and Uro-Oncology in particular. This congress reflects the spirit of bringing together clinicians, pathologists, and researchers to learn, share, and grow.

I look forward to the dynamic exchange of ideas, the meaningful conversations, and the lasting connections we will make over these days. Together, let us push the boundaries of knowledge and improve outcomes for our patients alleviating their suffering.

Welcome to what promises to be a truly remarkable congress.

Warm regards

Dr. Sushil Kumar Giri

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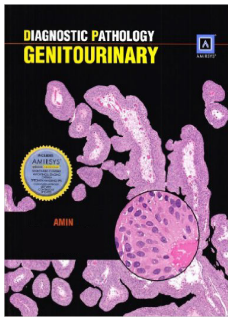
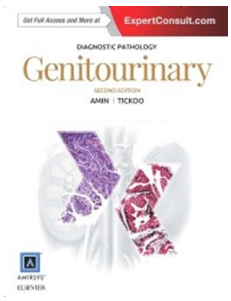
Faculty Write-ups

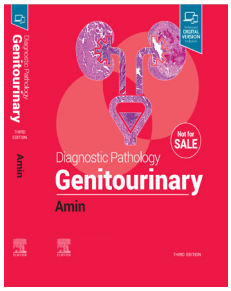
From Serendipity To Purpose: A Lifelong Journey In Urologic Oncopathology

Dr. Mahul B. Amin

Career paths rarely follow a meticulously charted blueprint; instead, they unfold as a tapestry woven from unexpected opportunities, pivotal moments, and serendipitous encounters—perhaps guided by destiny. When these moments are grounded in the principles of lifelong learning, innovation, and an unwavering commitment to excellence, and when nurtured by the guidance of inspiring mentors, collaboration of dedicated mentees, and a supportive environment, they culminate in a deeply fulfilling professional journey.







Achievements Thus Far:

Reflecting on my journey, I feel privileged to have played a role in shaping the field of urological oncopathology by advancing the understanding and diagnosis of urologic malignancies. I have been honored to be involved in the **discovery and description of several new pathological entities**, *including micropapillary carcinoma of the bladder, lymphoepithelioma-like carcinoma of the bladder, acquired cystic disease-associated renal cell carcinoma, clear cell-papillary renal cell carcinoma, thyroid-like carcinoma of the kidney, tubulocystic carcinoma of the kidney,* and *intratubular large cell hyalinizing Sertoli cell neoplasia of the testis*. In more recent years, I co-authored foundational studies on *fumarate hydratase-deficient renal cell carcinoma, succinate dehydrogenase-deficient renal cell carcinoma*, and we described a novel subtype: *low-grade oncocytic fumarate hydratase-deficient renal cell carcinoma*. My role in **setting standards for grading and staging prostate cancer** has been especially meaningful. As a co-organizer and co-author of the International Society of Urologic Pathologists Consensus Conference papers on Gleason Grading of Prostate Cancer (2007, 2014, 2015), I helped lead international consensus to refine morphological criteria of grading and promulgate clinically relevant nomenclature (grade grouping) that guide the treatment of countless patients worldwide. Similarly, my involvement in developing the 7th (2010) and 8th (2018) editions of the AJCC TNM staging of prostate cancer gave me an opportunity to promote the important role of "Pathology" in the multidisciplinary approach to classify and manage this prevalent disease. Additionally, I have had the honor of participating in the **WHO blue books authoring**, consensus meetings and/or editorial board

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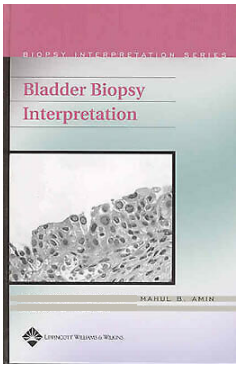
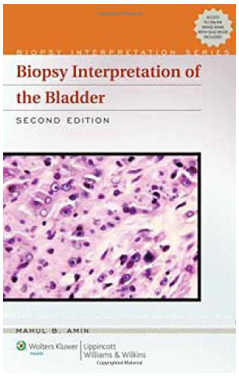
(2002, 2015, 2021) for classifications of genitourinary tumors and this has allowed me to contribute to global diagnostic and nomenclatural standards.

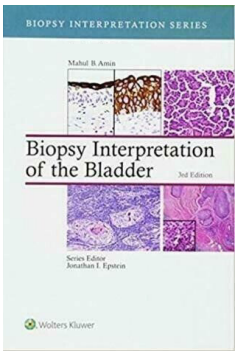
Holding leadership positions at international, national and institutional levels has helped enhance my influence as a thought leader. Serving as Vice Chair and later **Chair of the Cancer Committee of the College of American Pathologists (CAP)** from 2001 to 2009, I led efforts to standardize pathologic cancer reporting across the United States, a vital initiative that became central to the accreditation programs of the American College of Surgeons' Commission on Cancer, and the CAP's laboratory accreditation standards. One of the most defining chapters of my career was my appointment as **Editor-in-Chief of the 8th edition of the American Joint Committee on Cancer (AJCC) staging manual**. Collaborating with over 425 expert contributors from 184 institutions across 23 countries and five continents, I had a once in a lifetime opportunity to have profound global impact on cancer classification and management. This work resulted in a staging manual that continues to shape clinical decision-making, research, and healthcare policy worldwide. It is immensely rewarding to know that the AJCC manual reached the worldwide oncology community via 55,000 plus published copies, 11,000 kindle copies and through integration into approximately 50 electronic medical record systems.

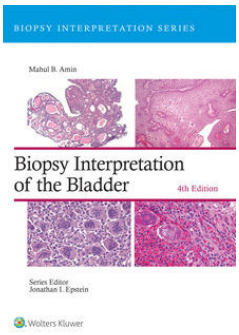
My institutional leadership roles have also been a significant part of my professional career. After just 5 years as junior faculty at Henry Ford Hospital, I was chosen to be the **Director of Surgical Pathology at Emory University Hospital**, rising to be a tenured Professor at Emory University School of Medicine, and Associate Director, Cancer Pathogenomics, Winship Cancer Institute (1998-2006). From 2006, I was the **Medical Director, Chairman, and Professor of the Department of Pathology and Laboratory Medicine at Cedars-Sinai Medical Center**. From 2016, I was the **Professor and Chair of the Department of Pathology and Laboratory Medicine, Professor of Urology, Gerwin Endowed Chair for Cancer Research at University of Tennessee Health Science System**. Since 2020, I am the **Divisional Medical Director and Vice President, West Division and Hospital Systems Operating Division at Labcorp**, which is a Fortune 500 and the largest laboratory company in the world. Since this is not a traditional role held by pathologists, I will explain my role a bit more here. As the Medical Director for 2 of the company's six divisions in the US, I lead the development and execution of the medical and science strategy for the Divisions to ensure delivery of the highest quality of Lab solutions and diagnostics to Labcorp physicians and patients. At an enterprise level, I provide senior medical leadership perspective to the Oncology, Digital Pathology, Artificial Intelligence, Anatomic Pathology and Bladder and Prostate programs.

Mentorship has been equally fulfilling. Since 1997, I have trained over 25 fellows and residents in urologic pathology, many of whom now hold esteemed positions at institutions such as M.D. Anderson, Cleveland Clinic, University of Chicago, Memorial Sloan Kettering, and the Mayo Clinic. Trained pathologists from more than a dozen countries have spent time with me in the United States to further their expertise. My passion for **teaching** extends to delivering over **435 lectures and workshops worldwide**, reaching audiences in **31 countries** and 75 cities outside the United States.









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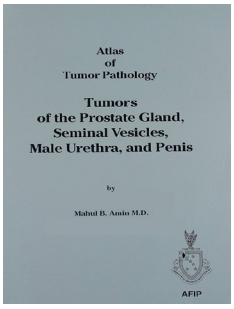
Scholarly work has been a cornerstone of my career. For those appreciating objective numbers, with **435 publications, 78 book chapters, and 16 co-authored books (and editions)**, including the Male genital system chapter in the Robbins' Pathologic Basis of Disease, and two of the 3rd series **Armed Forces Institute of Pathology (AFIP)** fascicles, I have sought to contribute to the collective knowledge of the field. Metrics such as my **H index of 133**, i10 index 405, and over 114,365 citations are gratifying, but the true impact lies in how these works are used to improve patient outcomes.

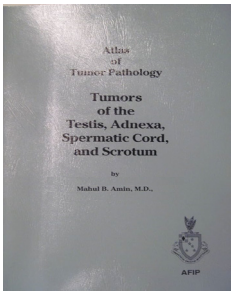
The advent of artificial intelligence and precision diagnostics represents a thrilling frontier and a forward continuation of my journey. My collaboration and team research in these areas allows me to explore clinical applications of cutting-edge technology to enhance diagnostic accuracy and patient care. Bringing new diagnostic markers into clinical practice and being an early adopter and passionate advocate of molecular diagnostics, digital pathology and AI has been gratifying as it directly impacts how diseases are managed in novel ways.

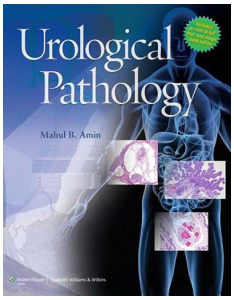
The Story Behind the Story… the rest of the Story:

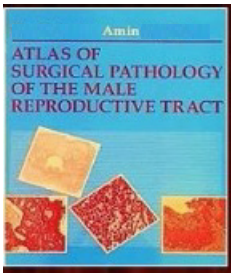
Behind the seemingly cohesive narrative of the above accomplishments in GU Pathology lies a story shaped by serendipity, good fortune, and the domino effect of one opportunity leading to another. This journey began nearly 40 years ago. In 1985, as a **postgraduate student of Pathology**, I was required to write a thesis. My guide, Dr. Suman Kinare, a globally renowned cardiac pathologist, was understandably expected to assign me a topic in cardiac pathology. However, due to her numerous commitments, she delegated me to a senior histopathologist with diverse interests, who suggested I explore prostate cancer—a relatively rare and poorly understood disease in India at the time.

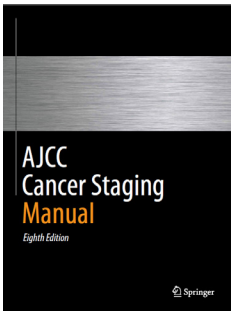
In 1988, I immigrated to the U.S., where my prior training in India allowed me to start as an advanced **resident in Pathology**. The Vice Chairman of my department, Dr. John Crissman, a Urologic and Head and Neck Pathologist, entrusted me with representing pathology at GU tumor boards in my second year, exposing me to invaluable clinical interactions. Recognizing my growing expertise, he invited me to teach at the American Urology Association's national Pathology course, attended by hundreds of Urology residents. This opportunity brought me into close collaboration with renowned pathologists, including Drs. David Grignon, John Srigley, and Mark Weiss, accelerating my understanding of the specialty and its collaborative dynamics with clinicians and eminent pathologists. The Chairman at Henry Ford Hospital recognized my potential and offered me a faculty position contingent upon completing a year of bone pathology training at the Mayo Clinic under Dr. K. Krishnan Unni. However, a mentor advised me to pursue a Surgical Pathology fellowship instead. Though I aspired to train under Dr. Juan Rosai, he informed me of his upcoming transition to Memorial Sloan Kettering Cancer Center as Chair and limited availability. Eager for diverse and prestigious training experiences, as a resident, I was able to negotiate a unique path- spending three months at the **Mayo Clinic** and then completing an **Oncologic Pathology fellowship** at **MD Anderson Cancer Center** under Dr. Alberto Ayala, a renowned bone pathologist. Through a combination of good fortune and opportunity, I was able to work alongside luminaries in GU pathology at both these institutions, including Drs. George Farrow, David Bostwick, Jae Ro, and Ayala, launching my early academic career. Thus, during these formative years, my career, directed











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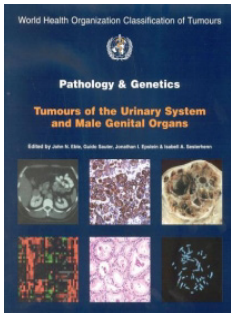
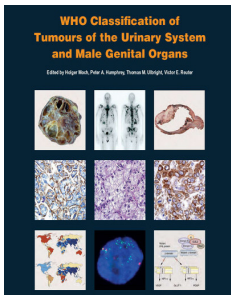
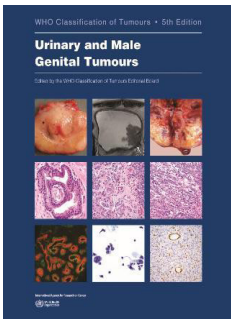
by **serendipity** and busy Chairs and Vice Chairs pivoted from possibly cardiac or bone pathology to Urologic Pathology - just as this field was emerging as a high-value subspecialty.

Along the way, opening one door, opened several doors along my career. Being on a self-motivated accelerated academic track at Henry Ford, I actively began publishing and giving national courses as a junior faculty and caught the attention of one of the preeminent pathologists, Dr. Robert Young who asked me to co-author **2 AFIP fascicles** giving me instant high impact visibility. In 1997, Dr. Mani Menon, the new Chairman of Urology at Henry Ford funded a fellowship position for me to offer and which was one of only two in Urologic Pathology (the other being offered by Jonathan Epstein) and from thereon until 2020, I have had the honor of training dedicated fellows and residents in Urologic Pathology. These fellows, through challenging consultations we received, were a continuous source of new questions with opportunities to solve them through their research enhancing theirs and in turn my career. The Director of Surgical Pathology at Henry Ford, Dr. Richard Zarbo, was very active with CAP and he motivated me to join it, which gave me the opportunity to become the Chair of its Cancer Committee.







I was at **Emory** at the right place at the right time. The institution was preparing for an NCI designation for their cancer center which opened a completely new opportunity for me in molecular pathology while developing a Pathogenomics program for the Cancer Center. This new knowledge base was extremely crucial for me at **Cedars-Sinai** where along with a few other select institutional leaders, I was asked to develop a Precision Medicine program for the institution with diagnostics being provided through my department. In 2014, when the **AJCC selection committee** was interviewing for an Editor in chief; my prior experience in leading the transformation of the CAP Cancer Protocols from guidelines to a mandate for clinical practice reporting across the US, and my experience with Precision Medicine and Diagnostics was instrumental in my selection to help AJCC develop a new paradigm and build a bridge from a population based to a more individualized staging paradigm. Also, at Cedars-Sinai, I acquired two other new skill sets – **Clinical Pathology** (I was the Medical Director of all the clinical pathology labs, giving me an excellent understanding of the overall principals of the field) which allowed me to more strongly promote **molecular pathology** that is built on strong foundations derived both from Anatomic and Clinical Pathology. **Digital Pathology** at that time was in its relative infancy, and exploring scanners for research and potential diagnostic uses opened doors for becoming an early adopter and promoter of this technology for clinical practice. This role attracted a Google AI team, Ibex Analytics (has the largest deployment of Prostate AI worldwide in clinical practice) and other industry innovators to engage with me as a subject matter expert. Finally, the experience in clinical pathology and dealing with innovation and industry opened doors for my current role at **Labcorp** to play an influential role as a Medical leader in one of the largest laboratory companies in the world and advocating the important role of Pathologists in the diagnostics, life sciences and healthcare space.

In conclusion:

I feel deeply fortunate to have pursued a career in Urologic Pathology. Guided by a passion to make meaningful contributions, shaped by a series of serendipitous opportunities, my journey has spanned multidisciplinary clinical practice across

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academia, industry, and international standard-setting organizations. Reflecting on this path, I am reminded that these achievements are not mine alone- they are the result of invaluable collaborations with mentors, colleagues, and mentees who have shared in this mission. Collaboration and strong relationships have been central to my work, enabling the formation of international cohorts to better understand rare diseases and drive international consensus. I am proud to witness how this tradition of collaborative research and publications continues to thrive in the urological pathology community worldwide. My values have served as a compass guiding me through challenges with a commitment to lifelong learning, calculated risk-taking, sharing knowledge, and learning from mistakes. Grounded in humility and a steadfast focus on the well-being of patients and the needs of physicians, I have sought to make contributions that matter. These principles have made the journey both rewarding and fulfilling. While I am deeply grateful for the milestones reached and the opportunities I've had to impact on the field, I remain energized and inspired by the work ahead. The rapid convergence of advancements in science, technology, AI, precision diagnostics, and computational pathology presents a once-in-a-generation opportunity to transform how we diagnose and manage urologic cancers. As new thought leaders emerge, I hope to continue contributing in a small yet meaningful way to this transformative journey.

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My Journey Through The Field Of Urologic Oncology

Dr. Sandy Srinivas

I started my fellowship in Heme/Onc at UCSF (USA) in 1991 and wanted to specialize in Bone marrow transplant. Through my rotations in different clinics, I had urology clinic within a few months of start of my fellowship. The attending at that time developed severe Meniere's disease and was off at home. As the fellow I became the conduit between him and the patient. I would present new patients to him on the phone and then convey the recommendations to the patient. Within a few weeks I became the point person in that clinic and even my co- fellows identified me as the trainee with maximum GU knowledge.

That was the beginning and since then I have never looked back. I got my first job in Baylor College in Houston as a GU oncologist and moved to Stanford a year later. I started at Stanford in 1997 participating in multi disciplinary clinic in GU and also had a practice in the VA hospital. Ultimately in 2003 moved full time to Stanford and had a very big GU practice.

My research interests have been clinical trials in GU oncology and have been involved in many of the trials that have led to FDA approvals in GU oncology

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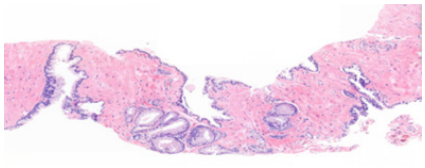
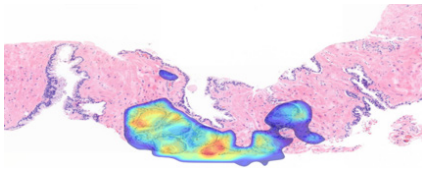
Applications of Digital and Computational Pathology and Artificial Intelligence in Genitourinary Pathology Diagnostics

Mahul B. Amin

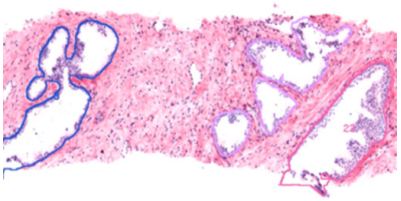


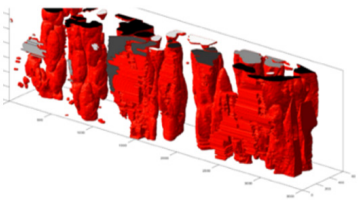


Accurate histopathologic diagnosis and comprehensive pathological assessment remain the cornerstones of managing genitourinary cancers. Over the past two decades, advancements in immunohistochemistry, standardized reporting of clinically relevant pathologic parameters, and molecular diagnostics have elevated the role of pathology, propelling precision medicine deeper into clinical care.

The emergence of digital pathology and whole slide imaging has opened new avenues for innovation, although adoption has been hindered by scanner costs, image management challenges, and workflow integration issues. Nevertheless, the rapid rise of artificial intelligence (AI) - combined with powerful cloud computing and robust data storage capabilities - has revolutionized digital pathology, ushering in the era of computational pathology. This field extracts medical knowledge from complex laboratory, digital, and patient data, revealing prognostic and predictive analytics that transcend traditional human interpretation. Alongside these developments, emerging concepts in pathogenomics demonstrate how molecular features can increasingly be inferred directly from H&E images, potentially triaging cases for molecular evaluation and making precision medicine more accessible. Emerging tools like generative AI, large language models, and even quantum computing promise to further expand the scope of computational pathology. We now stand on the cusp of a generational opportunity. The convergence of scientific breakthrough - spurred by the omics revolution - and transformative technologies such as high-throughput diagnostics, robotics, and AI have dramatically begun to reshape medicine.

This keynote address will concentrate on prostate cancer as an illustrative example, showcasing how accurate diagnosis, digital evaluation of clinically relevant pathologic parameters, and molecular diagnostics are being transformed through AI and computational pathology. These developments are redefining diagnostic workflows and expanding our ability to glean actionable insights from a single pathology slide. From diagnosis and prognosis to hereditary cancer risk stratification and predictive markers for therapy selection, AI-powered digital pathology is enhancing efficiency, accuracy, and quality assurance - while democratizing access to subspecialty expertise across diverse practice settings. The presentation will outline the current landscape of AI adoption, including FDA-approved algorithms and their integration into NCCN guidelines, and will hint at the nearly limitless possibilities on the horizon that fundamentally transform clinical decision making. This keynote aims to set an inspiring tone for our two-day multidisciplinary meeting, where we will explore these and other cutting-edge advances that promise to improve patient outcomes and elevate the standard of care.





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Human Papillomavirus and Penile Cancer: A Comprehensive Review

Dr. Philipe E. Spiess

Penile cancer, although rare, is a significant global health issue with profound psychosocial and physical consequences. It constitutes less than 1% of male malignancies in developed countries but accounts for up to 10% of cancers in regions like sub-Saharan Africa, South America, and in parts of Indonesia. One of the key etiological factors implicated in penile cancer is human papillomavirus (HPV), a common sexually transmitted infection. Understanding the relationship between HPV and penile cancer is essential for prevention, early detection, and effective treatment strategies.

HPV and its Role in Penile Carcinogenesis

HPV is a DNA virus with over 200 identified genotypes, classified into low-risk (e.g., HPV 6 and 11) and high-risk types (e.g., HPV 16 and 18) based on their oncogenic potential. High-risk HPVs are strongly associated with anogenital cancers, including cervical, anal, and penile cancers. HPV infection contributes to approximately 30–50% of penile cancer cases, with HPV 16 being the most frequently detected genotype.

Penile carcinogenesis linked to HPV involves the integration of viral DNA into host cells, leading to the expression of oncogenes E6 and E7. These viral proteins inactivate tumor suppressor proteins p53 and retinoblastoma (Rb), respectively, resulting in uncontrolled cell proliferation, genomic instability, and progression to malignancy. The molecular pathways of HPV-induced penile cancer mirror those observed in cervical and other HPV-associated cancers.

Epidemiology and Risk Factors

HPV-related penile cancer is more common in regions with a higher prevalence of HPV and limited access to preventive measures such as vaccination and circumcision. Risk factors include:
1. HPV Infection: Persistent infection with high-risk HPV types is the strongest risk factor.
2. Phimosis and Poor Hygiene: These conditions increase the likelihood of chronic inflammation and HPV persistence.
3. Multiple Sexual Partners and Early Sexual Activity: These behaviors heighten HPV exposure risk.
4. Smoking: Smoking exacerbates the carcinogenic effects of HPV by impairing immune response and inducing DNA damage.
5. Immunosuppression: Conditions such as HIV and organ transplantation increase susceptibility to HPV infection and cancer progression.
6. Circumcision Status: Men who are uncircumcised are at greater risk due to the accumulation of smegma and chronic irritation.

Pathology and HPV Subtypes in Penile Cancer

Penile cancer predominantly presents as squamous cell carcinoma (SCC), accounting for over 95% of cases. HPV-positive penile cancers are more likely to be basaloid and warty subtypes, which show a strong correlation with high-risk HPV infection. In contrast, HPV-negative penile cancers are often keratinizing SCCs, associated with chronic inflammation and non-viral etiologies.

HPV testing using polymerase chain reaction (PCR) and in situ hybridization methods has confirmed the significant prevalence of HPV 16 in penile SCC. Furthermore, p16INK4a overexpression, a surrogate marker of HPV oncogenic activity, is frequently observed in HPV-positive penile cancers.

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Diagnosis and Staging

The diagnosis of penile cancer involves clinical examination, biopsy, and HPV testing to determine viral involvement. HPV positivity can influence tumor behavior, prognosis, and response to treatment. The staging of penile cancer follows the TNM classification system (including the sub-classification of penile intraepithelial neoplasia into HPV dependent and independent histologies), considering the depth of invasion, lymph node involvement, and distant metastases.

HPV-positive penile cancers are generally associated with better outcomes than HPV-negative cancers, likely due to distinct tumor biology and increased sensitivity to radiation and chemotherapy.

Prevention and Vaccination

Primary prevention of HPV-related penile cancer focuses on reducing HPV transmission and persistent infection. Strategies include:

1. HPV Vaccination: Prophylactic vaccines such as Gardasil 9 target high-risk HPV types, including HPV 16 and 18. Vaccination programs for boys and young men can significantly reduce HPV prevalence and related cancers.
2. Circumcision: Circumcision has been shown to lower the risk of HPV acquisition and penile cancer, particularly in high-incidence regions.
3. Safe Sexual Practices: Condom use and reducing the number of sexual partners can lower HPV transmission risk.

Treatment of HPV-Related Penile Cancer

Management of penile cancer involves a multidisciplinary approach, including surgery, radiotherapy, and chemotherapy most notably for bulky nodal/metastatic disease. Early-stage disease may be treated with organ-sparing techniques such as laser therapy, topical agents, or partial penectomy. Advanced cases often require total penectomy, inguinal lymphadenectomy, and systemic therapy.

HPV-positive tumors are more radiosensitive, offering opportunities for conservative treatment approaches. Immune checkpoint inhibitors and HPV-specific therapeutic vaccines are under investigation, offering hope for targeted therapies.

Challenges and Future Directions

Despite advances in understanding HPV's role in penile cancer, significant challenges remain. Awareness and access to HPV vaccination programs are limited in resource-poor settings, where the disease burden is highest. Additionally, the stigma surrounding penile cancer and HPV often delays diagnosis and treatment.

Future research should focus on:

1. Expanding global vaccination coverage.
2. Developing HPV-targeted therapeutic strategies.
3. Investigating biomarkers for early detection and prognosis.

Conclusion

The association between HPV and penile cancer underscores the importance of preventive measures, including vaccination and circumcision, in reducing disease incidence. While HPV-positive penile cancers have better outcomes than their HPV-negative counterparts, early detection and treatment remain critical. Efforts to raise awareness, improve access to prevention, and advance research into HPV-targeted therapies will be pivotal in mitigating the impact of this malignancy worldwide.

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Multiparametric MRI in Prostate Cancer Diagnosis and Management: Pathologist Role

Dr. Cristina Magi-Galluzzi

Multiparametric MRI (mpMRI) is a non-invasive powerful imaging technique used in the diagnosis, staging, and management of prostate cancer (PCa). It combines multiple MRI sequences to provide detailed information about the prostate, allowing for better detection, characterization, and localization of neoplastic lesions. The Prostate Imaging Reporting and Data System (PI-RADS) has helped standardize the interpretation and reporting of mpMRI. MpMRI plays an important role in PCa diagnosis and management.

MpMRI improves PCa detection by helping to better differentiate benign from malignant lesions; mpMRI is highly sensitive for detecting clinically significant (GG≥2) prostate cancers and is especially useful in detecting cancers in areas that are challenging to biopsy, such as the anterior prostate. MpMRI is used for guiding targeted biopsy. If a lesion is identified on mpMRI, it can be biopsied with higher precision, improving the likelihood of detecting clinically significant cancer and reducing the number of unnecessary biopsies in areas that are unlikely to be cancerous. MpMRI helps in determining the extent of cancer spread, particularly extraprostatic extension and seminal vesicle invasion. This is crucial for planning treatment options and assessing prognosis. While mpMRI is highly sensitive, it is not perfect; some cancers may not be visible on mpMRI, leading to false negatives. Conversely, benign conditions can sometimes appear suspicious, leading to false positives. Pathologists play a key role since definitive diagnosis requires histopathological confirmation through biopsy.

MpMRI has a significant impact on the management of prostate cancer, influencing treatment decisions, and follow-up strategies. For low-risk prostate cancer, mpMRI can be used to monitor lesions over time (active surveillance). It helps identify lesions that may be more aggressive and need intervention, while avoiding unnecessary treatment for indolent cancers. By providing detailed information about the local extent of prostate cancer, mpMRI aids in decisions about whether radical prostatectomy is needed, or if focal therapy might be appropriate. MpMRI can delineate the cancerous areas more precisely than traditional imaging methods, essential for planning radiation therapy and ensuring that the tumor is adequately targeted while minimizing damage to surrounding healthy tissue. After treatment, mpMRI can be used to monitor for recurrence, particularly if PSA levels rise, and it can help in detecting local recurrence at an early stage.

MRI allows for more precise and individualized care by providing a wealth of information about the tumor's characteristics and extent, improving decision-making for both patients and clinicians. Efforts are also underway to integrate mpMRI with other diagnostic modalities, such as molecular imaging and biomarkers, to further enhance the accuracy and personalization of prostate cancer diagnosis and treatment.

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Large Gland Lesions of the Prostate

Dr. Rajal B. Shah

Many prostate lesions have 'large gland' morphology with gland size similar to or larger than benign glands, simple to complex glandular architecture including papillary, cribriform, and solid, and significant cytological atypia in glandular epithelium with nucleomegaly, prominent nucleoli, or anisonucleosis. The most common and clinically important lesions with 'large gland' morphology include high-grade prostatic intraepithelial neoplasia (HGPIN), PIN-like carcinoma, ductal adenocarcinoma, atypical borderline intraductal proliferation (AIP), and intraductal carcinoma (IDC-P). These lesions have diverse clinical significance and management implications. HGPIN refers to the proliferation of glandular epithelium that displays cytological atypia specifically prominent nucleoli visible at 20x within the confines of prostatic ducts and acini. HGPIN diagnosis particularly when focal in contemporary biopsies connotes a much reduced (~ 20%) risk of cancer detection in repeat biopsies. It has been accepted as the main precursor lesion to invasive carcinoma. PIN-like carcinoma is a variant of acinar carcinoma morphologically reminiscent of HGPIN and composed of large cancer glands lined with pseudostratified epithelium. Nuclei in the lining epithelium may exhibit acinar or ductal-like features. Limited data suggests that its clinical outcome is similar to usual acinar carcinomas and is graded as Gleason score 3+3=6. Ductal adenocarcinoma is a heterogeneous disease that in general comprises large complex glands with cribriform and papillary epithelium lined with tall columnar/elongated and pseudostratified nuclei. It is more aggressive than acinar carcinomas and is associated with higher-stage disease and a greater risk of PSA recurrence and mortality. Our experience suggests that ductal adenocarcinoma involving the central (urethra) part of prostate is biologically and molecularly distinct than one showing only peripheral involvement. IDC-P is an intraglandular/ductal neoplastic proliferation of glandular epithelial cells that results in a marked expansion of glandular architecture and nuclear atypia that often exceeds that in invasive carcinomas. In the majority of cases, it is thought to represent a retrograde extension of invasive carcinoma into pre-existing ducts and acini. It is considered an adverse pathological feature and is seen almost always in high-grade and volume carcinoma and harbingers worse clinical outcomes. NCI recommends a germline study of DNA repair genes for patients with IDC-P. Finally, AIP refers to lesions with more complex architecture and cytological atypia that exceeds HGPIN but does not reach the threshold to classify as IDC-P. PTEN loss and ERG overexpression are concordant in AIP associated with IDC-P and invasive cancer. It typically presents with a loose cribriform architecture. When detected in biopsy it is a marker of unsampled IDC-P and clinically significant cancer.

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Contemporary Update on Gleason Grading of Prostate Cancer

Dr. Ming Zhou

The Gleason grading system is based on the architectural patterns of prostate cancer, ie, how well-formed the cancer glands have become. Gleason patterns 3, 4 and 5 are assigned to cancer that is well-formed, moderately to poorly formed and cancer that lacks glandular differentiation. Since it was introduced by Dr. Gleason in 1960s, Gleason grading system has undergone many significant changes and modifications under the auspices of ISUP and GUPS in response to the needs of patient care and pathology practice. These changes have addressed the following 3 issues:

1. More precise definitions of the Gleason patterns and subpatterns (PMID: 26492179).

Gleason pattern 3 (GP3) exhibits well-formed glandular architecture. Modifications in the grading criteria for GP3 resulted in a relatively homogeneous GP3 entity with excellent clinical outcomes.

GP4 includes poorly formed glands, fused glands, glomeruloid pattern and cribriform pattern. Poorly formed glands are the most difficult pattern to grade, as they can be difficult to distinguish from tangential sectioning of well-formed GP3 cancer. Cribriform pattern is the most important GP4 subpattern to diagnose as it is associated with adverse clinical outcomes and unique treatment implications.

GP 5 represents the most poorly differentiated form of prostate cancer and includes solid, non-glandular patterns. The subpatterns within Gleason pattern 5 include: single cells, cords of cells, solid nests and cancer with comendonecrosis.

Gleason grading suffers sbuoptimal interobserver reproducibility. Studies have addressed the grading criteria of the Gleason patterns and subpatterns, such as poorly formed glands, cribriform pattern and GP5. These recommendations have helped improve the grading consistency by pathologists (PMID: 26099009; 25929349).

2. Gleason grading under special circumstances, including grading of prostate cancer subtypes and cancer after treatment.

Several morphological variants of prostate cancer can present grading challenges. In case of mucinous adenocarcinoma and cancer with signet-ring like cells, grading should be based on the underlying glandular architecture and ignores the name-sake morphology.

Neuroendocrine differentiation is rare in prostate cancer. When Paneth cell-like cells are present, they should be ignored and the grading is based on the cancer without Paneth cell-like differentiation. If cancer comprises of pure Paneth cell-like cancer cells, the cancer should not be graded and a note should accompany the diagnosis that these cancers have excellent prognosis. High grade neuroendocrine differentiation such as small cell carcinoma should not be graded. The concomitant acinar cancer can be graded.

Whether intraductal carcinoma of the prostate (IDCP) should be graded is controversial. It is universally agreed that isolated IDCP without coexisting prostate cancer should not be graded. When it is associated with > Grade Group 2 cancer, IDCP may be incorporated with invasive cancer for Gleason score and tumor volume. When it is found with Grade Group 1 cancer, it is controversial whether to include IDCP in the Gleason score, but it is prudent not to include it in the Gleason score (PMID: 38001579).

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3. Reporting of Gleason grade in prostate biopsies in special clinical settings, such as biopsies with multiple cores containing cancer of different grades, MRI-targeted biopsies, small focus of cancer, and radical prostatectomy with multifocal cancer.

Prostate cancer often has more than 2 patterns. Grading follows certain rules (PMID: 32589068). The most common pattern must always be included as the primary pattern. Higher/highest grade pattern of lesser amount should always be included in the Gleason score as the secondary or tertiary pattern. GP 3 should be ignored if it is the tertiary pattern 3. Grading rules may vary between biopsy and radical prostatectomy. In prostate biopsies, if the tertiary pattern is higher than the primary and secondary patterns, ie, the tertiary pattern is GP5, it should be included in the final GS as the secondary pattern, regardless of its amount. In RP, >5% Gleason pattern 5 is considered significant and should be included in the Gleason score as the secondary pattern even when it is the 3rd most common pattern.

MRI-targeted biopsies have been increasingly used. When multiple biopsy cores from the same MRI lesion contains cancer, the aggregate approach to calculate the mean grade and tumor volume of all the positive cores is recommended and is thought to correlate better with tumor volume and extraprostatic extension, although studies are inconclusive regarding the correlation with final grade in RP (PMID: 32589068).

When the cancer focus is small, usually <0.5 mm, or one 40X field, grading may not fully represent the heterogeneity of the tumor. As a result, pathologists may have difficulty assigning a reliable Gleason score based on small or fragmented specimens, leading to undergrading or overgrading. Pathologists should acknowledge the limitations of Gleason grading and it is prudent to indicate the presence of GP4 but an accurate grading and quantification of GP4 is difficult in such a case.

With the growing use of digital pathology and artificial intelligence (AI) in pathology practice, there is potential for enhanced accuracy and efficiency in Gleason grading. AI algorithms can assist in identifying and quantifying Gleason patterns, potentially reducing human error (PMID: 32759979). However, challenges remain in integrating these systems in the clinical workflow, financial resources in implementation and compliance with regulatory requirements.

With the advent of genomic testing (e.g., next-generation sequencing, RNA expression profiling), there is growing interest in correlating Gleason grading with molecular markers to refine risk stratification and treatment planning (PMID: 35243396). Some studies suggest that specific genetic alterations are more common in higher Gleason scores, which could aid in prognosis and therapeutic decision-making. However, integrating genomic data with Gleason grading remains in its early stages and poses practical challenges, including cost, accessibility, and the need for further validation.

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Communicating Prostate Pathology Results for Personalised Medicine

Dr. Murali Varma

Prostate cancer management is often based on biopsy findings but conflicting recommendations by different expert groups have led to significant reporting variation.

In this lecture, an alternative approach focusing on optimal communication of histopathological data is described. Communication is critical as clinicians rarely view histological material and are therefore dependent on the information included in the histopathology report.

Pathologists tend to focus on precise and reproducible reporting of tumour grade and extent, but precision/reproducibility would be less important if the biopsy findings are effectively conveyed by the pathologist and correctly interpreted by the clinician.

Strategies to effectively communicate the message in contentious scenarios such when a prostate needle biopsy set contains prostate cancer that is either discontinuous, of borderline grade, of disparate grades or associated with intraductal carcinoma of the prostate will be outlined. Terminology issues will also be discussed and use of ambiguous diagnostic terminologies such as atypical small acinar proliferation and atypical intraductal proliferation discouraged.

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Divergent Differentiations and Subtype Histologies of Urinary Bladder Carcinoma

Dr. Gladell P. Paner

Several divergent differentiations and histologic subtypes (variants) of invasive urothelial carcinoma are officially recognized in the 2022 WHO classification of urinary tract neoplasms. Most of these tumors have poorer outcomes due to their higher stage presentations and some are more aggressive than stage-matched conventional urothelial carcinoma. Contemporary clinical guidelines consider differing managements, including a more aggressive therapeutic approach and enrollment in clinical trials, for some of these unusual tumors. Thus, accuracy in diagnosis and reporting are important. Because of their unusual morphologies, these tumors can resemble other lesions or neoplasms in the bladder and pose a diagnostic challenge for pathologists. The 2022 ISUP consensus conference acknowledged the relevance of these tumors in risk stratification and management and highlighted the concern of under recognition and lack of standardization on some aspects in their diagnosis and reporting. This lecture will discuss the growing importance of divergent differentiations and subtypes of bladder carcinoma with special emphasis on clinically significant entities, their unique morphologies, challenges in diagnosis, new evolving entities, and best practice recommendations in their diagnosis and reporting.

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Pink Cell Tumors of The Kidney: Making Sense

Dr. Rohit Mehra

'Pink Cell Tumors' of the kidney encompass renal tumors with eosinophilic cytoplasm. These neoplasms include well established entities like renal oncocytoma, chromophobe renal cell carcinoma (RCC), hybrid oncocytic tumor, chromophobe RCC with eosinophilic features, FH-deficient RCC, SDHB-deficient RCC, MiTF family altered RCC, and some emerging entities. Molecular underpinnings of these tumors are facilitating our insight into the phenotypic heterogeneity that genitourinary pathologists have been observing at the microscopic level. Germline annotations for some of these tumors (for example, those related with FH and SDH deficiency) are changing how we perceive kidney cancer treatment and prevention. TSC-associated RCC does not equate to a single renal subtype, but rather represents multiple tumors which may harbor overlapping mTOR pathway alterations. Examples include eosinophilic solid and cystic renal cell carcinoma (ESC RCC), low-grade oncocytic tumor (LOT), and eosinophilic vacuolated tumor (EVT). Currently, the RCC seen within spectrum of TSC1/2/MTOR mutations are not considered as a formal renal tumor subtype in the 2022 WHO classification. From a 'nephronal mapping' standpoint, a subset of these eosinophilic tumors arise from the distal nephron, often with an interplay of cell of origin associated with distinct copy number changes, signature mutational profile, and pathogenic metabolic dysfunction. As we improve our understanding of eosinophilic renal neoplasia with better defined molecular perturbations and associated morphologic parameters, the treatment of RCC continues to evolve which hopefully contributes to a reduction in renal cancer-related mortality.

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Penile Cancer: A Pathologist's Perspective on Current Trends in Diagnosis, Staging and Treatment

Dr. Jasreman Dhillon

Penile cancer is a rare disease ranging from <1% - 10% in incidence depending on different regions/ countries of the world. High income countries like United States have <1% incidence whereas some Asian, South American, and African countries have a higher incidence which is contributed by low prevalence of circumcision, higher rates of HPV infection, and hygienic infrastructure among others. India is one of the countries where the incidence of penile cancer is among the highest in the world.

Squamous cell carcinoma (SCC) is the most common malignant penile tumor. It is broadly categorized either as HPV associated or as HPV independent. HPV DNA integration into the host genome of the epithelial cells is the hallmark of HPV associated penile intraepithelial neoplasias (PeINs) and cancers. Approximately 30-50% of penile SCC is HPV related. Currently there are no treatment differences between HPV related and HPV independent penile SCCs.

Immunohistochemical stain p16 and HPV RNA-ISH are commonly used for diagnosis of HPV associated SCCs. In a survey conducted among >120 GU pathologists worldwide routine HPV testing in penile cancer cases is performed by only 34% of respondents.

Minor changes in the subtypes of penile SCCs as reported in the 5th WHO edition are HPV associated papillary basaloid, warty, and warty basaloid carcinomas are clubbed as warty carcinoma; HPV independent pseudo hypertrophic carcinoma and pseudoglandular carcinoma are clubbed with SCC, usual type and carcinoma cuniculatum is clubbed with verrucous carcinoma.

Many studies are published regarding prognostic effect of HPV in penile SCC. It is now clear that HPV associated penile SCCs have a better prognosis compared to HPV independent penile cancers. Findings from a Norwegian cohort study spanning 50 years has shown that HPV associated penile cancers are associated with improved survival in node positive patients.

Histological features of prognostic significance in penile SCC include subtypes such as basaloid and sarcomatoid that are associated with poor prognosis whereas warty, verrucous, and papillary types are associated with good to excellent prognosis. Other histological features of prognostic significance include grade of the tumor, depth of invasion, pathological stage, lymph-vascular invasion, perineural invasion, resection margin status and metastasis to inguinal lymph nodes.

Per 8th AJCC edition of penile cancer staging, pTa stage represents non-invasive localized SCC, a term that includes pure verrucous carcinoma, carcinoma cuniculatum and papillary NOS carcinoma. This stage includes carcinomas that have no metastatic potential. pT1 stage is further subclassified into pT 1a and pT1b depending on the grade of the tumor, perineural invasion and/or lymph-vascular invasion (LVI). There is, however, poor reproducibility of grading among pathologists. In a survey among >120 GU pathologists world-wide, when asked about grading different subtypes, 64% would grade basaloid SCC as poorly differentiated (PD) and close to 10.5% would never grade it as PD. For carcinoma cuniculatum 74.5% would grade it as well-differentiated (WD) and 4.1% would never grade it as WD. Per CAP protocol, any proportion of anaplastic cells is sufficient to categorize a penile SCC as grade 3/PD. However, when asked the minimum proportion of PD cancer required to call it a grade 3, close to 50% responded ≥5% and many responded at least 20% or >25%. Hence, there is a need for better grading models and education about grading criteria among pathologists. The current staging system stages the invasion of corpus cavernosum including tunica albuginea as pT3. However, there is insufficient evidence regarding the inclusion of tunica albuginea as pT3. A study by Li et al, has proposed to further subclassify pT2 and pT3, depending on the presence or absence of LVI. Currently, the involvement of urethra is not included in the staging. However,

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invasion of the deep urethra may have adverse prognosis and needs to be re-evaluated.

It has been suggested to add lymph node density criteria, defined as number of positive lymph nodes out of total lymph nodes, to the nodal staging. Regional lymph node metastasis to the inguinal lymph nodes is the strongest predictive marker of clinical outcomes.

The most common genomic alterations found in penile SCC involve TP53, CDKN2A, NOTCH1 genes and TERT-promoter region. These alterations are more prevalent in HPV independent penile SCC. Tumor mutational burden (TMB) is higher in HPV associated penile SCC. There have been suggestions to add the HPV status of the tumor to the penile staging manual in future.

There are limited options for metastatic, advanced penile SCC including anti-EGFR antibodies, tyrosine kinase inhibitors and pembrolizumab (tumors with TMB (≥10) and/or deficient mismatch repair/MSI high). Programmed cell death ligand 1 (PD-L1) is expressed (33-69%) in penile SCC and is associated with a worse survival, lymph node metastasis and reduced cancer specific survival and overall survival. Currently, no differences have been reported in the outcome based on HPV status. Benefits of immune checkpoint inhibitor (ICI) monotherapy appear to be limited. Combination therapies for advanced tumors (platinum-based chemotherapy + anti-EGFR + anti-PD-1 ICI) are more effective than a single agent. Penile SCCs have a high expression (90%) of EGFR by immunohistochemistry (IHC); although at molecular level only 10-30% of penile SCCs have EGFR mutations. Down-regulation in the notch pathway may render tumors sensitive to PI3K/mTOR inhibitors. Certain cell surface biomarkers like Notch-4 and TROP-2 can serve as drug targets to monoclonal antibodies and small molecule inhibitors. These biomarkers can be detected via IHC and penile SCCs frequently express both. Clinical trials using Nectin-4 as a potential targeted to treat metastatic penile SCC are being conducted and biomarker TROP-2 is being considered in future.

The first Quadrivalent HPV vaccine was approved for use in males in 2009. Quadrivalent HPV vaccine has reduced external genital lesions in males by 90% and anal intraepithelial neoplasia by 77.5%. However, the impact of HPV vaccination in penile cancer is not clear yet due to lack of data as penile SCC is a rare disease, almost half the cases being HPV independent, large gap in time between HPV infection and development of cancer and low rate (<4%) of vaccination among boys.

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How New Developments Impact Diagnosis in Existing Renal Neoplasms

Dr. Sean R. Williamson

Recently there has been significant interest in emerging subtypes of renal neoplasms that can be discriminated from the more common counterparts by novel immunohistochemical and molecular techniques. However, understanding of long-established renal tumor types has also grown. In clear cell renal cell carcinoma (RCC), elucidation of tumor genetics has improved. In addition to the well known *VHL/3p* alterations, it is now recognized that several other genes have key roles in this tumor type, such as *SETD2, BAP1, PBRM1*, and others. For example, BAP1-deficient tumors are noted to have some distinct features, such as papillary/pseudopapillary architecture, hyaline globules, and increased staining for keratin 7 or AMACR. In general, diagnosis of clear cell RCC can be supported by diffuse membranous staining for carbonic anhydrase 9 (CA9), typically with minor or negative staining for keratin 7. Subtyping of papillary RCC has also been to be refined, with the former type 1 tumors representing the essence of these neoplasms, and the former type 2 tumors now being thought to include multiple diagnostic entities, such as MITF family translocation RCC and FH-deficient RCC. Clear cell papillary renal cell tumor (formerly RCC) has been designated as a "tumor" rather than "carcinoma" due to its highly favorable behavior, with questionable rare exceptions. These show a characteristic immunohistochemical profile of CA9 +, keratin 7 +, GATA3 +, high molecular weight keratin +, CD10 -/minimal, and AMACR -/minimal. Genetically, they lack the VHL/3p alterations of conventional clear cell RCC. In the oncocytic tumor spectrum, the recent Genitourinary Pathology Society (GUPS) consensus on renal neoplasms proposes the term oncocytic renal neoplasm of low malignant potential, not further specified, for tumors that largely resemble oncocytoma, yet which have minor atypical features of uncertain significance, since the behavior is likely favorable regardless. When diagnosing high-grade, infiltrative tumors involving the kidney, collecting duct carcinoma has become a diagnosis of extreme exclusion, to the point that some may debate its existence in modern practice. A differential diagnosis for infiltrative carcinoma in the kidney should usually include urothelial carcinoma, FH-deficient RCC, medullary carcinoma, and metastasis from another organ.

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Antibody-Drug Conjugates in Cancer Therapy: Transforming Oncological Treatment

Dr. Ajjai S. Alva

Introduction

Cancer remains one of the leading causes of death worldwide, and despite significant advances in chemotherapy, radiation therapy, and immunotherapy, the need for more targeted and effective treatments persists. Antibody-drug conjugates (ADCs) have emerged as a promising frontier in oncological therapeutics, providing a means to selectively target and destroy cancer cells while minimizing damage to healthy tissues. This article delves into the mechanisms, development, clinical applications, and potential future of ADCs in cancer therapy, exploring their transformative potential in the fight against cancer.

Mechanism of Action

Antibody-drug conjugates are complex molecules designed to combine the selectivity of monoclonal antibodies (mAbs) with the cytotoxic potency of chemotherapy drugs. The general structure of an ADC includes three critical components: the monoclonal antibody, the linker, and the cytotoxic drug.

Monoclonal Antibody

The monoclonal antibody component of an ADC is responsible for targeting and binding to specific antigens expressed on the surface of cancer cells. These antigens are often proteins that are overexpressed in tumors compared to normal tissues, thereby providing a degree of selectivity in targeting cancer cells. Examples of such antigens include HER2 (human epidermal growth factor receptor 2) for breast cancer and CD30 for Hodgkin lymphoma. The specificity of monoclonal antibodies allows ADCs to home in on cancer cells, thereby reducing off-target effects and adverse reactions commonly associated with conventional chemotherapy.

Linker

The linker is a crucial component that connects the monoclonal antibody to the cytotoxic drug. The stability of the linker is paramount, as it determines the release mechanism of the drug. Linkers can be classified into cleavable and non-cleavable types. Cleavable linkers are designed to release the drug in response to specific stimuli found in the tumor microenvironment, such as acidic pH, high glutathione concentrations, or the presence of specific enzymes like cathepsin B. Non-cleavable linkers, on the other hand, release the drug only after the entire ADC is internalized by the cancer cell and degraded in the lysosome. The choice of linker affects both the efficacy and safety of the ADC.

Cytotoxic Drug

The cytotoxic drug, or payload, is the component of the ADC responsible for killing the cancer cells. These drugs are typically highly potent and include agents such as auristatins, maytansinoids, and calicheamicins, which can disrupt critical cellular processes like microtubule assembly and DNA replication. The cytotoxic drug is only released once the ADC has been internalized by the cancer cell and the linker has been cleaved, ensuring that the potent compound exerts its effects predominantly within the target cells.

Internalization and Cytotoxicity

Following binding to the target antigen on the cancer cell surface, the ADC-antigen complex undergoes endocytosis and is internalized into the cell. Inside the cell, the linker is cleaved, releasing the cytotoxic drug. The drug then exerts its cytotoxic effects, leading to cell cycle arrest and apoptosis. This targeted approach allows for the delivery of highly potent cytotoxic agents directly to cancer cells, resulting in improved therapeutic indices and reduced systemic toxicity.

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Development of ADCs

The development of ADCs involves several critical steps, from target identification and antibody generation to linker-payload selection and preclinical evaluation.

Target Identification and Validation

Identifying an appropriate target antigen is the first and most crucial step in ADC development. Ideal targets are those that are highly expressed on cancer cells but have limited expression on normal tissues, minimizing the risk of off-target toxicity. Advances in genomics and proteomics have facilitated the discovery of novel tumor-specific antigens, opening new opportunities for ADC development.

Antibody Engineering

Once a target antigen is identified, monoclonal antibodies specific to the antigen are generated through techniques such as hybridoma technology or phage display. These antibodies are then humanized or fully human antibodies to reduce the risk of immunogenicity. Engineering modifications, such as improving binding affinity and optimizing Fc domain interactions, are performed to enhance the therapeutic potential of the antibody.

Linker and Payload Selection

Choosing the right linker and payload is equally important in ADC development. Linkers must be stable in the bloodstream yet cleavable within the target cell, whereas payloads must be potent enough to kill cancer cells at low concentrations. Advances in chemistry have led to the development of linkers with tunable stability and drug release profiles, as well as novel cytotoxic agents with varying mechanisms of action.

Preclinical Evaluation

Before advancing to clinical trials, ADCs undergo rigorous preclinical evaluation, including in vitro assays to assess binding specificity, internalization, and cytotoxicity, as well as in vivo studies to evaluate pharmacokinetics, biodistribution, and antitumor efficacy. Safety assessments, including toxicity studies in animal models, are also conducted to predict potential adverse effects in humans.

Clinical Applications

ADCs have shown significant promise in both hematologic malignancies and solid tumors, with several ADCs receiving regulatory approval and many more in clinical development.

Hematologic Malignancies

1. Brentuximab Vedotin (Adcetris): Brentuximab vedotin targets CD30, an antigen expressed in Hodgkin lymphoma and anaplastic large cell lymphoma. Approved in 2011, it was one of the first ADCs to gain regulatory approval. The conjugate consists of an anti-CD30 antibody linked to the microtubule-disrupting agent monomethyl auristatin E (MMAE). Clinical trials demonstrated significant response rates in patients with relapsed or refractory Hodgkin lymphoma.

2. Inotuzumab Ozogamicin (Besponsa): Targeting CD22, inotuzumab ozogamicin is approved for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The ADC is composed of an anti-CD22 antibody linked to calicheamicin, a potent DNA-damaging agent. Clinical studies have shown high response rates and improved outcomes in patients with relapsed or refractory ALL.

Solid Tumors

1. Trastuzumab Emtansine (T-DM1, Kadcyla): One of the most well-known ADCs, trastuzumab emtansine targets HER2-positive breast cancer. The ADC combines trastuzumab, an anti-HER2 antibody, with DM1, a maytansine derivative that inhibits microtubule assembly. Approved in 2013, T-DM1 has shown efficacy in patients with HER2-positive breast cancer who have progressed on prior therapies, significantly improving progression-free and overall survival.

2. Sacituzumab Govitecan (Trodelvy): Sacituzumab govitecan targets Trop-2, an antigen overexpressed in various epithelial cancers, including triple-negative breast cancer (TNBC). Approved in 2020, this ADC links an anti-Trop-2 antibody to SN-38, a topoisomerase I inhibitor. Clinical trials demonstrated significant clinical benefit in patients with metastatic TNBC.

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Emerging ADCs

The pipeline of ADCs continues to expand, with numerous candidates in various stages of clinical development:

1. Enfortumab Vedotin (Padcev): Targeting Nectin-4, enfortumab vedotin is approved for the treatment of advanced urothelial carcinoma. The ADC conjugates an anti-Nectin-4 antibody with MMAE, demonstrating significant responses in patients with previously treated urothelial cancer.

2. Margetuximab Deruxtecan (MGAH22-DX): Margetuximab deruxtecan targets HER2 and is in clinical development for HER2-positive cancers. The ADC links an anti-HER2 antibody with a topoisomerase I inhibitor, showing promising preliminary efficacy in HER2-positive breast and gastric cancers.

3. Polatuzumab Vedotin: Targeting CD79b, polatuzumab vedotin is in development for B-cell non-Hodgkin lymphoma. Clinical trials have shown encouraging results, with the ADC improving response rates and outcomes in combination with standard chemotherapy.

Challenges and Future Directions

Despite the success of ADCs, several challenges remain, including resistance mechanisms, toxicity management, and the development of more effective ADCs.

Resistance Mechanisms

Resistance to ADCs can arise through various mechanisms, such as antigen downregulation, efflux of the cytotoxic drug, or alterations in intracellular trafficking and drug metabolism. Overcoming resistance requires a multifaceted approach, including the identification of biomarkers to predict and monitor resistance, the development of next-generation ADCs with novel targets and payloads, and the combination of ADCs with other therapeutic modalities.

Toxicity Management

While ADCs are designed to minimize toxicity to healthy tissues, off-target effects and toxicity due to the release of the cytotoxic drug can still occur. Managing these toxicities involves optimizing the therapeutic window, improving patient selection through biomarker-driven approaches, and developing strategies to mitigate adverse effects, such as dose adjustments and supportive care measures.

Advances in ADC Technology

Continued advancements in ADC technology hold promise for the next generation of ADCs. Innovations include the development of site-specific conjugation techniques to ensure homogeneous and stable ADC preparations, the discovery of new cytotoxic agents with diverse mechanisms of action, and the design of multifunctional ADCs that can engage multiple targets or incorporate immune-stimulatory components.

Combination Therapies

Combining ADCs with other treatment modalities, such as immune checkpoint inhibitors, targeted therapies, or radiation, offers the potential to enhance therapeutic efficacy and overcome resistance. Synergistic combinations can leverage complementary mechanisms of action, potentially improving patient outcomes.

Personalized Medicine

The integration of ADCs into personalized medicine approaches is a significant advancement in cancer therapy. Biomarkers and companion diagnostics can identify patients most likely to benefit from ADC treatment, enabling tailored therapies that maximize efficacy and minimize toxicity. The development of precision medicine approaches, including next-generation sequencing and proteomics, will further refine patient selection and treatment strategies for ADCs.

Expanding Indications

Expanding the indications for ADCs beyond traditional cancer types is another exciting avenue. Exploring the use of ADCs in rare cancers, metastatic disease, and even non-oncological conditions, such as autoimmune disorders, opens new therapeutic possibilities. Investigating the potential of ADCs to target cancer stem cells, which contribute to tumor initiation, progression, and recurrence, is also an area of active research.

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Overcoming Tumor Microenvironment Barriers

The tumor microenvironment (TME) plays a critical role in cancer progression and response to therapy. Tumors can create barriers that limit the penetration and efficacy of ADCs. Strategies to modulate the TME, such as targeting stromal components, tumor vasculature, and the immune microenvironment, can enhance ADC delivery and activity. Combination approaches that address both tumor cells and the TME may lead to more comprehensive and durable responses.

Next-Generation ADCs

The future of ADCs lies in the development of next-generation designs that address current limitations and enhance therapeutic precision. Emerging concepts include bispecific ADCs that target multiple antigens, ADCs with immune-modulating components, and ADCs that deliver non-cytotoxic payloads, such as RNA-based therapeutics or epigenetic modulators. These innovations aim to expand the capabilities of ADCs and improve treatment outcomes for a broader range of patients.

Clinical Trials and Real-World Evidence

Ongoing clinical trials continue to investigate the potential of ADCs in various cancer types and settings. These trials evaluate the safety, efficacy, and optimal use of ADCs, generating valuable data to guide clinical practice. Additionally, real-world evidence from patient registries and post-marketing studies provides insights into the long-term outcomes and safety profiles of approved ADCs. The integration of clinical trial data and real-world evidence enhances our understanding of the benefits and limitations of ADCs in diverse patient populations.

The Role of ADCs in the Treatment Landscape

ADCs have already transformed the treatment landscape for several cancers, providing new options for patients who may have limited choices. In diseases where traditional therapies have shown limited success, ADCs offer the potential for improved outcomes and extended survival. They have demonstrated efficacy in both front-line and relapsed/refractory settings, and ongoing research aims to optimize their use in combination with other therapies. The successful integration of ADCs into standard treatment protocols requires collaboration between researchers, clinicians, regulatory agencies, and pharmaceutical companies to ensure that patients benefit from these innovative therapies.

Conclusion

Antibody-drug conjugates represent a significant advancement in cancer therapy, combining the precision of targeted antibodies with the potent cytotoxic effects of chemotherapy. Their ability to selectively target cancer cells has revolutionized treatment options for various malignancies, improving patient outcomes while minimizing systemic toxicity. Despite challenges, ongoing research and technological advancements continue to refine ADCs, addressing resistance mechanisms, optimizing therapeutic windows, and exploring combination strategies. As the field progresses, ADCs are poised to play an increasingly prominent role in the personalized treatment of cancer, offering new hope to patients and transforming the landscape of oncological therapeutics. The future of ADCs holds immense promise, ushering in a new era of targeted, effective, and personalized cancer care.

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Oligometastatic Prostate Cancer

Dr. Sandy Srinivas

Oligometastatic Prostate Cancer: Premise is it's an intermediate stage between localized disease and widely metastatic disease. Defined as fewer than 5 metastases. Exists in different states- De-novo oligometastatic state; oligo Recurrent- hormone sensitive with prior local Rx; Oligo progressive- usually in CRPC who has a few progressive sites. Sites of disease could be bone, nodal or visceral metastases.

Newer imaging modalities with PSMA based PET imaging has redefined this disease state. Novel imaging has shifted non metastases to oligo metastases and oligo metastases to poly metastases. The biology of this disease maybe different and more indolent than patients with widespread metastases.

The goals of treatment varies depending on the disease state. In de novo hormone sensitive state, the goal may be to increase longevity. In the oligo recurrent stat the objective may to delay systemic therapy and improve quality of life and in the castrate resistant state the objective maybe to not change systemic therapy.

No standard guidelines to manage this disease state and treatment is evolving De Novo Metastatic Hormone Sensitive Disease: Therapy for metastatic disease has dramatically changed over the last decade. Monotherapy with androgen deprivation therapy i(ADT) s inadequate and multiple trials have demonstrated improved longevity with the androgen receptor antagonist. Combining ADT with docetaxel improved survival compared to ADT alone in the CHAARTED, STAMPEDE and GETUG trials. However only patients with high volume disease benefited from chemotherapy. Similarly combining ADT with abiraterone was shown to improve survival compared to ADT alone in the STAMPEDE as well as LATITUDE studies. Unlike docetaxel, abiraterone had benefit across all tumor volumes. Other androgen receptor pathway inhibitors (ARPI) such as enzalutamide when combined with ADT was superior compared to ADT alone in the ARCHES study as was the combination of apalutamide plus ADT compared to ADT alone in the TITAN study. Again these combinations benefited patients with both low volume as well as high volume disease. Attempts at improving outcomes further with triplets using ADT, docetaxel and an ARPI were demonstrated in the PEACE 1 study with abiraterone and in the ARASENS study with darolutamide. Both these studies showed an improvement of the triplet regimen more in high volume disease.

Treating the primary in Hormone sensitive disease resulted in improvement in overall survival in patients with low volume disease and this was demonstrated in both the HORRAD and the STAMPEDE trial. Whether this benefit remains when systemic therapy is intensified remains to be seen but there is benefit in decreasing GU symptoms irrespective of the volume of disease.

Treating the metastases in hormone sensitive prostate cancer is taking this concept one step further and there is some benefit as was seen in the SABR-COMET study where there was an improvement in OS from 17% to 42%.

The largest body of evidence of treating oligometastases is in the oligo recurrent space where patients have had their primary treated and have few sites of metastases detected along with a rising PSA. The goals of treating these metastases are to delay systemic therapy. Two randomized trials the ORIOLE and STOMP have both demonstrated the benefit of treating the metastases with SBRT and have demonstrated a delay in start of systemic therapy. Much effort is now on who benefits from this therapy based on genomics and biology to help separate the rapid progressors who need systemic therapy as opposed to the slow progressors.

Treatment of olgometastases have been attempted in the castrate resistant state with the intent to delay change in systemic therapy. Number of studies are limited and there is ongoing research.

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Pathologic Sub-staging of Bladder Cancer: Updates, Controversies, and Guidelines

Dr. Ankur Sangoi

Both the current 9th edition AJCC and updated College of American Pathologists (CAP) staging synoptic summaries recommend pathologists to provide some assessment as to the extent of lamina propria invasion for urinary bladder biopsies/transurethral resections. In a 2024 International Society of Urological Pathology (ISUP) consensus meeting on bladder cancer, substaging of pT1 was endorsed in daily practice but with no agreement on the specific method or how it should be reported. Herein, a primer on pT1 substaging is provided including the following 3 overarching categories: descriptive, histoanatomic, and micrometric. A background into each of these 3 techniques is discussed including case examples and problematic scenarios. Recommended sustaging guidelines are highlighted including benefits/limitations of each method. The impact of updated restaging urologic society guidelines and novel en bloc resection concepts are also briefly addressed.

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Germ Cell Tumors of the Testis: Diagnoses that You Do Not Want to Miss

Dr. Andres M. Acosta

In recent years, there have been significant advances in the field of testicular pathology. Specifically, the use of new molecular techniques has led to the identification of mechanisms that underlie oncogenesis and disease progression in germ cell tumors and sex cord-stromal tumors. These molecular data will likely impact treatment and disease classification in coming years.

This talk focuses on recently identified entities that genitourinary pathologists must be familiar with due to their implications for clinical management. Four cases will be used to exemplify four entities with distinct clinicopathologic features. The first one corresponds to a so-called “somatic-type” malignancy of germ cell origin occurring in a primary testicular germ cell tumor. These neoplasms are chemo-resistant, and optimal management requires an aggressive surgical approach to achieve complete resection, including the possibility of upfront retroperitoneal lymph node dissection in the absence of clinically evident extra-testicular disease. The second entity is represented by post-chemotherapy cystic trophoblastic tumor and other indolent post-chemotherapy trophoblastic tumors. When encountered in post-chemotherapy retroperitoneal lymph node dissections or resection of metastatic lesions, these neoplasms behave largely as teratoma and, unlike choriocarcinoma, do not require additional chemotherapy. The third entity is a recently described sex cord tumor driven by EWSR1::ATF1, which had been historically interpreted as a phenotype of Sertoli cell tumor not otherwise specified. In contrast to other subtypes of sex cord stromal tumors, this fusion-driven neoplasm seems to be invariably malignant and, therefore, requires aggressive clinical management. Finally, the fourth entity is represented by fumarate hydratase-deficient sex cord stromal tumors, which typically exhibit a Leydig cell phenotype. The presence of loss-of-function fumarate hydratase variants in these tumors appears to correlate with aggressive clinical behavior. Additionally, some fumarate hydratase variants identified in these tumors are of germline origin, suggesting that they are part of the spectrum of lesions seen in hereditary leiomyomatosis and renal cell carcinoma. The objective of the presentation is that attendants become aware of these rare but clinically important entities and understand their clinical implications.

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Best Practice Recommendation for Immunohistochemical Markers in Renal Cell Tumors

Dr. Mahmut Akgul

In the last two decades, diagnostically and clinically relevant information on kidney tumors has significantly increased, particularly with the utilization of tools to better interrogate their genetic background. This reflects as a surge on the number of recognized and emerging renal neoplastic entities in the latest edition (2022) of the World Health Organization's tumor classification, and it has several impacts on pathologists' daily practice on kidney tumors for a few reasons:

1. Despite multiple new entities, the composition of most-commonly encountered kidney tumors in daily practice are largely unchanged, and their diagnostic criteria are refined with the better classification of other unusual "look-alike" kidney tumors and better understanding on the expression profile of most commonly used biomarkers, utilized as immunohistochemical (IHC) assays.

2. A new sub-category, molecularly defined renal carcinomas, requires demonstration of the canonical mutations identifying the carcinomas in the sub-category, including TFE3 rearranged renal cell carcinoma (RCC), TFEB altered (rearranged or amplified) RCC, succinate dehydrogenase RCC, fumarate hydratase RCC, ALK rearranged RCC, ELOC mutated RCC, and SMARCB1 deficient renal medullary carcinoma.

3. Most labs are not equipped with the necessary molecular or surrogate IHC tools to define molecularly defined renal carcinomas, and the expression profile of most commonly used IHC markers in these carcinomas are not well-established.

4. The diagnostic algorithms for the diagnosis of kidney tumors need to be updated for pathologists to guide in their daily practice.

In this talk, we will discuss morphology-driven and cost-effective IHC utilization in daily genitourinary pathology practice on kidney tumors. Multiple algorithms tailored for pathology laboratories in limited resource settings will be introduced, and main effort will be to a) to have refined morphologic and IHC criteria for common kidney tumors and b) to triage unusual kidney tumors with practical clues based on their morphology and immunoprofile.

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TERT Promotor Mutation in Diagnosis and Management of Urinary Bladder Cancer: A Bridge Too Far or An Extended Arm, A Pathologist's Perspective

Dr. Rajan Arora

Why It's Important

Histopathological diagnosis of urinary bladder is challenging specially in specific scenarios where the morphology is bland & deceptive i.e. Nested urothelial carcinoma (vs Florid Von- Brunn nest proliferation), Bladder Adenocarcinoma (vs Nephrogenic adenoma) and Inverted Urothelial carcinoma (vs Inverted papilloma). Although morphology is key in all these circumstances, molecular adjunct like Telomerase reverse transcriptase (TERT) Promotor Mutation analysis can be an extended arm in this modern pathology era but can be a bridge too far in a resource limited setting.

TERT Gene, Telomere and TERT Promotor Mutation

Telomeres are Ribonucleoprotein structures, located at the termini of linear chromosomes, composed of hundreds of tandem hexamaric Deoxyribonucleic acid (DNA) repeats. They function to protect the chromosome ends and progressively shorten with each mitotic division. In an individual cell, critically short telomere length triggers p53 pathway usually leading to proliferative arrest, senescence, and apoptosis. To escape this telomere attrition and attain immortality, majority of cancers preserve telomere length using Telomerase, a reverse transcriptase enzyme (TERT) and its RNA template (TERC). In mature cells TERT gene, located on chromosome 5p is repressed, while in cancer cells TERT promoter mutations result in increased TERT mRNA and TERT protein leading to uncontrolled proliferation.

TERT Promotor Mutation and Bladder Cancer

TERT promoter mutation (TERTPM) is a key driver mutation that occurs in 60-80% cases of bladder cancers. TERTPM occurs in entire spectrum of Urothelial carcinoma (including Papillary Urothelial Neoplasm of Low Malignant Potential) and its various subtypes across age, gender, tumor grade & stage, and spatial location; while TERTPM are rare/absent in Benign Urothelial proliferations e.g. Cystitis cystica, Cystitis glandularis, and Inflammatory myofibroblastic tumor (IMT) which pose a diagnostic conundrum in routine, day to day, pathology practice. As mentioned before, it's particularly relevant in innocuous looking cancers e.g. Nested urothelial carcinoma, inverted urothelial carcinoma and adenocarcinoma specially in small/superficial biopsy specimens (A nightmare for General histopathologist! and a challenge for expert Uropathologist) where TERTPM are negative in their benign mimics e.g. Florid Von Brunn nest proliferation, Inverted Papilloma, and Nephrogenic adenoma respectively. These entities can be a morphological trap for the unwary! and TERTPM detection can be a friendly hand to hold on to.

TERT Promotor Mutation in Urine and Plasma Samples

Long term follow up and surveillance is imperative in bladder cancer patiens. Urine based TERTPM analysis holds great promise as a non-invasive approach for detection of bladder cancer that can save not only millions of dollars spent annually worldwide but more importantly ameliorate the pain & predicament of these cancer patients. Urine cell free DNA TERTPM are detectable up to 10yr before clinical diagnosis of bladder cancer!

TERT Promotor Mutation Detection Analysis

TERTPM could be detected in formalin fixed, paraffin embedded, tissue; urine cells, urine cell free DNA, and plasma cell free DNA in variety of analytical platforms e.g. IHC, Sanger DNA sequencing, PCR (real time & reverse trarnscriptase), and NSG etc.

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TERT Promotor Mutation And Bacillus Calmatte-Guerin (BCG) Treatment Response

Intravesical BCG therapy is most common and standard treatment for early stage bladder cancer. Presence of TERTPM appears to be independent predictor of BCG responsiveness.

To Conclude

TERT promoter mutation is a critical mechanism for Telomerase activation, a key driver in majority of Urothelial cancers along the entire spectrum.

TERT promoter mutation is an emerging clinical tool for early detection, diagnosis, differential diagnosis, prognostication, and prediction of treatment response in bladder cancer that can serve as an extended arm in tertiary care setting.

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Collaborative Multidisciplinary Team Working and the Value of Pathology Input in the New Era of Personalised Medicine

Dr. Aiman Haider

Sir William Osler wrote 'The good physician treats the disease; the great physician treats the patient who has the disease.' This is the very essence of personalised medicine which is focussed on assigning the right patient with the right diagnosis at the right time for appropriate management. Therefore, in this new era of personalised medicine, pathologists need to understand the clinical implications and utility of reports. Effective and efficient multidisciplimnary working needs mutual respect and trust, an equal voice, resolution of any conflicts with constructive discussion/debate and an ability to request and provide clarification. This helps facilitate effective clinical pathways and decision making and fosters a high quality collaborative working on translational research and interventional trials that need pathology input for validation.

The last decade has seen colossal changes in clinical management and practice with regards to prostate cancer and I summarise a few of the multidisciplinary international multicentre trials led by UCLH that have bought about these changes and how pathology contributed.

1. PROMIS led by Prof Hash Ahmed was a NIHR funded nonrandomised trial that tested the value of Multi Parametric Magnetic Resonance Imaging (MP-MRI) for men with a suspicion of prostate cancer who had been recommended to have a prostate biopsy. It investigated whether MP-MRI could be used to advise whether or not men might safely avoid biopsy and to help us do better biopsies for men who have them.

PROMIS was multicentre and recruited 740 men to the trial. The pathology of these were centrally reviewed at UCLH. The trial demonstrated the following (1):

1. TRUS is a poor test for the diagnosis of clinically significant prostate cancer. The sensitivity was only 48% and thus missed over half the cases.

2. mp-MRI is a highly sensitive test (93%) for the detection of clinically significant cancer and if performed prior to the biopsy, it can identify about 25% of men who might safely avoid a biopsy.

3. A subsequent cost effectiveness analysis demonstrated that performing an mp-MRI scan prior to biopsy was highly cost effective.

A unique dataset was created which gave way to numerous new studies and projects exploring digital evaluation of prostate biopsies and secondary analysis and follow up(2,3).

2. PRECISION Trial led by Dr. Veeru Kasivisvanathan is a landmark, international multi-centre randomized controlled trial, in which 500 men, who had been referred with clinical suspicion of prostate cancer without prior biopsy, were randomised to either standard 12-core TRUS biopsy or a MPMRI arm (4). The study was published in the New England Journal of Medicine and was awarded the Fritz Schröder EAU Prostate Cancer Research Award in 2019. The histology for all cases recruited to the trial were centrally reviewed at UCLH. The potential implications of this trial: were introduction of an alternative prostate cancer diagnostic pathway in biopsy naive men, an increase in the number of patients with clinically significant cancer diagnoses, a reduction in the over-diagnosis of clinically insignificant prostate cancer, reduction in the number of patients undergoing prostate biopsy, a reduction in the number of biopsy cores taken per patient, a reduction in biopsy-related sepsis, pain and other side effects.

Formal guidance published by the National Institute for Health and Care Excellence (NICE) (09/05/2019) approved multiparametric MRI (mpMRI) as a first line investigation for men suspected of having clinically localised prostate cancer.

The decision by NICE, followed two clinical trials (PROMIS and PRECISION) led by UCL in partnership with University College London Hospitals (UCLH). The PRECISION trial won UK Research Paper of the Year at last

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month's 2019 BMJ awards.

3. PEOPLE: PatiEnt prOstate samPLes for rEsearch" was a multidisciplinary collaboration to collect high-quality fresh tissue for research use, using magnetic resonance imaging (MRI) and biopsy data to target areas of tumor and benign tissue (5).

4. The NeuroSAFE study (6,7) led by Prof Greg Shaw is the first single-blinded, multi-centre, randomised controlled trial (RCT) of intra-operative frozen section during radical prostatectomy in the world. It is properly powered to evaluate a difference in the recovery of erectile dysfunction for men undergoing radical prostatectomy assessed by patient-reported outcome measures. The multidisciplinary team effort and pathology input has been crucial to this trial and the results will provide evidence to guide the use of the NeuroSAFE technique around the world.

These are just a few examples of clinical studies that have had significant pathology input leading to change in clinical practice. Other studies including PRIME, HIST-MRI, RECONCILE, LIMIT are looking to improve imaging modalities and early detection. Sir William Osler also wrote 'The pathologist is the doctor's doctor'. The central review and validation pf pathology reports and results provides a high-quality control and quality assurance for the trials to succeed. This is only possible when there is understanding, respect and consideration of pathology time and input in the multidisciplinary teams.

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Neuroendocrine Tumors of The Prostate Gland – Insights into The Current Classification, Nomenclature and Molecular Updates

Dr. Anandi Lobo, Dr. Sourav K. Mishra, Dr. Ranjana Giri & Dr. Sambit K. Mohanty




Introduction

Neuroendocrine tumors (NETs) represent a distinct entity within the spectrum of prostate cancer, characterized by neuroendocrine differentiation on morphology and unique clinical behavior. They constitute less than 0.5% of prostate cancers (PC).

This class of tumors encompasses various entities, ranging from the mixed neuroendocrine carcinoma (NEC) in an otherwise conventional prostatic acinar adenocarcinoma to a SCNEC or LCNEC, and can arise either as a de novo disease (in a treatment-naïve setting) or a post-therapy transdifferentiated phenotype that arises from an adenocarcinoma of the prostate gland. It is estimated that up to 10% of the PC in patients with androgen-resistant disease following long-term androgen deprivation therapy (ADT), are high-grade NEC, mostly associated with acinar adenocarcinoma. The WHO Blue Book, 2022, provides an excellent framework and classifies these neoplasms as well-differentiated neuroendocrine tumors (WDNET), small-cell neuroendocrine carcinoma (SCNEC), large-cell neuroendocrine carcinoma (LCNEC), mixed neuroendocrine neoplasms and paraganglioma. Previously incorporated entities such as neuroendocrine cells in the usual PC and adenocarcinoma with Paneth cell-like differentiation, do not find any mention in the current WHO classification. Treatment-related neuroendocrine PC (t-NEPC) is a distinctive category mentioned in the current WHO scheme due to its unique pathobiology, that arises after intensive suppression of the androgen receptor by next-generation therapeutic inhibition of androgen receptor signaling.

NE differentiation in PC involves the acquisition of NE features; a process is driven by various factors, including ADT, genomic alterations, and microenvironmental cues. There have been several hypotheses regarding the origin of NEPC, most of them supporting the idea that a majority of these carcinomas arise from the conventional prostatic adenocarcinoma cells, and the transition being influenced by ADT. The most accepted prevailing concept is that of transdifferentiation or lineage plasticity, wherein the cells switch off from one pathway to another to escape from adverse milieu. Lineage plasticity has emerged as an important mechanism of treatment resistance in PC. Treatment refractory PCs are increasingly associated with loss of luminal prostatic markers, and in many cases induction of developmental programs, stem cell–like phenotypes, and neuroendocrine/neuronal features. However, what these theories do not directly explain is the genesis of de novo NEPC. It has been demonstrated that some SCNEC of the prostate have been found to share immunohistochemical characteristics with the multipotent basal progenitor cells, which are positive for p63 and KIT; thus, suggesting a probable origin from these cells as well as a possible assumption for the origin of de novo tumors.

Molecular Mechanisms facilitating Neuroendocrine Differentiation in Prostate Carcinoma

Several key pathways and a constellation of molecular events are associated with a process of transdifferentiation along with a parallel reduction either in the androgen receptors or in the overall androgen receptor signaling pathway. Targeting key signaling pathways and transcriptional regulators involved in NE differentiation represents a promising approach for the treatment of NEPC with improving patient outcomes.

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The key genes and molecular events facilitating the lineage plasticity and NE differentiation include:

1. Androgen Receptor Downregulation

NEPC cells often exhibit decreased or absent expression of the androgen receptor (AR) compared to adenocarcinoma cells and this downregulation can occur through various mechanisms. ERG gene fusion with one of the androgen-regulated genes (TMPRSS2, SLC45A3, and NDRG1) was encountered in around 50% of SCNEC cases. This gene fusion, in conjunction with AR gene amplification, was found to downregulate the ERG gene and lead to NE differentiation of typical adenocarcinoma cells.

2. Inactivation of Tumor Suppressor Genes

The most common genetic alterations seen with NEPC include loss of retinoblastoma suppressor gene (RB1), TP53, and PTEN genes along with downregulation or loss of REST (RE1-silencing transcription factor) gene. Concomitant inactivation of both RB1 and TP53 are believed to be an early predispose towards NEPC transformation. Loss of both these genes are thought to contribute towards an accelerated proliferation of the tumor cells, and beyond that, facilitates the lineage plasticity towards a NE phenotype by inducing SOX2 expression, at transcription factor implicated in this lineage plasticity phenomenon. An upregulation of E2F, is considered a hallmark of RB1 deficient tumors.

3. Amplification of oncogenes

NMYC and Aurora kinase A (AURKA) overexpression/amplification is one of the most common genetic events found in clinical NEPC. AURKA gene, a regulator of mitosis/meiosis binds to NMYC and stabilizes it, and overexpression of either of these oncogenes in normal human epithelial cells increases the expression of NE markers, including synaptophysin and chromogranin. NMYC also directly binds with AR enhancers through EZH2-mediated transcriptional programs to drive NE differentiation, which forms the rationale for testing EZH2 inhibitors for NMYC–driven NEPC. Moreso, the combined loss of RB1 and overexpression of NMYC in genetically engineered mouse models has shown the progression of poorly differentiated NE-like tumors and reduced median survival. Inhibition of AURKA leads to reduced NMYC levels and thus decreases NEPC tumor burden, thus, potentiating the use of AURKA inhibitor alisertib in NEPC with NMYC overexpression. AURKA and NMYC amplifications are now increasingly considered prognostic biomarkers that may help predict aggressive NE disease progression, with or without ADT.

4. Transcription Factors

Transcription factors play a crucial role in the regulation of gene expression programs that contribute to the development and progression of NEPC. Key transcription factors regulating the expression of NE genes include ASCL1 (achaete-scute family bHLH transcription factor 1), REST (RE1-silencing transcription factor), and FOXA (forkhead box A) family. FOXA family genes, chiefly FOXA1 and FOXA2 play a primal role in prostate development as well modulate AR signaling and PC progression. ASCL1 has been found to regulate delta-like ligand 3 (DLL3) expression, an inhibitor of the NOTCH signaling pathway which is known to be strongly associated with NE differentiation in the lung and prostate. Upregulation of ASCL1 in RB1-mutated high-grade pulmonary NEC (SCLC and LCNEC) was associated with DLL3 overexpression compared with normal tissues. DLL3 has also been shown to be overexpressed in many NE neoplasms, implicated in tumor progression, and is typically associated with poor clinical outcomes, particularly in patients with NEC. Targeted therapies using DLL3 as a homing beacon for cytotoxic activity mediated via several different mechanisms (e.g., antibody-drug conjugates, T-cell engager molecules, CAR-Ts) have shown promising clinical activity in small-cell lung cancer (SCLC). DLL3 may be a clinically actionable target across neuroendocrine neoplasms.

5. Epigenetic Modifications

There are multiple epigenetic alterations that contribute to the development, progression, and characteristics of this aggressive subtype of PC. Methylation of DNA at CpG sites is a common epigenetic modification that can silence tumor suppressor genes or other genes involved in cancer progression, leading to changes in gene expression that promote NE differentiation and aggressive tumor behavior. As much as 20% of CRPC metastasis are known to exhibit DNA hypermethylation, consequently increasing the expression of AR, MYC, and ERG. Expression of the histone methyltransferase EZH2, is also increased in NEPC. Conversely, it has been reported that inhibition of EZH2 reactivated AR signaling and decreased the expression of NEPC genes and subsequently resensitize the tumor to ADT.

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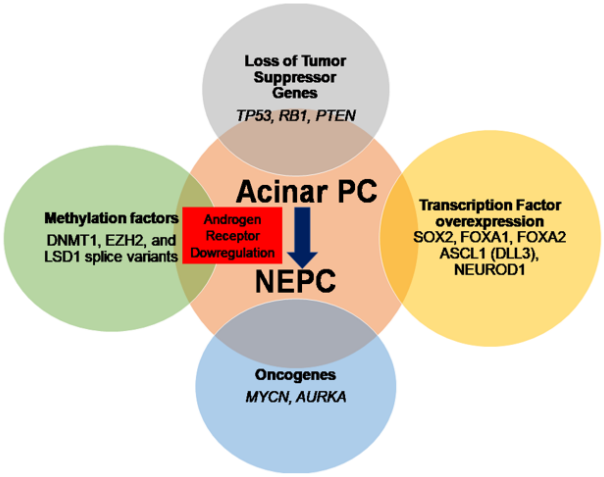

Classification of Neuroendocrine Prostate Tumors and Neuroendocrine Differentiation in Prostatic Adenocarcinoma

1. Well-differentiated Neuroendocrine Tumor

This tumor represents a low-grade tumor showing NE differentiation. To identify as a prostatic WDNET, these tumors must originate from the prostatic parenchyma, without any association with typical PC or extension from the urethra or bladder, must be positive for NE markers and negative for prostatic markers. These tumors are composed of bland, monotonous tumor cells, arranged in cords, nests, acini, and trabeculae, with mild nuclear pleomorphism and typical speckled chromatin. The mitotic rate and Ki-67 labeling index is usually low. Immunohistochemically, the tumor cells are reactive for chromogranin A, synaptophysin, and CD56. Reactivity for prostate specific antigen (PSA) and TTF1 has been reported to be negative. There is no established grading system for these tumors in the genitourinary tract; however, grading using the mitotic rates and Ki-67 index as is done in other sites can be recommended. Primary WDNET of the prostate, is extremely rare, with few individual case reports in the literature. Majority of the cases were diagnosed in males in the third decade or younger, and in patients of multiple endocrine neoplasia (MEN) syndrome, Type IIB.

2. Small Cell Neuroendocrine Carcinoma

Small cell neuroendocrine carcinoma (SCNEC) represents an aggressive NEPC with a poor prognosis, that may occur either in its pure form or adjacent/admixed with the conventional PC, reflecting a transdifferentiation from a conventional PC. These tumors can develop either de novo, or more commonly in the setting of ADT for typical PC. Primary SCNEC account for 1-5% of all the PCs. Therapy-associated tumors are commoner than the de novo counterpart. Molecular data suggest that many cases may arise from the transdifferentiation of a PC, even in patients who are treatment-naïve. ERG gene rearrangements are commonly concordant between the SCNEC and adenocarcinoma components. In these cases, there are usually recognizably distinct components of both conventional PC and SCNEC. The transition between the two components is usually sharp, and can be easily differentiated by routine morphology as well as IHC.

SCNEC exhibit a prototype morphology comprising of a solid, nested infiltrative architecture with small cell morphology (< 3 lymphocyte diameters) and high-grade features including high nuclear-to-cytoplasmic ratio, nuclear molding, speckled salt and pepper chromatin pattern, lack of prominent nucleoli, significant crush artifact, apoptosis and necrosis, and a high mitotic rate. Pure prostatic SCNEC should not be graded using the Gleason grading system.

SCNEC is characterized by diffuse reactivity for NE markers like synaptophysin, chromogranin, a markedly high Ki-67 proliferation index in the order of >50% and are usually negative for prostatic markers like AR, PSA, NK3 homeobox 1(NKX3.1) and prostate-specific membrane antigen (PSMA), though IHC is not necessary to make the diagnosis in the presence of classic morphology. Less than 20% of these cases retain PSA positivity, and in these cases, PSA immunostaining can confirm a prostatic primary in the setting of a metastatic SCNEC. TTF1 positivity has been reported in majority of prostatic SCNEC; TTF1 is often positive in

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SCNEC, regard less of the primary site of origin. Insulinoma-associated protein 1 (INSM1), has been shown to be positive in those SCNEC cases that lack reactivity to the conventional NE markers like synaptophysin and chromogranin A, however it lacks complete specificity. Occasionally, these tumors may be completely negative for synaptophysin or chromogranin expression; and be diagnosed entirely based on nuclear morphologic features in well-preserved tumor samples. IHC usually aids to establish a diagnosis in cases of a poorly differentiated morphology, especially at a metastatic site in the presence of extensive crush artifact of a small biopsy tumor. In such cases, NE marker positivity with negative to patchy weak staining with PSA and PAP can be suggestive of unequivocal evidence of SCNEC.

The incidence of TMPRSS2::ERG rearrangements in prostatic SCNEC have been reported as ~45%. Multiple reports have uniformly demonstrated that there is concordant ERG rearrangement status between concurrent usual PC and SCNEC components, indicating a shared clonal origin.

Surgery, platinum-based chemotherapy and radiation remain the mainstay therapy for SCNEC.

3. Large Cell Neuroendocrine Carcinoma (LCNEC)

Large cell neuroendocrine carcinoma (LCNEC) describes an expectedly rare and aggressive high-grade NEC whose cytology is characteristically distinct from SCNEC. These tumor cells tend to arrange in an organoid, trabecular or palisading manner with more abundant amphophilic cytoplasm and tumor nuclei tend to have coarse, clumpy chromatin, and prominent nucleoli, unlike the SCNEC tumors. Frequent geographic necrosis and brisk mitotic rate is present. Morphologically, there is significantly overlap with high-grade prostatic adenocarcinoma, which may cause challenges in the interpretation on H&E stain alone.

The NE differentiation should be supported by at least one NE marker. There may either be complete negative staining or only focal positivity for prostate luminal cell markers, such as PSA and prostatic acid phosphatase (PAP). Ki-67 proliferation index generally exceeds 50% but is lower than that seen in SCNEC. As these tumors show either negative staining or patchy positivity with PSA and PAP, these markers should not be solely used to rule out prostatic origin of metastatic LCNEC.

LCNEC in its pure form is exceptionally rare and most cases represent a progression from prior PC following long standing hormonal therapy. Most of what is reported suggests that LCNEC morphology most commonly arises in the setting of an already existing PC with history of long-standing hormone therapy.

4. Mixed Neuroendocrine Neoplasms

Approximately 50% of high-grade NE carcinomas are composite/mixed tumors with conventional PC. There is typically a clearly demarcated component of conventional PC, with an abrupt transition from the NE component. The acinar component usually is of high Gleason grade. The high-grade NEC component of these tumors should not be assigned a Gleason grade. The transition of PC into high-grade NE morphology also frequently occurs in the setting of anti-androgen therapy. The immunophenotype of this tumor is typical, with a strong labeling for PSA in most PC and diffuse NE marker reactivity in the NE component and substantially less staining in the usual PC. TP53 gene mutations are shared between both the components, further suggesting a common clonal origin. However, a loss of RB1 gene by deletion is a common event in prostatic SCNEC, which may be detected in these lesions and ~ 50% of concurrent acinar PC by loss of Rb IHC expression, compared with a very low percentage of otherwise conventional high-grade acinar PC.

5. Paraganglioma

Paragangliomas (PGLs), also referred to as extra-adrenal pheochromocytomas as rare and highly vascular tumors, originating from sympathetic or parasympathetic extra-adrenal autonomic paraganglia. PGLs involving the prostate are extremely rare tumors with a few anecdotal case reports. Prostatic PGL is a usually benign tumor, which should be considered in the differential diagnosis of prostate tumors in young males. PGLs have a characteristic nested growth pattern with a Zellballen appearance, separated by a delicate fibrovascular network and supported by sustentacular cells.

IHC for synaptophysin and chromogranin A yields diffuse strong staining. S100 and SRY-box transcription factor 10 (SOX10) staining highlights the sustentacular cells and are negative for cytokeratin (KRT). GATA3 reactivity poses as a serious pitfall while diagnosing these lesions in the genitourinary tract due to its expression in normal as well as neoplastic tissues such as urothelial carcinoma and collecting duct carcinoma of the kidney. Recognition of this finding will aid pathologists in preventing a misdiagnosis of a urothelial tumor based on GATA3 expression, which is critical given the differences in treatment, follow-up and prognosis between PGLs and urothelial carcinoma. A loss of succinate dehydrogenase B (SDHB) reactivity in tumor cells with supports the diagnosis of SDH-related disease.

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6. Treatment-related Neuroendocrine Carcinoma

Treatment-related neuroendocrine carcinoma (t-NEPC) refers to a subtype of PC that develops after treatment with ADT or other treatments for conventional PC and displays partial or complete high-grade NE differentiation. Because of its unique clinical and therapeutic significance, t-NEPC is classified as a distinct tumor type of prostatic neoplasms in the recent WHO 2022 classification.

T-NEPC arises by the transdifferentiation of a CRPC in 10-15% of patients with CRPC; shared clonal origin demonstrated by concordance of ERG rearrangements between t-NEPC and matched hormone-naïve carcinomas or in mixed tumors. This transdifferentiation is typically manifested by a downregulation of AR, PSA, and PSMA expression in tumors. AR expression is typically low but even when AR is expressed, NEPC tumors tend to be indifferent, to recognized AR signaling. The constellation of molecular alterations involving key tumor suppressor genes TP53, RB1, and PTEN; epigenetic reprogramming; dysregulation of transcription factors and upregulation of oncogenes NMYC and AURKA that occur concurrent to the reduction in AR, ultimately results in the NE phenotype.

T-NEPC has a spectrum of morphological features ranging from pure NE morphology, most commonly SCNEC, rarely LCNEC, to mixed tumors with a poorly differentiated PC and high-grade NEC components. The SCNEC component in a t-NEPC is morphologically identical to its counterpart at other body sites. LCNECs are exceedingly rare. Mixed tumors, consisting of admixed typical PC and high-grade NEC components, account for more than half of these cases. The transition between both components is usually abrupt, and the concomitant PC is often high-grade. The high-grade NE component is not graded, whereas the conventional PC component in such tumors can be graded and usually has a Gleason score of > 8. Clinically, these tumors manifests with predominantly visceral or lytic bone metastases, bulky tumor masses, low PSA levels relative to tumor burden or a short response duration to androgen deprivation therapy.

7. De Novo Neuroendocrine Carcinoma

De novo NEPC is an exceptionally rare but very aggressive form of this disease. It represents <2% of all NEPCs. Studies have shown that de novo progression is facilitated by the genomic loss of tumor suppressor genes like RB1 or TP53 that expedites this transition of PC away from a luminal epithelial phenotype. Similar to t-NEPC, about half of these tumors usually coexist with typical adenocarcinomas, while the remaining cases present as pure SCNEC. Morphologically and immunohistochemically, these tumors are similar to their counterparts previously discussed. A primary prostatic SCNEC can be distinguished from a metastatic SCNEC from other sites by the presence of TMPRSS2::ERG fusion gene, strongly suggestive of a primary prostatic tumor. This diagnostic differentiation from a usual PC with NE differentiation and carcinoid is crucial, as it is typically non-responsive to androgen signaling targeted therapies. Prognosis is dismal with a median overall survival to less than 12 months.

8. Prostatic Carcinoma with Diffuse Neuroendocrine Differentiation

This group represents a class of tumors that do not neatly fit into the proposed classification system for NE tumors in the prostate gland. They have been variously termed “amphicrine” carcinoma and “hybrid carcinoma with mixed luminal and NE phenotype. They comprise an unknown percentage of primary/metastatic lesions and most commonly are reported in patients in a post ADT/androgen receptor signaling inhibitor (ARSI) setting. It has been hypothesized that this group may represent tumors in transition from usual PC to tumors with well-developed NE features. Such “in transition’ tumors, or prostatic adenocarcinoma with diffuse NE transdifferentiation demonstrate features intermediate in between pure conventional/acinar prostatic adenocarcinoma and SCNEC. It has been reported that ADT/ARSI therapy may induce a phenotypic change in the usual acinar PC from an AR+/NE- phenotype to AR-/NE+, AR-/NE- (dual negative tumors) and AR+/NE+ phenotypes. Ki67 proliferative index can also be utilized to segregate these tumors, ranging from low Ki67 levels in AR+ tumors to high Ki67 levels in NE+ tumors.

This group of tumors are known to metastasize to sites common to PC like lymph nodes and bone as well as to sites favored in high grade NEC like lung and liver. Morphologically, the tumor is composed of nests and sheets of tumor cells, some displaying rosette-like architecture, with abundant amphophilic to pale cytoplasm, salt and pepper chromatin, prominent central nucleoli with brisk mitotic activity. The overall impression is one of a PC with overlapping NE-like morphology. The cells display diffuse (or non-focal, confluent) positivity for at least 1 NE marker, commonly synaptophysin or chromogranin, and at least 1 prostatic marker, such as NKX3.1, AR or PSA. Ki67 proliferation index is moderately high (~50%), but not at that seen in SCNEC. TMPRSS2::ERG rearrangement has been noted in ~50% cases. As there is still a lack of large

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series describing these tumors in terms of morphology, grading, clinical behavior and outcomes as well as molecular signatures, there is a clear lack of well-defined diagnostic criteria for this set of neoplasms.

Role of Immunohistochemical Markers in the Diagnostic Workup for NEPC

Current recommendations of the ISUP molecular pathology working group state that for clinically localized PC, unless there are clear morphologic NE features, IHC for NE markers is not recommended. In well preserved tumors, a diagnosis of SCNEC and LCNEC is usually based entirely on the morphology of the tumor and routine use of IHC is not recommended. Moreso, NE markers can show reactivity in few high-grade acinar PC as well, at least focally; thus, rendering these markers are not entirely specific for NE differentiation. Thus, NE marker expression in isolation does not confirm to the diagnosis of a SCNEC or LCNEC in the absence of typical morphology. Also, a worse outcome has not been attributed to NE marker positivity in those cases of localized usual PC that do not exhibit any high-grade NE features, thus further relegating the practical utility of routine use of NE IHC.

However, NE markers may be useful in small tissue metastatic site biopsy or in prostate core needle biopsies, in the presence of crush artifacts and for confirmation of suspicious high-grade morphology such as nuclear molding, high N:C ratio, diffuse architecture and large sheets of cells with geographic necrosis. A combination of prostate specific / AR related markers such as PSA, NKX3.1 and PSMA along with the NE markers (synaptophysin, chromogranin, and INSM1) is most commonly utilized.

Given its clinical implications, the term NEC is best reserved for high-grade cancers and not the usual type PC or well-differentiated NE tumors. Ki-67 appears to have some role in NEPC, with NECs having much higher Ki-67 proliferative index (>50%) compared to conventional high-grade PC.

Future Directions and Conclusion

The diagnosis of NE tumors of the prostate relies on histopathological examination and IHC staining for NE markers. Occasionally, distinguishing between focal NE differentiation and pure NE tumors can be challenging, leading to variability in classification and treatment. There may be cases of NE neoplasms within the prostate that are morphologically difficult to classify under the WHO criteria. A diagnosis of "High-grade neuroendocrine carcinoma, not otherwise specified" has been recommended for these lesions.

The outcome of these tumors varies, with paragangliomas and WDNETs having a better prognosis on one end of the spectrum with a dismal prognosis for SCNEC and LCNEC at the other end of the spectrum. Advances in molecular profiling, imaging modalities, and targeted therapies hold promise for improving the diagnosis and management of NEPC. Future research efforts should focus on validating molecular markers, refining diagnostic criteria, and conducting prospective clinical trials to evaluate novel therapeutic approaches. A comprehensive understanding of the molecular and clinical heterogeneity of neuroendocrine prostate tumors is essential for guiding clinical decision-making and improving patient outcomes.

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Metastatic Castration Sensitive Prostate Cancer – "Choose Wisely"

Dr. Krishnakumar Rathnam

Prostate cancer is the second most common cancer in men in India. It accounts for about 3% of all cancers in India. In 2020, the Indian Council of Medical Research (ICMR) estimated that there were around 40,000 new cases of prostate cancer in India. The average annual incidence rate for prostate cancer in India is between 5.0 and 9.1 per 100,000 people per year. The 5-year survival rate for prostate cancer in India is 61.9%, and the 10-year survival rate is 36.2%. The burden of prostate cancer in India is expected to increase due to population growth, life expectancy, and an aging male population. Many patients in India are diagnosed with prostate cancer in advanced stages where the journey of these patients begin in the hormone sensitive phase. Given the overall younger age and higher disease burden disease in Indian population it is prudent to augment existing hormonal back bone of Androgen Deprivation Therapy (ADT), in the hormone "sensitive" phase to improve overall outcomes.

ADT includes Surgical Orchiectomy or Medical Orchidectomy like LHRH agonist - Leuprolide, Goserelin, Triptorelin or LHRH antagonist - Degarelix or relugolix or a combination of both; which most use in clinical practice. Augmenting the defence against progression includes - next generation Androgen Receptor Blockers (ARB) – enzalutamide, apalutamide and daralutamide; Abiraterone Acetate (AA) that inhibits androgen synthesis and chemotherapeutic agents. Selecting the best additional drug that provides the best symptom relief and improve overall survival without adding to drug toxicity or financial toxicity can get very challenging. Patients can be differentiated into 2 subsets - Low Burden and High Burden disease. The "low disease burden" continue to get standard ADT and a first generation ARB which seems to have a reasonably good control over disease progression and overall survival. Adding radiotherapy to the primary in addition to ADT enhances local control and improves survival in this subset (STAMPEDE, HORRAD trials).

On the other hand patients with "high disease burden" defined as presence of visceral metastasis or with 4 or more bone metastases with atleast 1 lesion outside the vertebral column or pelvis seem to be more aggressive in their behaviour and needed fortification in Indian population. In CHAARTED TRIAL addition of 6 cycles of docetaxel with ADT caused a 40% decrease in risk of mortality and improved survival; however with increased side effects of chemotherapy. Adding AA with prednisolone to ADT improved survival (LATTITUDE and STAMPEDE trials). Newer ARBS – like Enzalutamide (ENZAMET study) and Darolutamide (ARASENS study) decrease mortality when added on early along with ADT, however the benefit post chemotherapy in the HSPC setting was not significantly better over 1st generation ARBs like Bicalutamide, Nilutamide and Flutamide. APALUTAMIDE also improved time to radiological events and survival (TITAN study).

Now how to choose which drug to give in Indian practice is a multifactorial process that includes patient factors like age, comorbidities versus availability and cost of each additional drug into a treatment protocol that usually run for years at a stretch (especially hormonal backbone). The very young and fit patient with heavy burden disease could be initiated on Docetaxel +ADT chemotherapy as it is a "time-limited" approach and then continue on combination ADT with first generation ARB or Darolutamide (ARASENS Study) till progression.

For the patient who is unable to tolerate or receive docetaxel, AA plus prednisolone in addition to ADT is non inferior to addition of Docetaxel in terms of survival and provides better PSA control and Quality of life. For patients with relative/absolute contraindication to steroids, enzalutamide, apalutamide or darolutamide are good alternatives and the choice depends on the availability and cost of each regimen in the practicing context.

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Recent Advances in Advanced Endometrial Cancer: New Poster Girl for Precision Oncology

Dr. Ghanashyam Biswas, Dr. Piyush Ranjan Sahoo & Dr. Inimerla Bhavya

Endometrial cancer is the second most common and fourth leading cause of death due to gynecological malignancy worldwide as recorded in 2020. In India, the incidence of endometrial cancer is lower as compared to developed countries with a reported incidence of 16,413 cases in GLOBOCAN 2020. While early-stage endometrial cancer is typically curable with surgery, advanced and metastatic disease remains a challenge.

Between the two main subtypes namely endometrioid and non-endometrioid, endometrioid tumors are more common (75-80% of uterine cancers), are typically diagnosed at an early stage, and may have a favorable prognosis. Non-endometrioid tumors (including serous, clear cell, carcinosarcoma, and other, rarer types of endometrial cancer) are often more aggressive and have a poor prognosis. Major advances in the field of endometrial cancer are the adoption of molecular and genomic profiling and then risk stratifying.

The TCGA established four molecular subtypes, termed copy-number high (serous-like), copy-number low, microsatellite instability (MSI, hypermutated), and POLE (ultra-mutated). Copy-number high tumors comprise all serous carcinomas and many high-grade (FIGO grade 3) endometrioid carcinomas.

Chemotherapy, hormonal therapy and targeted therapy

While chemotherapy remains a cornerstone of treatment for many patients with advanced endometrial cancer, efforts are underway to improve the efficacy of existing regimens and develop novel drug combinations.

Most of the endometrial cancers are hormone receptor (ER, PR) positive and does benefit with drugs like Tamoxifen, Aromatase inhibitors, Megestrol acetate, Fulvestrant and even CDK4/6 inhibitors in advanced and recurrent settings. Alternate use of Tamoxifen with Megestrol acetate every three weeks gives a decent response rate in good number of patients.

Research into combining chemotherapy with targeted therapies, immunotherapy, and agents like VEGF inhibitors (Bevacizumab) is showing promise in overcoming resistance and improving patient outcomes.

Adding certain targeted therapies like anti Her2 neu agents to chemotherapy will benefit patients with HER2 positive advanced endometrial cancer.

Immunotherapy alone in Advanced Endometrial Cancer

Immunotherapy has gained significant attraction as a treatment for advanced endometrial cancer, especially in patients with mismatch repair deficiency (dMMR) or microsatellite instability (MSI-H). MMRd/MSI-H is an important (agnostic) biomarker. Approximately, 30% of endometrial cancer patients harbor this type of alteration. Patients characterized by a ultra-mutated (POLE) and hyper-mutated (MSI-H) profile are likely to respond to immune checkpoint inhibitors. Pembrolizumab (PD-1 inhibitor), was the first FDA approved immunotherapy for this subgroup of patients, showing promising survival benefits. Other immune checkpoint inhibitors, such as nivolumab and dostarlimab, have also demonstrated clinical efficacy in both first-line and later-line settings. The GARNET study shows the beneficial effect of dostarlimab monotherapy in MMRd/MSI-H in 2L+ endometrial cancer patients.

Immunotherapy combination in Advanced Endometrial Cancer

The use of targeted agents like lenvatinib (anti-angiogenic agent) has been approved in combination with pembrolizumab for advanced or metastatic endometrial cancer that is not MSI-H or dMMR previously

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treated with at least one prior platinum based chemotherapy regimen in any setting. The Study 309 (KEYNOTE-775) highlighted that this combination has shown improved PFS, improved OS and median DOR.

DUO-E was an international, randomized phase 3 study for advanced stage and recurrent uterine cancer that evaluated the addition of durvalumab to paclitaxel and carboplatin with and without olaparib compared to standard paclitaxel and carboplatin and placebo maintenance. DUO-E built upon prior immunotherapy trials of durvulamab in endometrial cancer for patients with both pMMR and dMMR tumors. It was hypothesized that combining poly(ADP-ribose) polymerase (PARP) inhibitor with an immune checkpoint inhibitor may improve outcomes in both dMMR and pMMR tumors.

PARP Inhibitors

PARP inhibitors, such as olaparib and niraparib, have been investigated in the treatment of endometrial cancer, particularly in patients with BRCA mutations or homologous recombination repair defects. These therapies exploit the concept of synthetic lethality, where the inhibition of the PARP enzyme, critical for DNA repair, leads to tumor cell death in cancers with certain genetic defects. A phase 2 clinical trial is studying the efficacy of olaparib and cediranib maleate in treating patients with recurrent, resistant or metastatic endometrial cancer.

Other targeted therapy in Advanced Endometrial Cancer

Moreover, endometrial cancer shares genomic features with serous ovarian cancer, the basal-like subtype of breast cancer, and colorectal cancer. Some endometrioid and serous endometrial tumors are molecularly distinct, while others are similar, suggesting some may benefit from a common treatment. Moreover, exportin-1 inhibitor (e.g., selinexor) and WEE1 inhibitor seem to correlate with promising anti-tumor activity in TP53 wild type and TP53 mutated tumors.

Conclusion

Significant progress has been made in recent years, particularly in the areas of targeted therapies, immunotherapy, and personalized treatment approaches besides backbone chemotherapy and hormonal treatment. The rise of precision medicine has also brought about more individualized treatment strategies. These therapies are beginning to provide improved survival outcomes and quality of life for patients with advanced disease. We know that advanced lung cancer (especially, adenocarcinoma) is known to be a poster boy for precision oncology, while endometrial cancer today is a New Poster Girl for Precision Oncology.

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Improving Outcomes in Prostate Cancer Care with AI-based Risk Stratification

Dr. Uttara Joshi

Prostate cancer is one of the most common cancers among men worldwide, with millions of new cases diagnosed annually. Accurate diagnosis and risk stratification are crucial to distinguishing aggressive cancers requiring immediate intervention from indolent ones that may benefit from active surveillance. Current diagnosis and risk stratification methods like histopathology-based nomograms and genomic classifiers, while invaluable, face limitations in terms of speed, consistency, and precision. Artificial intelligence (AI) emerges as a transformative force, poised to improve prostate cancer care through enhanced risk stratification, enabling personalized therapy regimens and improved treatment outcomes.

Gleason grading and risk stratification in prostate cancer suffer from inter- and intra-observer variability, leading to suboptimal selection of treatment regimens. In addition to this, a significant amount of crucial information remains untapped when tissue slides are reported manually. Artificial Intelligence/Deep Learning (DL) histopathology solutions for prostate cancer grading hold promise to:

1. Improve accuracy and reproducibility over human grading
2. Increase usage and utility of quantitative grading metrics (percent pattern 4, quantification of tumor involvement, cribriform pattern quantification)
3. Use morphology-based biomarkers to predict tumor trajectory for events like biochemical recurrence, time to metastasis, metastasis, and Prostate Cancer-Specific Mortality.
4. Make available accurate grading and risk stratification in low-resource settings without subspecialist pathologists, ensuring equitable healthcare.

In this talk, we will present AIRAProstate a suite of Artificial Intelligence-based solutions that automate Gleason grading, ISUP grade grouping, and prognostic markers quantification in core needle biopsies and radical prostatectomies. Trained on datasets from thousands of PCa patient data, AIRAProstate improves risk stratification by removing inter and intra-observer variability seen in manual pathology reads, leading to better treatment decisions.

- We will present how the AI was trained, tested, and validated, not only against Pathologist Gleason grading but also against actual clinical outcomes.
- We will demonstrate results on two cohorts: An Active Surveillance cohort followed up for 15 years, and a GG2 post-RP cohort.
- In addition, we will also discuss our recently published histopathology AI/DL algorithms for molecular subtype prediction and prediction of lethal PCa directly from histopathologic images.

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The Key Role Urology is Playing in Defining Pathology's Digital Future

Dr. Matthew. O. Leavitt

Digital transformation in pathology has been discussed for decades. Despite all the talk, progress has been frustratingly slow. Over the last 10 years building and supporting digital pathology labs, we've found progress has been less about imaging technology and more about efficient workflow. Urology is the first subspecialty poised to broadly adopt a standardized pre-analytic pathology workflow, setting the stage for significant breakthroughs.

In urology clinics, providers are focused on managing their day-to-day responsibilities. Asking them to consider the nuances of pathology processes is often a significant challenge. To address this, we reimagined the specimen procurement process—not to make life easier for the pathology lab, but to streamline workflows for urologists and their staff during biopsy procedures. This patient- and provider-centric approach garnered adoption because it addressed what matters most to clinic teams: efficiency.

Similarly, histology labs face immense pressure to produce slides quickly. Change is often met with resistance unless it demonstrably improves their processes. Introducing digital workflows, including whole-slide imaging, required us to simplify mundane, manual tasks for lab technicians. By focusing on reducing inefficiencies, we were able to drive standardization and adoption—not through mandates, but by creating solutions that made their work easier.

This shift toward clinic- and lab-centric improvements has had transformative results. In 2015, much of community-based urology in the U.S. relied on small highly variable in-office labs. By 2025, we expect over 20% of all U.S. prostate biopsies to be performed in standardized, fully digital labs. Urology clinics that adopted these practical workflow improvements have leap-frogged larger better-funded academic center labs, setting a new standard for the field.

These advancements in urologic pathology are paving the way for the next generation of pathology.

In this talk, I will share insights from a decade of implementing digital workflows in urology clinics and pathology labs, as well as our vision for the next 10 years of innovation.

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Application of Digital Pathology and the Role of AI in Prostate-Specific Cases

Dr. Matthew. O. Leavitt

When Dr. Leavitt first decided to dive into digital pathology, he knew it wouldn't be easy—but he wasn't alone. He convinced his friend Dr. Jared Szymanski to join him. Their journey began much like many others, by purchasing an expensive slide scanner. It wasn't long before they faced a hard truth—glass was faster and cheaper than digital. Worse yet, Dr. Leavitt and Dr. Szymanski found themselves missing the familiarity of working with microscopes over monitors.

The Turning Point

As their high-throughput digital dinosaur sat idle, they began questioning the inefficiencies in the digital workflow. Why was it so cumbersome for the lab? And why did signing out cases digitally feel so unappealing? Confronting these questions became a pivotal moment for them. They realized that a digital pathology workflow only makes sense if every step—from patient to bedside, tissue to block, image acquisition to diagnosis, report building to ancillary test ordering—is integrated into a cohesive digital system. This epiphany opened their eyes to a harsh reality: histopathology, as they knew it, had been an innovation desert for decades.

Revolutionizing Prostate Biopsy Workflow with Lumea

Determined to address these challenges, Dr. Leavitt and his team assembled a small group of engineers, software developers, and histotechnologists to reimagine the entire workflow. Their efforts began with prostate needle-core biopsies, which are notoriously challenging for labs due to their variability in quality and processing demands.

The result? They created new innovations like the BxBoard and BxChip, which have completely revolutionized prostate biopsy workflows. The BxBoard, a six-lane tissue transportation device, fixes tissue on a formalin-soaked sponge to maintain orientation and enable even geometric planes. Labs have reported dramatic improvements, including increased tissue yield on slides and better preservation of molecular biomarkers. Once in the lab, tissues are transferred to the BxChip, a clinical tissue array that reduces technician time by 76%, biohazard waste by 136%, and slide and stain costs by 83%.

AI and the Digital Leap

Standardizing the transportation, documentation, processing, and embedding of specimens has unlocked massive efficiency gains in digital workflows. By combining AI tissue detection with Lumea's artificial tissue fiducial, Dr. Leavitt and his team have further amplified these efficiencies. AI algorithms now recognize and track tissues in the BxChip lanes, enabling accurate measurements and real-time pathology report updates as pathologists review cases. Lumea's open-platform approach also allows labs to choose from various AI vendors for quality control checks or automated tasks.

These advancements have cut diagnostic time per case for some pathologists by 50%. Among labs adopting the system, notable increases in biopsy core length and prostate cancer detection rates have been observed. Finding a solution that enhances both efficiency and quality is rare, but harmonizing standardized tissue handling with digital imaging tools has achieved that.

Transforming Patient Care

Over the past decade, Dr. Leavitt's innovations through Lumea have impacted hundreds of thousands of patients worldwide. By aligning standardized tissue handling with digital imaging innovations and AI, his team has demonstrated how labs can achieve tangible returns on investment while advancing prostate cancer care. As the field prepares for the inevitable waves of digital transformation, those leveraging Lumea's solutions are poised to lead the way, combining efficiency with unparalleled quality in patient outcomes.

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Augmenting Prostate Cancer Diagnosis with AI: Real-World Insights, Challenges & Solutions

Dr. Shriya Kumar

About Qritive

Qritive is a cutting-edge digital pathology company that leverages artificial intelligence (AI) to enhance diagnostic accuracy, consistency, and efficiency for laboratories worldwide. Our AI-powered solutions reduce slide reading times, minimize pathologist bias, and enable healthcare providers to make data-driven decisions that improve patient outcomes. We serve a global clientele, including leading institutions such as Singapore General Hospital and Mayo Clinic.

Our portfolio consists of three main components:

- ***Pantheon:*** An image management system that enables physicians to view physical microscopic slides in digital form. Pantheon provides features for case management and image analysis.
- ***AI Modules:*** Specialized tools that analyze WSIs to identify and grade disease areas. These include:
  - Tumor-specific modules for Prostate, Colon, and Lymph Nodes.
  - The IHC (Immunohistochemistry) module, applicable to various cancers such as breast, lung, and gastrointestinal cancers, which are analyzed using immunohistochemistry methods.
- Pathologist Analytics Network which provides pathologist expert services to support research projects.

QAi Prostate Grade: Augmenting Prostate Cancer Diagnosis with AI

QAi Prostate Grade is Qritive's AI module designed to assist pathologists in the detection and grading of prostate cancer on core needle biopsy whole slide images (WSIs). By employing deep learning algorithms, it enhances diagnostic accuracy and supports consistent clinical decision-making.

Key Features:

- ***Tumor Detection:*** Identifies tumor regions, distinguishing benign from malignant tissue with high sensitivity and specificity.
- ***ISUP Grading:*** Assigns International Society of Urological Pathology (ISUP) grades to tumor regions.
- ***Explainability:*** Provides clear segmentation of tumor regions, enhancing pathologist confidence.
- ***Flexible Deployment:*** Available as an on-premise or cloud-based solution adaptable to laboratory needs.

Performance Metrics and Validation Studies

Study 1: ECP 2023 Publication: A Deep Learning-based Tool for Histological Detection of Malignancy in Prostate Core Needle Biopsies

- ***Design:*** 10 pathologists analyzed 150 WSIs in two phases (without and with AI assistance). Ground truth (GT) was established by senior pathologists.
- ***Findings:***
  - AI aligned with GT in 148/150 cases.
  - Sensitivity: 100%, Specificity: 95.1%.
  - Pathologist concordance improved by 17.1% for benign cases with AI assistance.
- ***Conclusion:*** AI improves pathologist concordance in challenging cases.

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Study 2: USCAP 2023 Publication: A Deep Learning Approach to Identify Tumor on Prostate Biopsies

- ***Design:*** 99 WSIs analyzed by two pathologists first without and then with AI annotations.
- ***Findings:***
  - AI improved pathologist agreement from 95 to 97 out of 99 cases.
  - Sensitivity: 98.3%, Specificity: 82.1%.
- ***Conclusion:*** AI assists in reducing workload and improving diagnostic accuracy.

Study 3: USCAP 2024 Publication: A Deep Learning Algorithm to Help Identify and Grade Tumor into ISUP Grades on Prostate Needle Biopsies

- ***Design:*** 160 WSIs analyzed by 11 pathologists and compared with AI predictions.
- ***Findings:***
  - AI identified all malignant cases (100% sensitivity) versus pathologists who missed 2 cases.
  - ISUP grading: AI and pathologists aligned with GT in 57/109 cases.
- ***Conclusion:*** AI is effective in both screening and grading.

Why QAi Prostate Grade?

- ***Accuracy:*** High sensitivity for malignancy detection.
- ***Efficiency:*** Automates routine tasks, reducing workload.
- ***Explainability:*** Offers clear segmentation of tumor regions.
- ***Global Validation:*** Validated through multiple studies at international institutions.

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Abstracts of Oral Presentation

Diagnostic Accuracy of The Paris System 2 for Detection of Urothelial Cancer in Comparison to TPS1 and Conventional Reporting of Urine Cytology

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University College of Medical Sciences, New Delhi, India

Abstract:

Background:

In 2016, The Paris System 1.0 (TPS 1.0) was introduced to overcome the problem of the lack of a standardized reporting system, leading to diagnostic dilemmas for treating physicians. Following this, TPS 2.0 was introduced in 2022 to deal with the certain limitations of TPS 1.0.

Objectives:

To evaluate the diagnostic accuracy and risk of malignancy (ROM) with risk of high-grade malignancy (ROHM) of urinary tract by TPS 2.0 in comparison to TPS 1.0 and Conventional reporting (CR) of urine cytology. Methods: Data were collected from 2017 to 2023 from the departmental archives. The cases were reviewed and categorized as per TPS 2.0, TPS 1.0 and CR.

Results:

Of 835 urine samples studied, 128 urine samples of patients with histology correlation were analyzed. TPS 2.0 had a maximum sensitivity, specificity, PPV and NPV 43.6%, 94.1, 95.3% and 37.6% in comparison to TPS 1.0 and CR (33.0%, 85.3%, 31.5%, 86.1%, and 22.3%, 91.2%, 29.8%, 87.5%) respectively. TPS 2.0 has significantly high sensitivity (P= 0.0075), and maximum ROC AUC score (0.6887) compared to TPS 1.0 and CR. ROM for AUC, SHGUC and HGUC categories 78.3%, 96% and 94.1%, whereas ROHM 21.7%, 56%, and 88.3%, respectively. CR and TPS 1.0 predicted ROM for AUC, SHGUC, HGUC categories (80.9%, 84.6%, 92% and 72.7%, 93.7%, 89.5%) and ROHM (33.3%, 61.5%, 92.8% and 30.3%, 62.5%, 73.7%), respectively.

Conclusion:

Implementation of TPS 2.0 revealed maximum diagnostic accuracy for urinary tract malignancy, with the highest ROC AUC compared to TPS 1.0 and CR. Our study results highlight the impact of TPS 2.0 for detection Urothelial cancer.

Keywords:

TPS 2.0, Urothelial Cancer, Risk of Malignancy, Diagnostic Accuracy, Urine Cytology

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Immunohistochemical Expression of Enhancer of Zeste Homolog2 (EZH2), p53 and Ki-67 in Patients of Prostate Carcinoma: Association with Clinicopathological Parameters and Serum PSA Level

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Abstract:

Introduction:

Prostate cancer is a major health problem throughout the developed world leading to substantial mortality and morbidity.At present adequate prognostic markers are lacking.Most cases are diagnosed microscopically before metastatic spread. Thus by differentiating these groups we can help patients remarkably.

Aims And Objectives:

1. To study immunohistochemical expression of EZH2,p53 & Ki-67 in patients of prostate carcinoma.
2. To study their correlation with the clinicopathological parameters and serum PSA level.
3. To predict the prognosis of the disease based on histo-morphological parameters and IHC findings.

Materials And Methods:

This study was a cross-sectional prospective study conducted in the Department of Pathology, IMS & Sum Hospital for 2 years. Clinical information of all the cases was collected from test requisition forms along with biopsy samples and medical records available in the department of urology.After histological confirmation of carcinoma, histopathological parameters were studied and representative blocks were selected for IHC. IHC expression was detected through routine immunohistochemical staining protocols and assessed by 2 pathologist independently.The Collected data was analyzed statistically.

Results:

We observed a statistically significant correlation of EZH2 with tumor differentiation (i.e. Gleason score ≥8), LVI and high Ki 67 index. However no significant correlation of EZH2 with PSA, grade group, tumor burden, PNI, metastasis, and with p53 observed.Similarly, p53 and Ki67 expression didn't reveal any significant correlation with above-mentioned clinicopathological parameters.

However, we found a significant correlation of p53,Ki 67and EZH2 expression in prostate carcinoma compared with BPH cases .

Conclusion:

We concluded that these markers are upregulated in malignancy compared to benign lesions. Thus, such patients can benefit from the appropriate targeted therapy, leading to an increase in survival time. However further studies on larger samples with long-term follow-up and molecular genetic analysis need to be undertaken to understand the biology of these markers, to assess their prognostic significance in patients with prostate carcinoma, and whether they can be future targets for treatment in aggressive prostate carcinoma.

Keywords:

Prostate Carcinoma, EZH2, p53, Ki-67

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Granulomatous Reaction in Renal Cell Carcinoma - Immunohistochemical Subtyping of the Macrophages and Their Clinicopathological Correlation

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Abstract:

Introduction:

Granulomatous reaction in renal cell carcinoma (RCC) is an uncommon feature. The clinicopathological impact of this granuloma in RCC is still unexplored. We aimed to study the clinicopathological features of RCC with granulomatous reaction, the type of macrophages within the granuloma, and their clinicopathological correlation.

Materials and Methods:

A retrospective study included the RCC cases from January 2022 to October 2024. Six cases showed a granulomatous reaction. The clinicopathological features were reviewed. Immunohistochemistry for CD68 and CD163 were performed.

Results:

The mean age was 56 years (ranges 29 -68). Male: Female: 5:1. Five cases showed clear cell RCC and one showed clear cell RCC and papillary RCC. WHO/ISUP histologic grade was 2 and 3. Most cases were pT1a (3 cases). Both intra and peri-tumoral granulomas were seen in four cases, and only intra-tumoral granuloma was seen in two cases. Special stains were negative. CD68 was diffusely positive in all six cases of granuloma. CD163 showed diffuse positive in one case, occasional to focal positive in three cases, and negative in two cases. No recurrence was noted in four cases on follow-up; one case showed bone metastasis and one case lost follow-up.

Discussion:

Among the macrophage subtypes in granuloma, CD68-positivity is the dominant finding compared to CD163. CD68-positive macrophages in the granuloma are associated with unfavorable prognosis. In contrast, most cases in the present study showed no recurrence. This observation might help further research to study the role of granuloma in tumor progression and for further treatment and prognosis.

Keywords:

RCC, Macrophage, Granuloma, CD68, CD163

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Low Grade Oncocytic Renal Tumours – A Small Study Highlighting the Need for Careful Microscopic Assessment and Immunohistochemistry

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Abstract:

In light of recent updates in the classification of oncocytic renal tumours, we aimed to see if we could re-classify tumours with a low grade oncocytic morphology based on careful histologic assessment and immunohistochemistry (IHC).

Between January and September 2024, out of 6 cases diagnosed purely on morphology as either oncocytoma and/or chromophobe renal cell carcinoma, three cases fit our inclusion criteria of low grade oncocytic morphology. All were nephrectomies.

On re-evaluation of histology and a panel IHC performed on representative areas of tumour by tissue micro-array, we could re-classify two cases; one as Eosinophilic vacuolated tumour (EVT) based on the presence of cytoplasmic vacuoles supported by other histologic features (IHC: CD117 weak+, CK7 one occasional cell+, PAX8 weak+) and the other as Eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) with predominantly solid, focally cystic areas and cells with voluminous granular eosinophilic, stippled cytoplasm, multinucleated giant cells among other features (IHC: CD117-, CK20+, CK7-, PAX8+). One tumour morphologically diagnosed as oncocytoma did not undergo reclassification after IHC and review of histology. FH and SDHB were retained and Melan A, HMB45 and CA9 were negative in all tumours.

In this small cohort, we could re-classify two out of three tumours by looking for typical histologic features and IHC which could indicate that these recently described members of the low grade oncocytic renal tumour family, may prove to be not so uncommon if adequately worked up.

Keywords:

Oncocytic, Renal Cell Carcinoma, Low Grade, Eosinophilic Solid and Cystic Renal Cell Carcinoma, Eosinophilic Vacuolated Tumour

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Papanicolaou Society of Cytopathology System vs World Health Organization of Reporting System for Pancreaticobiliary Cytopathology-Comparison of Risk of Malignancy and Diagnostic Predictive Values: A 3 Year Retrospective Study in a tertiary care centre in India

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Abstract:

Introduction:

Pancreatic carcinoma is a rare entity with a poor survival rate due to late presentation and limited diagnostic modalities.

Materials and Methods:

This retrospective study aimed to evaluate the diagnostic performance of the Papanicolaou Society of Cytopathology (PSC) system and the World Health Organization (WHO) system for pancreaticobiliary cytology reporting. Total of 77 cases with pancreatic lesions were evaluated at the Department of Pathology, Vydehi Institute of Medical Sciences and Research Centre for a period of 3 years, i.e. from January 2021 to December 2023, using both PSC and WHO systems. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated for both systems. The Risk of Malignancy (ROM) was also estimated for each diagnostic category.

Results:

ROM for both systems with statistical significance was established at P=<0.05. Both the systems had a P value of less than 0.05, hence performing well in distinguishing between different categories. Both systems showed high sensitivity, specificity, and diagnostic accuracy. However, the WHO system had higher sensitivity (95.65% vs 93.47%), NPV (93.75% vs 90.90%) and diagnostic accuracy (96.10% vs 94.81%) compared to the PSC system.

Conclusion:

Both PSC and WHO systems are reliable for pancreaticobiliary cytology reporting having estimated ROM accurately. However, the WHO system may be more effective for risk stratification and diagnosis of pancreaticobiliary lesions, with a better performance in estimating sensitivity, NPV and diagnostic accuracy. Future studies with larger sample sizes and longer follow-up periods are needed to further substantiate these findings.

Keywords:

Pancreas, PSC, WHO, FNAC, Malignancy

ISBN: 978-93-92106-53-8

Tumors of Mullerian Origin in the Urinary Tract: Insights from Five Cases

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Abstract:

Tumors of Mullerian origin within the urinary tract are exceedingly rare, with limited literature describing their clinical and pathological characteristics. They are subdivided into clear cell carcinoma (CCC) and endometrioid carcinoma (EC). The histogenesis of these tumors remain controversial, however, their morphology shows a striking resemblance to their female genital tract counterpart. This case series details five patients treated at a tertiary cancer care center, each diagnosed with tumors of Mullerian origin in the urinary tract. Because of no specific characteristics for symptoms, signs, and accessory examinations compared with common urothelial carcinoma, diagnosis is mainly on histopathological examination. 4 out of 5 cases had CCC and 1 case had EC of the urinary tract. This study provides a brief discussion about its morphological and immunohistochemical characteristics with emphasis on differential diagnosis. The prognosis of these tumors is unclear due to their rarity. However, studies have shown a poorer prognosis compared with all other carcinomas of the urinary bladder, attributable to their high stage at presentation and unresponsiveness to radiation and/or chemotherapy. Thus, it is important to accurately recognize these tumors due to their clinical outcomes and management implications, underscoring the importance of multidisciplinary management in achieving favorable outcomes.

Keywords:

Clear Cell Adenocarcinoma, Endometrioid Carcinoma, Mullerian Tumors, Urethra, Urinary Bladder, Urinary Tract

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Renal Neuroendocrine Tumors – Unveiling the Rarity

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Abstract:

Renal neuroendocrine tumor (NET) is an extremely rare entity and only few cases have been reported worldwide. They have a frequent association with horseshoe kidneys & may also be seen as a component of prepubertal-type teratomas. In the kidney, NETs are thought to arise from tubular stem cells or from native neuroendocrine cells or stem cells located in the urothelium lining the renal calyces. Morphology & immunohistochemistry (IHC) studies form the mainstay in the diagnosis of these tumors. Nephrectomy is the standard treatment of renal NETs. These are indolent tumors associated with prolonged survival even in patients having metastatic disease. At present, we don't have an established grading system for renal NET's. However, the latest WHO 5th edition of urogenital and male genital tumors recommends the use of the gastrointestinal and pancreatic NET grading systems. The rarity of these tumors poses a diagnostic and therapeutic challenge. We hereby report 2 cases of this rare entity. Case 1 was of a 39 year old female whose renal mass showed features of a well differentiated NET, WHO grade 1. Case 2 was of a 57 year old female whose renal mass showed features of a well differentiated NET, WHO grade 2. At 6 months follow-up, both the patients remain asymptomatic. Our aim is to highlight the existence of this rare entity and emphasize the usage of appropriate IHC markers to confirm the diagnosis and exclude other mimics such as papillary renal cell carcinoma and adenomas.

Keywords:

Kidney, Neuroendocrine Tumor, Immunohistochemistry

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A Comprehensive Study of Renal Cell Carcinoma in Children and young Adults: Data from a Referral Centre

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Abstract:

Introduction:

Renal cell carcinoma (RCC) is rare in children and young adults. This comprehensive study outlines the prevalence and types of RCC in individuals aged 40 years or younger, along with their morphological characteristics, immunohistochemical profiling, and clinical outcomes.

Materials and Methods:

A total of 132 renal cell carcinomas diagnosed in individuals aged 40 years or younger were identified at our institution between January 2021 and March 2024. Demographic data, clinical characteristics, and follow-up information were collected from the electronic database. Tumor classification and categorization were performed using the WHO 2020 criteria. Immunohistochemical markers, such as CK7, CK20, CA-IX, TFE3, AMACR, CD117, SDH-B, and FH, were analyzed in selected cases in conjunction with hematoxylin and eosin (HE) slides.

Results:

The mean age was 34.43 years, with a distribution that was positively skewed towards the 30–40-year age group (n=114, 86.36%). The male-to-female ratio was 2.57:1. Of the 132 patients, 66 underwent partial nephrectomy and 66 underwent radical nephrectomy. Multifocal tumors were found in 3 cases. Clear cell renal cell carcinoma (CCRCC) was the most common histological subtype (n=99, 75%), followed by TFE3-rearranged RCC (n=9 6.81%), chromophobe RCC (n=9, 6.81%), and papillary RCC (n=7, 5.30%). Rarer subtypes were identified, with two cases of Mucinous Tubular Spindle Cell Carcinoma, and one case each of Clear Cell Papillary Renal Tumor, Eosinophilic Solid Cystic RCC, SDHB-deficient RCC, and Oncocytic Renal Tumor of Low Malignant Potential (LMP). Despite extensive immunohistochemical workup, one case remained unclassified. The median follow-up period is ~ 404 days[13 months].

Conclusion:

This series elaborates the clinicopathological profile of renal cell carcinomas in children and young adults (< 40 years), with emphasis on the importance of using ancillary tests in correct diagnosis.

Keywords:

RCC, Children, young adults, Clear cell RCC, and TFE3-RCC

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Steering through Uncommon Waters: Three Bladder Tumours Beyond the Common Spectrum

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Abstract:

We share our encounters with three rare tumours of the Urinary bladder. Urachal Mucinous Cystic Neoplasm of Low Malignant Potential, Polyoma virus driven Sarcomatoid Urothelial Carcinoma in a Renal Transplant recipient and Mixed NeuroEndocrine Carcinoma.

Case 1: 76 years old female presented with suprapubic mass. Intraoperatively she was found to have a midline cystic mass with bladder dome infiltration. The resected mass revealed extensive calcification of cyst wall. Microscopy revealed a cyst with neoplastic proliferation of mucinous epithelial cells, pushing pattern of invasion, extravasated mucin and calcification. The lining epithelium had no connection with the bladder mucosa. The tumour cells were CK20 and CDX2 positive. GATA 3 was negative. Ovarian or gastrointestinal tract tumours wre excluded. Diagnosis of Urachal Mucinous Cystic Neoplasm of Low Malignant Potential was made.

Case 2: 31 years old renal transplant recipient presented with hematuria and bladder mass. TURBT specimen revealed a sarcomatoid carcinoma with GATA3, p63, SV40, p16 and p53 positivity. EBER- ISH was negative. His serology revealed high Polyoma viral load. A diagnosis of Polyoma virus driven sarcomatoid urothelial Carcinoma was made. Patient underwent Radical Cystectomy which revealed the tumour with perivesical soft tissue infiltration.

Case 3: 71 years old male presented with myoinvasive bladder tumour. TURBT specimen revealed an admixture of High grade urothelial and small cell neuroendocrine carcinoma components, supported by mutually exclusive expression of GATA3, INSM1 and synaptophysin. The patient underwent Radical Cystectomy and extended pelvic lymphadenectomy.

Keywords:

Urachal Tumour, Mixed Neuroendocrine Tumour, Polyoma Virus Associated Bladder Cancer

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Molecular Classification of Muscle Invasive Bladder Cancer by using Immunohistochemistry and Its Association With Her2 Neu Expression in a Tertiary Care Hospital

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Abstract:

Introduction:

Muscle Invasive bladder carcinoma (MIBC) remains a major challenge in urological oncology, with significant implications for patient prognosis and treatment strategies. Recent advances in molecular classification have highlighted the potential for tailored therapeutic approaches, particularly in identifying key biomarkers that influence tumour behaviour and therapeutic response.

Aim:

Molecular classification of MIBC using immunohistochemistry and explore its association with expression of HER2neu.

Materials:

We conducted a retrospective analysis of MIBC tissue samples, applying IHC to classify tumours based on molecular subtypes, including luminal, basal and p53 subtype. The expression of HER2 neu was assessed and correlated with clinicopathological parameters and patient outcomes.

Results:

IHC analysis done till date revealed that 25% of tumours were luminal type, 50% of tumours were basal type and 25% of tumours were p53 subtype. Correlation with clinicopathological parameters demonstrated that basal type MIBC have better response to neoadjuvant chemotherapy. Luminal subtype MIBC are more likely to benefit from HER2 while p53 subtype are chemo resistant and require further treatment.

Conclusion:

Molecular classification of Muscle invasive bladder carcinoma by immunohistochemistry may allow easier definition of molecular subtypes in daily clinical practice contributing to the therapeutic planning, thereby improving the overall survival/disease free survival.

Keywords:

Muscle Invasive Bladder Carcinoma Molecular Classification Immunohistochemistry

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Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Upper and Lower Tract Urothelial Carcinomas: A Comparative Study and Histopathological Correlation

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Abstract:

Background:

Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are inflammatory markers which have gained more attention recently as prognostic factors in several malignant neoplasms. Numerous studies have analysed their prognostic and predictive utility in urothelial carcinomas. This study evaluates the association of NLR and PLR with tumour grade and its extent.

Materials and Methods:

This retrospective analysis included 123 patients with urothelial cancer for whom biopsies and radical surgeries were performed during January 2022 to December 2024. They were divided into two groups- upper tract comprising of 26 cases, and lower tract comprising of 97 cases based on site of the lesion. Pre-procedural NLR and PLR were calculated for all the patients. These values were correlated with tumour grade and extent obtained from the histopathology reports using Pearson's correlation and logistic regression.

Results:

Our study included patients aged 36 to 90 years, with a male to female ratio of 5.5:1. 22 out of 26 patients with upper tract urothelial carcinoma (UTUC) and 52 out of 97 patients with lower tract urothelial carcinoma (LTUC) showed high grade features. The mean NLR and PLR values were found to be higher among cases with high grade tumours (mean NLR= 5.72, mean PLR=190.05) as compared to low grade tumours (mean NLR=3.29, mean PLR=141.42). Tumour grade was found to have significant correlation with NLR but not PLR. NLR and PLR values were also found to have association with tumour extent in LTUC.

Conclusion:

The pre-procedural NLR and PLR values showed significant correlation with tumour extent. Similarly, positive correlation was established between pre-procedural NLR and tumour grade.

Keywords:

Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio, Urothelial Carcinoma, Tumour Grade

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From Rarity to Recognition: The Journey of Eosinophilic Solid Cystic RCC

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Abstract:

Eosinophilic Solid-Cystic Renal Cell Carcinoma (ESC-RCC) is a rare and recently recognized entity with an incidence of 0.2% worldwide. Included in the WHO 2022 classification of urinary and male genital tumors, ESC-RCC is characterized by distinctive histopathological and immunohistochemical features. It is associated with TSC gene mutations and mTOR pathway activation, providing opportunities for targeted therapy and favorable prognosis. This case report details a 44-year-old female who presented with left flank pain and a history of left nephrectomy for an unspecified tumor. Imaging revealed a recurrent mass in the left renal fossa, confirmed as ESC-RCC by histopathological and immunohistochemical analysis. Tumor cells showed abundant eosinophilic cytoplasm, prominent nucleoli, and cystic changes, with a CK20-positive/CK7-negative immunoprofile and a Ki67 labeling index of 40%. Molecular studies highlighted TSC mutations, distinguishing ESC-RCC from other renal neoplasms, including chromophobe RCC and high-grade oncocytic tumors. ESC-RCC typically manifests as small, organ-confined tumors with a favorable prognosis, though its metastatic potential is yet to be fully determined. Awareness of this novel entity is crucial for accurate diagnosis and appropriate management, emphasizing the need for differentiation from other renal cell carcinomas to enable targeted treatment strategies.

Keywords:

Eosinophilic Solid-Cystic Renal Cell Carcinoma (ESC-RCC), TSC Gene Mutations, mTOR Pathway, Immunohistochemistry (CK20, CK7), Renal Tumor Differential Diagnosis

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Evaluation of TLE1 as a Diagnostic Immunohistochemical Marker in Synovial Sarcoma

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Abstract:

Synovial Sarcoma is a malignant soft tissue tumour which is defined by the translocation t(X;18) that produce the oncogene SYT-SSX. TLE1 has emerged as a useful marker for the diagnosis of synovial sarcoma. We investigated the utility of TLE1 expression agains histomorphological and other immunohistological markers in synovial sarcoma cases. Conventional sections from 107 synovial sarcoma cases were subjected to TLE1 immunohistochemical staining along with traditional markers including EMA, AE1\AE3, CD99, Bcl2 and CD34. TLE1 staining was graded as 0, 1+, 2+, 3+. All the tumours were positive for TLE1 of which, 72(67%) displayed 3+ staining, 29(27%) displayed 2+ staining and 6(6%) displayed 1+ staining. EMA was positive in 86(80%), AE1\AE3 in 65(61%), CD99 in 93(87%), Bcl2 in 82(77%) and CD34 was negative in all the cases wherever performed. Our study showed TLE1 as more sensitive than traditional immunohistochemical markers for synovial sarcoma and may have implications for understanding the biology and for developing new therapies for this malignancy.

Keywords:

Synovial sarcoma, Immunohistochemistry, TLE1

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Comparative Evaluation of Microsatellite Instability, PDL-1 Expression and Molecular Subtypes of Upper and Lower Tract Urothelial Carcinoma

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Abstract:

Background:

Predictive biomarkers like PDL-1 expression and mismatch repair status are advocated for immunotherapy in advanced urothelial cancer. The frequencies of microsatellite instability (MSI) range between 1-3% for muscle-invasive bladder carcinoma (MIBC), while 3-46% for upper tract urothelial carcinoma (UTUC).

Design:

This ambispective study included 60 cases (30 each of UTUC and MIBC). MSI was detected using fluorescent PCR-based assay, comparing allelic profiles of microsatellite markers from matching normal and test samples. Immunohistochemistry (IHC) performed for MMR proteins (MSH2, MSH6, MLH, PMS2); CK5/6 and GATA3 for molecular subtyping and PDL-1 expression in subtypes. Findings were correlated with clinical parameters and outcomes.

Results:

Distal ureter (50%) was most common site for UTUC. Basal subtype (60%) was predominant in MIBC and luminal (60%) in UTUC. MSI was seen in 20%(5/30) cases of UTUC, while only 6.6%(2/30) of MIBC cases. Fifty-percent(3/6) MSI cases of UTUC showed basal/squamous subtype, two luminal, while one was double negative. In UTUC, 50%(3/6) of MSI cases showed PD-L1 positivity in tumor cells, while 67%(4/6) cases in immune cells. PD-L1 positivity rates in tumor cells (TPS≥1%) was 46% in MIBC, while 50% in UTUC, being 83.3% in MIBC basal(p=0.003) and 77.8% in UTUC basal subtypes. PD-L1 positivity in immune cells(ICS≥5%) observed in 36.6% cases in both cohorts. Overall survival was least in basal subtype and worse in MSI tumors, but PD-L1 expression had better survival.

Conclusion:

MSI is more prevalent in UTUC than MIBC and PD-L1 expression varies by molecular subtypes at both sites. Our results indicate that lower and UTUC have different molecular landscapes and both can be differentially stratified for prognostic and therapeutic benefits of immune checkpoint therapy.

Keywords:

Urothelial carcinoma, MSI, PDL-1, molecular, PCR

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Renal Neoplasm with Oncocytic Features: A Single Institutional Experience

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Abstract:

Introduction:

Renal tumors with oncocytic morphology are the most challenging to classify, with divergent biological behavior ranging from indolent to most aggressive tumors. Hence, it is essential to distinguish them from the rest of the tumors for appropriate management. In this study we identified the renal neoplasms with oncocytic morphology and classify them with the available resources.

Materials & Methods:

It is a retrospective study conducted in the Department of Pathology, IMS &SUM Hospital, from January 2023 to November 2024. All HE & IHC stained slides of renal neoplasm of nephrectomy/biopsy specimens were reviewed, and cases with eosinophilic morphology were selected for inclusion in the study. Representative paraffin blocks were collected, and additional IHC staining was performed using keratin 7, 20, KIT, AMACR, PAX8, GATA3, Ki67, CAIX, SDH B, TFE3, FH, ALK1 & SMARCB1/INI1 where ever previously not available. The tumours were re-classified.

Result:

Of 89 cases of renal neoplasms,14 had eosinophilic morphology (15.73%). In total 8 cases, the diagnosis remains unchanged. Three cases were ALK-rearranged RCC, of which two were Eosionophilic Clear cell RCC and one was Eosinophilic chromophobe RCC, respectively. The remaining 3 cases could not have been classified. The ALK-rearranged RCC have aggressive behaviour with multiple lymph node metastasis.

Conclusion:

Renal tumors with oncocytic morphology are the most challenging to classify, IHC enables to classify these special group of tumors in majority of the cases for better management of the patients.

Keywords:

Renal Cell Carcinoma, Eosinophilic Renal Neoplasm, Immunohistochemistry

ISBN: 978-93-92106-53-8

Evaluation for Diagnostic Accuracy of The Paris System (TPS 2.0) in Urine Cytology Specimens: An Institutional Experience from a Large Cohort of a Tertiary Care Centre

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Abstract:

Background:

Urinary cytology is a valuable, non-invasive diagnostic tool for bladder malignancy screening. The 2016 implementation of The Paris System (TPS) introduced a standardized approach, which was updated in 2022 (TPS 2.0) to include both upper and lower urinary tract specimens, regardless of collection method. However, comprehensive data on this topic remains limited.

Aim:

1) Reclassification of urine cytology reporting into TPS 2.0 categories and determining risk of high grade malignancy.
2) Comparison of diagnostic accuracy with TPS 1.0 and FTRS (four tiered reporting system) in our institute.

Methodology:

The retrospective study included 789 urine cytology specimens from 240 patients including 12 UTUC cases with corresponding histological diagnoses and clinical details. Cytological diagnoses were made according to TPS1.0, TPS2.0 and FTRS (including UNS, NEG, INC and POS categories). LGUNs in TPS1.0 were reclassified into NHGUC in TPS 2.0. INC category of FTRS included AUCs and SHGUCs and the POS category included HGUCs and LGUNs.

Results:

Both TPS1.0 and TPS2.0 showed a combined sensitivity of 70.91% , specificity of 90.77%, PPV of 86.6%, NPV of 78.67% and diagnostic accuracy of 81.67% (in comparison to 59.09%, 81.54%, 73.03%, 70.2% and 71.25% respectively in FTRS). Further TPS 2.0 showed a greater ROHM of 29.7% for AUC in comparison to 19.7% in TPS1.0. The number of AUC diagnoses were significantly reduced in TPS2.0 (37 cases in comparison to 61 cases in TPS1.0). Only 3 cases were diagnosed as LGUN in TPS1.0 in contrast to 94 corresponding histological diagnoses, most of them being classified in NGHUCs making this category redundant.

Conclusion:

TPS 2.0 enhances diagnostic clarity, accuracy, and ROHM prediction. Integrating TPS 2.0 with AI and molecular testing holds promise for future clinical applications.

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Nested Subtype of Urothelial Carcinoma-Clinicopathological Profile of 15 Cases from a Single Tertiary Care Institute

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Abstract:

Introduction:

Nested subtype is a rare variant of urothelial carcinoma, morphologically consisting of nests of urothelial cells without overt cytological atypia, albeit having an aggressive behavior. It may mimic von Brunn nests, neuroendocrine tumor, paraganglioma and prostatic adenocarcinoma in biopsy samples.

Aim:

We retrospectively analyzed the clinicopathological spectrum of patients diagnosed in our institute as nested urothelial carcinoma.

Result:

Out of total 15 cases, all but one patient were males, with age at presentation ranging from 48-76 years. Most common symptom was hematuria. Radiologically, primary site in all cases was urinary bladder. 14 patients underwent TURBT and 1 underwent radical cystectomy. 4 cases showed pure nested pattern, and 11 showed admixture of solid, papillary, micropapillary, glandular and squamous patterns in variable proportion (3 with large nested morphology). Detrusor muscle invasion was present in 14 cases. Lymphovascular emboli and perineural invasion were present in 4 cases each. On immunohistochemistry, the tumor cells were positive for GATA-3 (10/10), p40 (7/7), p63 (2/2), CK7 (4/5), CK20 (1/5), while negative for synaptophysin (5/5) and chromogranin (4/4). Majority of the patients received adjuvant chemotherapy followed by radiotherapy. Follow-up period ranged from 2 months to 16 years. Tumor recurred in 2 patients and metastasized to distant sites in 2 others. 6 patients are alive with disease, and 5 are alive with no evidence of disease, with no death due to disease reported.

Conclusion:

Nested urothelial carcinoma has an aggressive biological behavior. Distinction of this entity from its mimickers is essential to avoid misdiagnosis.

Keywords:

Urothelial Carcinoma, Nested, Variant Histology

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Worse Pattern of Invasion and p16 Expression in Squamous Cell Carcinoma of Penis: A Clinicopathological Study in a Tertiary Care Hospital

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Abstract:

Introduction:

The 2022 WHO classification followed this paradigm to subclassify penile squamous cell carcinoma into HPV-associated and HPV-independent types. p16 is a surrogate immunohistochemical marker for HPV association. HPV-associated SCCs are basaloid, warty, clear cell, and lymphoepithelioma like SCCs In oral squamous cell carcinoma (OSCC) the pattern of invasion is classified into 5 types and is an independent prognostic factor in early OSCC(T1/2N0M0) Till now Worse pattern of invasion (WPOI) is not studied in penile carcinoma

Aim:

To study the patterns of invasion and immunohistochemical expression of p16 and their association with the clinicopathological parameters.

Methods:

Cross-sectional hospital-based study and total 30cases of resected penis specimens were included. Univariate analysis by Fischer's exact test was used.

Results:

Age group ranged from 28-74yrs with a mean age of 55.26yrs. Commonest site was glans(81.48%) followed by prepuce. 48.2% cases are of stage pT2 and pT1 ,while pT3 in 3.7% cases.WPOI-3 observed in 52% cases followed by WPOI-4 in 40% and WPOI-2 in 8% cases .Grade-1 tumor was the commonest(57.14%),followed by grade 2(25%) and grade 3(17.85%). Expression of p16 present in 16.7% and negative in 83.33% cases. Association between p16 overexpression with LVI,PNI,POI and tumor grade was not statistically significant.

Discussion:

HPV is a common cause of penile SCC and can be diagnosed by p16 IHC overexpression. We observed a lesser p16 expression in comparison to other studies. The p16 protein overexpression is not associated with the histologic prognostic parameters in our study.

Keywords:

Penile SCC, p16, WPOI, HPV

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Immunohistochemistry as a Surrogate for Molecular Subtyping of Basal and Luminal Types of Urothelial Carcinoma

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Abstract:

Urothelial bladder carcinoma (UC), has been conventionally divided into non muscle invasive bladder cancer (NMIBC) and muscle invasive bladder cancer (MIBC). Recent mRNA expression profiling studies have suggested a schema of molecular subtyping urothelial bladder carcinoma related to the prognosis of cases. The MIBC molecular classification includes Luminal, Basal, Neuroendocrine-like and Stroma rich subtypes. Our current study uses immunohistochemistry markers p53, FGFR3, Uroplakin and CD-44 to identify molecular subtypes of histologically diagnosed UC. Study group included 200 cases of UC including 129 NMIBC and 71 MIBC cases. Mutant type p53 expression was significantly higher in MIBC and was seen in 35% (n=46) MIBC cases and 42%(n=30) NMIBC cases. FGFR3 expression was seen in 15 cases of MIBC and 51 cases of NMIBC thus classifying them as luminal subtype (of MIBC) and class 1a subtype (of NMIBC) respectively. Uroplakin expression was seen in 34 cases of MIBC and 80 cases of NMIBC thus classifying them as luminal subtype and class 1a subtype respectively. CD-44 expression was seen in 41 MIBC cases and 85 NMIBC cases thus classifying these cases as Basal subtype of MIBC and class 3 molecular subtype of NMIBC. 19 cases of MIBC had an overlap of both luminal and basal subtype of markers. Uroplakin expression classified 80 cases as class 1a whereas FGFR3 expression classified 51 cases as class1a. Significant overlap in IHC markers designated for different subgroups has been observed and IHC panel used does not appear to clearly assist in molecular classification in 10% cases.

Keywords:

Urothelial Bladder Carcinoma, Immunohistochemistry, Molecular subtyping, Novel Molecular Classification

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Expression of PDL-1 in Urothelial Carcinoma of Bladder and Its Correlation to Histopathological Parameters

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Abstract:

The aim of this study is to determine the expression of the PD_L1 protein in human bladder cancer, and significant correlations between these parameters and clinico pathologic variables like (grade and stage), and also exploring the use of PDL-1 immunostain expression in immunotherapy.

As per the GLOBOCAN 2018, bladder cancer was estimated to have 549,000 new cases and 200,000 deaths per year and was ranked 10th among all cancers in the world; it contributed 3.4% to the total cancer burden worldwide. In India, there were 18,921 new cases and 10,231 deaths with an incidence rate (per 105) of 2.4 and 0.7 in males and females, respectively, and mortality rates (per 105) as 1.3 and 0.3 in males and females, respectively; it is ranked 17th in incidence and 19th in mortality.

The current study is designed to detect the role of pD_L1 expression in bladder carcinoma as a possible marker for detecting the biological behavior of malignancy and its correlation with grade and muscle invasiveness for both diagnostic and prognostic purposes.

The study focuses on a technique of immunohistochemistry for detection pD_L1 expression in bladder cancer. The samples are collected randomly in SUM ultimate medicare hospital, bhubaneswar. Number of samples is 60. Results of this study reveal that pD_L1 expression is positive in 38 of 60 sample. The study demonstrated pD_L1 expression is increased in high grade bladder cancer represent (44.19%), while in low grade (33.33%). Expression pD_L1 excessive in muscle invasive (42.86%), whilst the low expression for pD_L1 in the non-muscle invasive type (35.71). The results indicated the potential benefit of anti-PD-L1 immunotherapy for patients with high tumor grades.

This study represents an important step because there are few of studies about this topic in India and we are need more studies to prove the function of this pD_L1 in biological behavior of bladder cancer.

Keywords:

Sertoli Cell Tumor, Testis, Immunohistochemistry

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To predict the Efficacy of Vesical Imaging-Reporting and Data System (VIRADS) in Predicting Muscle-Invasive Bladder Cancer (MIBC): A Prospective Observational Study

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Abstract:

Introduction & Objectives:

Muscle-Invasive Bladder Cancer (MIBC) poses considerable diagnostic difficulties, as timely and precise detection is essential for effective treatment. The Vesical Imaging-Reporting and Data System (VIRADS) provides a systematic method for evaluating bladder tumors, although its effectiveness in predicting MIBC has yet to be thoroughly confirmed. This prospective cohort study intends to assess the effectiveness of VIRADS, in conjunction with demographic and clinical factors, in anticipating the presence of MIBC.

Materials & Methods:

In this prospective cohort investigation, we carefully selected patients who had been diagnosed with bladder cancer, utilizing the VIRADS criteria on multiparametric MRI (mpMRI) to effectively predict the likelihood of muscle-invasive bladder cancer (MIBC) status. Our analysis focused on exploring the relationships between various factors, including the patients' age, the size of the tumors, the histological grade of the cancer, and the presence of hydronephrosis, which may affect the disease's progression. To rigorously assess the predictive accuracy of the VIRADS system for determining MIBC, we employed fisher exact and chi square tests ensuring that we accurately identified statistical significance in our findings.

Results:

The cohort was comprised of 53 patients with a mean age of 62 years (SD:12.52). The mean tumor size was 3.90 cm (SD:2.33). VIRADS scores were distributed as follows: 19 patients had a score of 5, 16 had a score of 4, 7 had a score of 3, 8 had a score of 2, and 3 had a score of 1. Fisher's exact test was used to explore the association between 'VIRADS' and 'T Stage'.There was a significant difference between the various groups in terms of the distribution of T Stage (χ^2=57.948, p=<0.001).The strength of association between the two variables (Bias Corrected Cramer's V)=0.55 (High Association).The models effectiveness is underscored by a Receiver Operating Characteristic (ROC) Area Under the Curve (AUC) of 0.8172.

Conclusions:

Our study results suggest that the VIRADS 5 scoring system has high specificity, and positive and negative predictive value to predict muscle invasive bladder cancer. In VIRADS 5 patients, additional randomized controlled studies could be conducted to randomly assign patients to either undergo TURBT or to proceed directly to radical cystectomy.

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Clinical Profile and Survival outcomes in Carcinoma Penis Patients: A Retrospective Observational Study and Case Series from a Single Centre from Eastern India

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Abstract:

Background:

Carcinoma penis is a rare malignancy with paucity of data on the impact of systemic therapy on long term survival outcomes. Our aim is to determine the clinical profile and management patterns, survival outcome and safety profile.

Methods:

Retrospective observational study of patients with a histological diagnosis of carcinoma penis from April 2021 to December 2024, irrespective of stage were included in our study. Demographics, histopathology, clinical profile, and outcomes were obtained from the case records. Primary objectives were progression free survival (PFS) and overall survival (OS); secondary objectives included assessment of clinical characteristics, management pattern, and toxicity.

Results:

Case records of 10 patients were retrieved, who were treated during the above period at our institute. Common presenting symptoms were ulcer proliferative growth (60%), pain (50%), and dysuria (40%). Median age was 56years (interquartile range [IQR], 49.25-59.25). 9(90%) patients had localised/ locally advanced disease and had undergone surgery upfront (9 Patients had undergone primary surgery ;8 had undergone partial penectomy (80%), one (10%) had undergone total penectomy) followed by adjuvant chemotherapy and radiotherapy according to their stages. one (10%) patient was upfront metastatic and received palliative chemotherapy upfront. Median DFS for non-metastatic disease was 14 months (95% CI 12.61-15.38). Post progression these patients were treated with palliative intent and had median PFS and OS of 12 months (95% CI 11.29-12.71) and 28months (95% CI 24.9-31.09), respectively. 2 (20%) had grade 3 or above neutropenia, one had hypothyroidism. There was no treatment related mortality.

Conclusion:

Penile cancer is diagnosed a decade earlier in India and at more advanced disease at presentation. Overall survival is poor for nodal and the presence of metastatic disease at diagnosis. Carcinoma penis patients with recurrent/metastatic disease have poor outcome, even with optimum palliative systemic therapy. So, there is an unmet need for better systemic therapy in these patients.

Keywords:

Clinical Profile; Survival; Penis; OS; DFS; PFS

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Response Assessment of PSMA Therapy in Metastatic Ca prostate: A Retrospective Observational Study and Case Series from a Single Centre in Eastern India

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Abstract:

Background:

Prostate-Specific Membrane Antigen (PSMA) is a promising target for the treatment of Castration-Resistant Prostate Cancer (CRPC) patients. The latest published papers about Radioligand Therapy (RLT) with 177Lu- PSMA-617 showed that the treatment is well tolerated and has a low toxicity profile. Our aim is to assess biochemical and radiological response in patients following PSMA therapy.

Methods:

Patients with a histological diagnosis of ca prostate with metastasis who received PSMA therapy from January 2022 to November 2024 were included in our study. Demographics, histopathology, clinical profile, and outcomes were obtained from the case records. Sr PSA values and SUV max on PSMA PET were studied prior to PSMA therapy and post PSMA therapy.

Results:

Data of 13 patients who received PSMA therapy at our institute was retrieved. Retrospective analysis of data including Sr PSA values and SUV max in PSMA PET scan, pre-PSMA therapy and following PSMA therapy was studied. Median age of population was 58 years(Interquartile range: 52-64). Majority of patients showed skeletal (92.3%)and Lymph node(84.6%) metastatic lesions at the time of diagnosis. A large number of population received PSMA therapy late in the course of illness with an average of 2 sessions per individual. 53% of population (7 patients out of 13) were noticed to have decline in Sr PSA values following PSMA therapy compared to baseline Sr PSA prior to PSMA therapy. However these patients differ in their clinical profile and chemotherapy received . SUV max in PSMA PET scan was studied to assess radiological response to PSMA therapy. 46% (6 out of 13 patients) were noticed to have decline in SUV max value on PET scan following 2-3 sessions of PSMA therapy however no much decline was appreciated following single session of PSMA therapy. Both radiological and biochemical response were noticed to be better in patients with higher baseline SUV max value on PSMA PET SCAN (Median SUV max is 16.4, Interquartile range: 12.8-23.2). Renal insufficiency and myelosuppression related to therapy was not noted. 2 patients out of 13 defaulted.

Conclusion:

Majority of study population received PSMA therapy at a later course after diagnosis of metastatic ca prostate. This is owing to the difficulty in accessing PSMA therapy in Low and Middle Income Countries like India. Large portion of study population couldn't complete the advised number of PSMA therapy sessions and some lost follow up pertaining to accessibility issues and logistic reasons.

However, in the studied population, most response benefit radiologically is noted in patients with a higher SUV max value in PSMA PET scan.

Limitations of this study are it's retrospective nature, small study population, accessibility issues.

Keywords:

Clinical Profile; Survival; Penis; OS; DFS; PFS

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Clinicopathological features and Multidisciplinary Management of Malignant Ovarian Germ Cell Tumors : A Single Center Experience from Eastern India

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Abstract:

Introduction:

Malignant ovarian germ-cell tumors (MOGCTs) account for about 5% of all ovarian malignancies and typically present at young age. Before mid-1960s, these patients had dismal outcome but subsequent introduction of chemotherapy and surgery proved to increase survival outcome. There is limited data on treatment outcomes of patients with MOGCT.

Objectives:

The aim of this study was to determine the clinicopathological characteristics and treatment outcomes in patients with MOGCTs undergoing multimodality treatment.

Materials and Methods:

16 patients from a single institution were included in the study for retrospective analysis from 2016 to 2021 . Data encompassing patient age distribution, histological subtype, clinical presentation, histopathological features and treatment strategies were collected and analyzed. Survival analysis was performed using the Kaplan–Meier method.

Results:

The median age was 10.5 years (1- 35 years). The most common complaint was pelvic or abdominal mass (62.5%, n=10). More than half (68.75%, n=11) had advanced stage disease (stages III). The most common histopathology was mixed (37.5%, n=6) followed by dysgerminoma (31.25%, n=5). Primary surgery was performed in 62.5%(n=10) of cases and Interval surgery in 31.25% (n=5). Of 15 patients, 1 did not receive adjuvant treatment and 14 received chemotherapy (BEP). Of 16 patients who were evaluable for responses, 9 patients (56.2%) had complete response, 3 (18.7%) had partial response while 3(18.7%) had stable disease. The 5-year PFS in overall population was 87.5%, Stage I and II was 100% and stage III was 71.4%. The 5-year OS in overall population was 93%, Stage I and II was 100% and stage III was 85.7%.

Conclusion:

Majority of patients were in advanced stage (FIGO stage III). MOGCTs had good prognosis with with surgery and chemotherapy in advanced disease proving it to be highly curable disease with multimodality management.

Keywords:

Malignant Ovarian Germ Cell Tumor, Surgery, Chemotherapy

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To Assess the Prognostic Value of Absolute SPSA in MHSPC in Era of Docetaxel and Abiraterone

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Abstract:

Aim:

To assess the prognostic value of absolute SPSA in MHSPC in current era of docetaxel and abiraterone

Methods:

In a retrospective audit of 2000 patients of MHSPC from 2015 to 2022, patients are categorised into low volume and high volume MHSPC. All patients received ADT along with either Docetaxel or Abiraterone as primary therapy. Serum PSA levels were observed at 3 months and 6 months.Primary end points analysed were PSA free survival, disease free survival(DFS) and secondary end point was overall survival

Results:

928 patients were eligible as per study criteria

Mean PSA free survival for PSA < 0.2 is 74 mths, for 0.2-4 is 38 mths and for > 4 is 18 mths, ($p<0.0001$), mean DFS for PSA < 0.2 is 83 mths, 0.2-4 is 47 mths and for > 4 is 25 mths ($p<0.0001$) and mean overall survival for PSA < 0.2 is 107 mths, for 0.2-4 is 79 mths and for > 4 is 76 mths($p<0.0001$).

In sub group analysis, increased PSA free survival and DFS are seen in low volume groups who received LHRH agonists for patients with PSA < 0.2 and 0.2-4 but no difference for patients with PSA >4 . There was no statistically significant difference in overall survival between different groups.

Conclusion:

Absolute SPSA of 4ng/ml or less after 6 months of ADT+ DOECTAXEL/ ABIRATERONE is a strong predictor of survival.This data can be used for future trial design and for counselling and prognostication of patients of MHSPC.

Keywords:

MHSPC, SPSA, DOECTAXEL, ABIRTERONE

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Unveiling the Rare: Largest Case Series of Genitourinary Ewing's Sarcoma with Key Insights into Treatment and Survival

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Abstract:

Ewing's sarcoma of the genitourinary tract is an exceptionally rare condition, with limited data on optimal treatment approaches and long-term outcomes. This study aims to evaluate the clinical features, treatment strategies, and long-term results of genitourinary Ewing's sarcoma. To our knowledge, it represents the largest case series of this rare condition managed at a tertiary cancer center. We retrospectively analyzed all patients diagnosed with genitourinary Ewing's sarcoma between January 2010 and December 2022, spanning a 12-year period.

Of 425 Ewing's sarcoma cases diagnosed across all sites, 18 (4.25%) involved the genitourinary tract. The median age was 26 years (range: 14–48), with a slight female predominance (61.1%). Pain was the most common symptom (94.5%). Most patients (83.3%) had localized disease at diagnosis, with the kidney being the primary site in 83% (n=15) of cases. Bulky tumors (>8 cm) were seen in 55.5% (n=10). Neoadjuvant chemotherapy was given in 26.6% (n=4) of localized cases, surgical resection in 86.6% (n=13), and adjuvant chemotherapy in all patients.

After a median follow-up of 20 months (range: 2–165 months), 8 of 18 patients (44.4%) were alive, 8 (44.4%) had died, and the status of 2 patients (11%) was unknown. The median disease-free survival was 13 months, and the median overall survival was 20.5 months.

Compared to existing literature, our cohort had slightly younger patients, with most presenting with localized but bulky primary disease. However, survival outcomes in our study were slightly lower than those reported in the literature.

Keywords:

Genitourinary Ewing's Sarcoma, Extraskeletal Ewings, Rare Tumors, Long Term Outcomes

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Retrospective Study of Risk Factors for Post Operative ileus After Radical Cystectomy with Ileal Conduit at a Tertiary Centre

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Abstract:

Background:

Radical cystectomy has been associated with high rate of perioperative morbidity (50-70%) including infections, wound related complications or ileus. Our study aimed to retrospectively identify the risk factors for post operative ileus among patients who underwent radical cystectomy and ileal conduit.

Methods:

Between 2021 and 2023, a total of 206 patients were included. For the above patients postoperative ileus was considered when return of bowel sounds was on day 3 or more. The retrospective data was analyzed statistically using licensed IBM SPSS v25. Univariate association was done using Chi square test. Significant variables were incorporated in multivariate model.

Results:

Out of 206 patients, 70 patients developed post operative ileus. Median BMI of our patients was 22.89. 147 patients underwent upfront surgery while 58 patients were post neoadjuvant therapy. In our study, we found that longer operative time was significantly associated with higher risk of developing post operative ileus. Patients with higher stage of disease (stage 3) had higher odds of developing ileus with odds ratio of 2.8. On multivariate analysis, we found that stage of the disease, substance abuse (tobacco, smoking or alcohol) were significantly associated with risk of ileus. We also found that delay in removal of Ryles tube beyond post operative day 1 and postoperative opioid analgesia significantly increased the possibility of ileus.

Conclusion:

Post operative ileus is a significant scenario after radical cystectomy which may be attributable to advanced disease, substance abuse, prolonged surgery and post operative use of opioids.

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A Prospective Observational Study to Evaluate the Biochemical Response of Radical Local Therapies in Patients with Locally Advanced and Oligometastatic Carcinoma Prostate

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Abstract:

Introduction & Objectives:

This prospective observational study assessed the role of radical local therapy in treating locally advanced prostate cancer and oligometastatic prostate cancer by evaluating the biochemical response. Specifically, the study assessed PSA reductions at three-month interval following radical prostatectomy or EBRT and quality of life at 3 months.

Materials & Methods:

In this prospective cohort study, we enrolled patients diagnosed with locally advanced and oligometastatic prostate cancer,to either undergo external beam radiotherapy or open radical prostatectomy. We analyzed correlations including age, initial PSA levels, PIRADS scores, ISUP grades, and TNM staging. Additionally, short-term biochemical responses, PSA at three months as well as change in PSA were analyzed in relation to T stage, nodal involvement, metastatic burden, surgical margins which served as key clinical determinants of treatment success.Change in serum PSA was compared using paired t test or Mann Whitney test,correlation between change in serum PSA and other continuous variables was done using the Pearson or Spearman coefficient.

Results:

A total of 30 participants were enrolled, with 73.3% undergoing radical prostatectomy and 26.7% receiving radiotherapy.The mean age of patients were 64.03 with SD (7.89).In our study 26.7% of the participants were T2 stage, 10.0% were T3a stage, 56.7% T3b stage, 6.7% were T4 stage.In terms of metastasis, 66.7% had M0 stage,33.3% of the participants M1b stage.The mean (SD) of change in PSA (ng/mL) at 3 Months in the radical prostatectomy group was -39.18 (33.10). The mean (SD) of change in PSA (ng/mL) at 3 Months in the radiotherapy group was -59.52 (62.27).There was no significant difference between the groups in terms of change in PSA(ng/mL) at 3 months ($W = 108.000, p = 0.368$).

Conclusions:

The combination of radical prostatectomy and radiation therapy with systemic treatments shows considerable potential for treating Locally advanced prostate cancer and Oligometastatic prostate cancer. These treatment methods have proven effective, safe, and have minimal short-term negative effects, making them viable options for these group of patients.

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Abstracts of Poster Presentation

Spleno-Gonadal Fusion in Cryptorchid Testis- A Rare Union Between Two Organs

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Abstract:

Introduction:

Spleno-Gonadal Fusion (SGF) is a rare congenital anomaly characterised by fusion between splenic and testicular tissue. Many cases are associated with undescended testis/ cryptorchidism. The splenic tissue, most commonly can be an ectopic splenic tissue or a fully developed spleen. Two types are identified, continuous and discontinuous variants. In continuous variant ,the main spleen is connected to the gonad by a cord like band of fibrous /splenic tissue. In the discontinuous variant , the spleen is fused to the gonad, but there is no connection with the main spleen. Less than 200 cases are reported to date in literature.

Case presentation:

We present a rare case of SGF in a 2 year male child who presented with left undescended testis. The child was otherwise asymptomatic. Routine blood investigations were normal. Ultrasonography of the upper abdomen appeared normal. Lower inguino-scrotal region showed a hypoechoic mass with moderate vascularity in the lumbar region with absence of testis in the left scrotal sac, suggestive of undescended testis. MRI showed the same features reported as suspicion of testicular neoplasm. Tumor markers were normal. The child underwent laparoscopy, intra-op findings showed presence of normal spleen and noted an intra-abdominal mass in the lumbar region. The patient underwent laparoscopic excision of the intrabdominal mass/undescended testis due to suspicion of neoplasm. Gross and histomorphology confirmed the diagnosis of Spleno-Gonadal fusion, left undescended testis of discontinuous type. There was no evidence of neoplastic component.

Conclusion:

SGF in an undescended testis is a rare benign entity. Clinically it may mimic a neoplasm due to its radiologic vascularity and size. Hence serum marker study with histopathological evaluation is essential to exclude neoplastic component.

Keywords:

Spleno-Gonadal Fusion, Cryptorchidism, Testis, Spleen, Ectopic Spleen

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Foamy Gland Carcinoma: Chasing the Chameleon

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Abstract:

A 77-year-old man presented with acute urinary retention with a history of irritative lower urinary symptoms for 3 months. Serum prostate-specific antigen (PSA) was elevated. MRI scan revealed an enlarged prostate with an ill defined lesion involving the posterior midline and peripheral zone. TRUS-guided 12-core biopsy was performed. Microscopic examination of the biopsy cores revealed predominantly fused glandular structures with focal cribriform pattern with individual cells exhibiting voluminous foamy cytoplasm, increased nucleo-cytoplasmic ratio, pyknotic nuclei and small nucleoli. Subsequently Transurethral Resection of Prostate was performed and subsequent histopathological examination confirmed the biopsy findings of foamy gland carcinoma. This case is of interest as foamy gland carcinoma presents a challenging diagnosis on needle biopsies due to its deceptively benign appearance, requiring a high index of suspicion for accurate diagnosis.

Keywords:

Prostatic Carcinoma, Foamy Gland Carcinoma, Gleason Score

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Series of Nephrectomy Specimens Received at a Newly Opened Tertiary Care Hospital in West Bengal

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Abstract:

Introduction:

Nephrectomy is a major surgical procedure that is performed for indications ranging from non- functioning kidney/irreversibly damaged kidney to tumours such as renal cell carcinoma and the procedure ranges from simple nephrectomy in benign conditions to radical nephrectomy in malignant.

Aims and Objectives:

To review the clinicopathological spectrum of cases requiring nephrectomy in a newly opened tertiary care centre

Materials and Methods:

It is an observational study done in the department of pathology and laboratory medicine, AIIMS Kalyani where all consecutive nephrectomy specimens received in the last one year (from the onset of Histopathology investigation in the department till date) were reviewed and a descriptive analysis of the data was done.

Results:

A total of 16 cases of nephrectomy were received out of which six (37.5%) cases were of non-neoplastic aetiology and 10(62.5%) cases neoplastic. All the neoplastic cases were malignant tumours of which five (50%) were clear cell renal cell carcinoma (RCC), three (30%) cases of urothelial carcinoma, one (10%) case of chromophobe RCC and one (10%) case was papillary RCC. The most common finding in the renal parenchyma adjacent to the tumour in cases of RCC was chronic pyelonephritis.
Of the non-neoplastic lesions all six cases where of chronic pyelonephritis where three cases had features of hydronephrosis and one had renal calculi. One of the cases of chronic pyelonephritis had congenital bifid ureter.

Conclusion:

This case series highlights the spectrum of nephrectomy cases received at inception of a new tertiary care centre.

Keywords:

Nephrectomy, Renal Cell Carcinoma, Chronic Pyelonephritis

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Female Form Persistent Mullerian Duct Syndrome with Bilateral Cryptorchidism and Seminoma Testis

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Abstract:

Introduction:

Persistent mullerian duct syndrome (PMDS) is a unusual sexual development disorder characterized by presence of mullerian duct derivatives in a phenotypic male with 46xy karyotype. Anatomically PMDS is classified as male form and female form .Female form PMDS is least common. 80% of PMDS cases are associated with cryptoorchidism, which increases the risk of testicular malignancies.

Materials and Methods:

A wide local excision specimen of pelvic mass received for histological examination. H&E stained tissue sections were examined microscopically and panel of immunohistochemical markers were done. Karyotyping of patient was obtained.

Results:

24years phenotypic male came with intermittent lower abdomen pain for 1 month. Imaging showed a cystic mass in right lower abdomen and umbilical region with septations and debris in it. Karyotyping report was 46XY. Gross examination revealed presence of uterus, cervix, bilateral tubes with 2 globular structures attached to each tube. Histomorphology and IHC confirmed the diagnosis of female form PMDS with bilateral cryptorchidism and seminoma testis.

Conclusion:

PMDS is rare genetic disorder in males with normal external genitalia and normal karyotype. Risk of developing testicular malignancies increases in these cases as they are associated with cryptorchidism.

Keywords:

Persistent Mullerian Duct Syndrome, Female Form, Cryptorchidism, Seminoma

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Utility of Smartphone Technology for Capturing Videos and Images of Semen Analysis Samples: A New Emerging Technology

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Abstract:

Background:

Semen analysis is an essential indicator of male infertility potential. The study aims to assess the diagnostic accuracy of smartphones compared to manual microscopy for semen analysis.

Method:

It is a cross-sectional analytical study with investigator blinding. Data were collected from August to September 2023. Pictures of semen analysis were captured through light microscopy and stored in a coded format on a smartphone. Later, the results of both methods were compared.

Results:

A total of 50 adequate semen samples were included. The age of enrolled males was Mean±SD 29.4±5.9 years. The sensitivity, specificity positive predictive value (PPV) and negative predictive value (NPV) were 100% for smartphones compared to light microscopy for total sperm counts. Sensitivity, specificity, PPV, and NPV for total sperm motility were 97.9%, 100%, 100%, and 66%, respectively. For normal morphology sperm, the sensitivity, specificity, PPV, and NPV of smartphones were 72.7%, 82.1%, 53.3%, and 91.4%, respectively, and for abnormal morphology sperm, they were 100%, 98%, 50%, and 100%, respectively. Smartphones exhibited a sensitivity, specificity, PPV, and NPV 98%, 100%, 100%, and 50%, respectively for assessing sperm vitality. The diagnostic agreement between smartphones and light microscopy was very good (κ value -0.6 -1) for detection of total count, vitality, and total motility of sperm.

Conclusion:

Smartphone technology demonstrates high sensitivity and specificity for semen analysis compared to manual microscopy. It also shows excellent agreement with manual microscopy for most parameters in semen analysis. We recommend smartphone reporting for semen analysis in remote areas and poor resource settings.

Keywords:

Smartphone, Manual Microscopy, Semen Analysis, Diagnostic Accuracy

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Smooth Muscle and Adenoma-like Renal Tumor (SMART)-A Rare Biphasic Renal Tumor with a Review

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Abstract:

Background:

Smooth muscle and adenoma-like renal tumor (SMART) is a biphasic tumor composed of cytologically bland stromal and epithelial components. The histomorphological differential diagnoses are mixed epithelial stromal tumor (MEST), angiomyolipoma with epithelial cysts, renal angiomyoadenomatous tumor, or a low-grade papillary renal cell carcinoma.

Case details:

A 57-year-old man presented with a left renal mass. He underwent a left radical nephrectomy, which showed a 13.5 cm predominantly solid tumor involving the entire kidney. The microscopic examination showed an unencapsulated, well-circumscribed biphasic tumor predominantly composed of intersecting bundles of spindle muscle admixed with focal epithelial components arranged in cyst, tubular, tubulopapillary, nests, and cords. The cysts were lined by a single layer of cuboidal cells. There was no evidence of nuclear pleomorphism, high mitotic activity, or necrosis in either of the components. The surrounding renal parenchyma was compressed and showed a xanthomatous reaction. The tumor was confined to the kidney. Lymphovascular invasion and perineural invasion were not identified. On immunohistochemistry (IHC), the spindle tumor cells were diffusely and strongly positive for desmin and SMA, focally positive (10%) for CD10, and negative for ER, PR, and HMB45. The epithelial cell component was positive for PAX8 and Keratin 7 and negative for CD10.

Conclusion:

We report this additional case of SMART, which has distinct clinical, morphological, and immunohistochemical features and only seven cases described in the literature to date. This would, in turn, lead to a better understanding of the clinicopathological associations and histogenesis of biphasic renal tumors.

Keywords:

SMART, MEST, Biphasic Renal Tumor, Desmin, Keratin 7

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Rare Case of Tuberculous Mastitis Diagnosed by Fine Needle Aspiration Cytology (FNAC)

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Abstract:

Introduction:

Tuberculous mastitis (TM) is a rare manifestation of tuberculosis, constituting <1% of breast lesions globally. Mimics malignancy or abscess, leading to diagnostic challenges.

Case Presentation:

32-year-old female with a history of lactation presenting with a painful lump in the right breast from 6 months.
On examination-Single well-defined swelling over upper outer quadrant of right breast measuring 3×3cm, firm, mobile, tender.
Imaging: Ultrasound: Hypoechoic mass with irregular margins.

FNAC Findings:

Smears revealed focal aggregates of epitheloid cells along with presence of chronic inflammatory cells in a necrotic background.
AFB Staining: Positive for acid-fast bacilli.

Discussion:

Pathogenesis: Tuberculous mastitis arises from lymphatic spread or hematogenous dissemination.
Differential Diagnosis:
Breast carcinoma.
Pyogenic abscess.
Chronic granulomatous mastitis.
FNAC is critical for early, non-invasive diagnosis in resource-limited settings.

Conclusion:

FNAC is an effective diagnostic tool for tuberculous mastitis.
Tuberculous mastitis is a rare and underdiagnosed condition requiring a high index of clinical suspicion.
FNAC and ZN staining remain crucial diagnostic tools, especially in resource-limited settings.
Early diagnosis and ATT lead to excellent outcomes.

Keywords:

Tuberculous mastitis, FNAC, ZN Stain, Breast Lump

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A Case Report on A Rare Neoplasm of Breast-Metaplastic Breast Cancer

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Abstract:

Metaplastic breast cancer represents a very rare and histopathologically diverse subtype of breast cancer. It shows neoplastic epithelial differentiation into squamous cells and/or mesenchymal-like components, resulting in its aggressive behaviour and poor prognosis compared to other types of breast cancer. Here, we describe the case of a 43-year-old woman diagnosed with metaplastic carcinoma of the breast who presented like any other case of breast lump in the right breast for six months. The tumor had a large size with an ulcerative lesion of the breast. Ultrasound showed heterogeneous echogenicity and lymph node involvement. Surgical resection with axillary lymph node dissection was done. The microscopic examination after tissue processing showed highly pleomorphic tumor cells along with chondromyxoid stroma and osseous differentiation, suggestive of metaplastic breast cancer which was triple-negative for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 on immunohistochemistry. The axillary lymph nodes identified were negative for tumor cells. The rarity and aggressive nature of this cancer pose diagnostic challenges and highlight the importance of multidisciplinary approaches for effective management.

Keywords:

Triple-Negative, Aggressive, Pleomorphic Tumor Cells and Diagnostic Challenges

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Papillary Renal Neoplasm with Reverse Polarity Along with Papillary Adenoma in A Non-Functioning Kidney- A Rare Report

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Abstract:

Background:

Papillary renal neoplasm with reverse polarity (PRNRP) is a newly proposed emerging entity. It shows papillary architecture with peculiar placement of nuclei away from the basement membrane and is frequently associated with KRAS mutation. Type D papillary adenoma is assumed to be a precursor of papillary renal cell carcinoma with reverse polarity. It is mostly discovered as an incidental finding.

Case Details:

A 65-year-old male patient presented with left proximal ureteric calculus causing obstructive uropathy. The radiological findings were consistent with the left non-functioning kidney. He underwent a left simple nephrectomy. The gross examination showed hydronephrosis with a thinned-out cortex without any lesion. The microscopic examination revealed a 4 mm-sized cystic lesion with an intracystic papillary pattern of tumor cells. The tumor cells lining the papillae had abundant eosinophilic cytoplasm and a single layer of the apically placed nucleus with ISUP/WHO grade 1. On IHC, the tumor cells were strongly and diffusely immunopositive for GATA3, PAX8, and CK7 while immune negative for AMACR. The morphological and immunohistochemical findings were consistent with papillary renal neoplasm with reverse polarity. In addition, a focus of papillary adenoma was also noted in the adjacent parenchyma. The rest of the renal parenchyma showed features of chronic pyelonephritis with hydronephrosis. The pathological stage was pT1a N0 M (not applicable). No features of recurrence after four months of follow-up.

Conclusion:

We report a rare case of papillary renal neoplasm with reverse polarity with an uncommon association of papillary adenoma both were incidentally diagnosed histopathologically in a non-functioning kidney.

Keywords:

Papillary Renal Neoplasm, Reverse Polarity, Renal Papillary Adenoma, GATA3, Keratin 7

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Metastatic Prostatic Acinar Adenocarcinoma Presenting as a Penile Malignant Tumor

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Abstract:

Introduction:

Penile metastasis from occult prostatic acinar adenocarcinoma is extremely rare and limited to a couple of case reports in literature. The incidence of metastasis of known prostate adenocarcinoma to penis is <0.3%.

Case Report:

A 72-year-old male presented with a hard penile mass measuring 2 x 1.5 x 1 cm since 3 months. He also had lower urinary tract symptoms, 2-3 episodes of hematuria, anorexia, weight loss, and low back pain. A wedge biopsy of the penile mass was reported as adenosquamous carcinoma.

On CECT scans, a heterogeneously enhancing, irregular distal penile lesion measuring 2 x 1.5 x 1 cm was seen. Mild prostatomegaly of 36 cc was noted.

Three weeks later, the patient developed acute urinary retention and serum PSA rose to 54ng/ml. A total penectomy and TRUS guided biopsy of prostate was done, showed prostatic adenocarcinoma with Gleason score 8 (4,4)/Grade Group 4, while the penectomy showed metastasis of prostatic adenocarcinoma. Immunohistochemistry (IHC) markers were

positive for NKX 3.1 and PSA confirming a prostatic origin of the penile mass. FDG PET scan followed and showed diffuse FDG avidity in the enlarged prostate. PSMA scans showed diffuse intermediate grade expression in the prostate, left sided paraaortic nodes and skeletal system.

Conclusion:

Unlike the present case, most patients of metastatic adenocarcinoma of prostate to the penis have a typical history of prostatic adenocarcinoma, diagnosed years prior to the penile metastasis. A thorough clinical examination of the prostate in patients with genitourinary malignancies is essential especially with rising PSA levels.

Keywords:

Occult Malignancy, Penile Mass, Prostatomegaly, PSA

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Unveiling Primary Penile Epithelioid Hemangioendothelioma: A Case Report with Histopathological Insights

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Abstract:

Background:

Epithelioid vascular tumors, particularly epithelioid hemangioendothelioma (EHE), are rare mesenchymal neoplasms characterized by their epithelioid morphology. EHE displays an intermediate behaviour between benign hemangiomas and malignant angiosarcomas. Penile

EHE is a rare tumor, representing less than 5% of penile cancers. We present an unusual case of low grade epithelioid hemangioendothelioma of the penis, which was diagnosed aptly at an early stage and treated with complete resection of the tumor via total penectomy.

Case Report:

A 77-year-old male, a known case of type 2 diabetes, presented with burning sensation during micturition and a non-healing wound over the glans penis for 5 days. Imaging studies and physical examination revealed an ill-defined, ulcerated lesion measuring 3.1x1.6x0.1 cm. This was followed by an incisional biopsy, which on histopathological examination showed infiltrative cords and nests of large endothelial cells with round to oval nucleus, vesicular chromatin, conspicuous nucleoli at places and abundant eosinophilic cytoplasm embedded in a myxohyaline stroma. Also seen were, few intracytoplasmic vacuoles containing erythrocytes. On immunohistochemistry, the tumor cells were strongly positive for ERG and CD31, and patchily positive for CD34. The Ki-67 labelling index was 6-8%. Finally, a diagnosis of low grade epithelioid hemangioendothelioma was made. The patient underwent total penectomy and currently is free of any residual disease which was confirmed with whole body CT imaging to check for any metastasis.

Conclusion:

This case study highlights the need for accurate diagnosis of painful penile lesions, emphasizing careful assessment, imaging, histopathology, and local excision to prevent recurrence, while encouraging further research on EHE.

Keywords:

Penile Epithelioid Hemangioendothelioma, Rare Vascular Tumor, Immunohistochemistry

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Unveiling Small Cell Carcinoma of Urinary Bladder – A Rare Entity

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Abstract:

Introduction:

Primary small cell carcinoma of urinary bladder is extremely rare and constitutes less than 1% of urinary bladder tumors. It is very aggressive and refractory to treatment due to its higher metastatic capability, compared to other bladder tumors. Small cell carcinoma of bladder originates from multipotential undifferentiated stem cells as supported by the fact that small cell carcinoma frequently coexists with other histological types of bladder carcinoma. The typical patient is a 60-year old Caucasian male with a history of smoking presenting with gross painless hematuria.

Case Report:

We report a case of a 59 year old male who presented with complaints of hematuria and burning micturition since 2 months. Histomorphological and IHC study suggested the diagnosis of Small Cell Carcinoma of Urinary Bladder.

Conclusion:

Awareness of this entity, as well as histopathology and IHC correlation are crucial for establishing a correct diagnosis. Clinical findings are inconclusive and patients present at a later stage than in urothelial carcinomas. The accurate recognition of this entity is of paramount importance due to the diagnostic dilemma that they may present, as well as prognostic and therapeutic implications this entity may have. Treatment options are not standardized, though so far it seems that neoadjuvant platinum-based chemotherapy followed by cystectomy offers the best outcome, except when metastases are present, in which case chemotherapy alone offers palliative support.

Keywords:

Urinary Bladder, Small Cell Carcinoma, Immunohistochemistry

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Renal Medullary Carcinoma-A Rare, Aggressive Renal Carcinoma

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Abstract:

Introduction:

Renal medullary carcinoma is a rare type of cancer that affects the kidney, which makes up less than 0.5% of all renal carcinomas. It tends to be aggressive, difficult to treat, and is often metastatic at the time of diagnosis. Typical RMC patients are mostly young males (2:1 male to female predominance) with sickle cell trait, who presents with pain and haematuria and are found to have metastatic disease at diagnosis. Prognosis is extremely poor, with a mean survival of less than a year in most cases.

Case Report:

A 32-year-old male presented with complains of right flank pain for 3 years, which was aggravated for 2 months, associated with haematuria. CECT KUB scan suggested large heterogeneously enhancing right renal mass with retroperitoneal lymphadenopathy with encasement of right renal artery. Patient then underwent Right Radical Nephrectomy for the same. Histopathological features were suggestive of renal medullary carcinoma. And IHC confirmed the above diagnosis.

Conclusion:

Renal Medullary Carcinoma is a rare and aggressive form of kidney cancer found almost exclusively in patients with sickle cell trait. Treatment options are limited, as most standard therapies have not been found to be efficacious in RMC. This case is being presented to emphasize the importance in conducting a search for Renal Medullary Carcinoma as it is rare and research opportunities will emerge and novel treatment options will be developed for this rare and dismal disease.

Keywords:

Renal Medullary Carcinoma, Sickle Cell Trait, Immunohistochemistry

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Adult Bladder Rhabdomyosarcoma: A Case Report

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Abstract:

Rhabdomyosarcomas (RMS) are the mesenchymal tumors originating from striated muscle fibres. It usually affects the children and adolescents but in adults RMS is an extremely rare malignant neoplasm that develops from the bladder wall and approximately 35 cases have been reported till date. Approximately 15 to 20% of all cases of RMS are of genitourinary origin. Most of these urinary bladder tumors are embryonal RMS, mainly the botryoid subtype. The differential diagnosis of RMS in adults includes sarcomatoid urothelial carcinoma with extensive rhabdomyosarcomatous differentiation and other small round cell tumors occurring at this site including small cell carcinoma, plasmacytoid urothelial carcinoma, primitive neuroectodermal tumor, and lymphoma. Immunohistochemistry has an important role in the differentiating these tumors. Myogenin and MyoD1 are equally sensitive (97% positivity) and specific (90% and 91% respectively) for the diagnosis of RMS. There is no significant difference in stage, lymph node status, gender, and site between adults and children. The 5-year survival for pediatric RMS is 66% and for adults 22%. We report a case of bladder rhabdomyosarcoma in a 30-years old patient who presented with gross hematuria.

Keywords:

Bladder Cancer, Rhabdomyosarcoma, Adult, Embryonal Subtype

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When Skin Tumours Reveal a Genetic Syndrome: A Case of Muir Torre Syndrome

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Abstract:

Introduction:

Muir-Torre syndrome (MTS) is a rare Lynch syndrome variant caused by mutations in mismatch repair (MMR) proteins, including MLH1, MSH2, MSH6, and PMS2. It accounts for less than 10% of Lynch Syndrome, with a slight male predominance. MTS is characterized by sebaceous neoplasms and visceral malignancies, most commonly colorectal cancer. Cutaneous lesions may be undifferentiated, showing features of malignancy and high microsatellite instability (MSI).

Case Report:

We report a case of a 55 year old male who presented with raised skin lesions over left cheek since 4 years. He is a known case of carcinoma of ascending colon, diagnosed 2 years before, for which he underwent radical right hemicolectomy. He also has a family history of colon cancer. Histopathological examination of the skin lesions showed Sebaceous carcinoma. Immunohistochemistry and molecular studies showed high MSI and mutations in expression of MSH2 and MSH6.

Conclusion:

This case underscores the importance of early recognition of Muir-Torre Syndrome, a rare genetic disorder linked to sebaceous neoplasms and systemic malignancies, especially colorectal cancer. Due to its connection with DNA mismatch repair defects, MTS should be considered in patients with sebaceous tumours or a history of colorectal cancer. Genetic testing and immunohistochemistry for mismatch repair proteins are essential for diagnosis, enabling proper surveillance and management.

Keywords:

Sebaceous carcinoma, Muir Torre Syndrome, Immunohistochemistry, Familial

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Sarcomatoid Variant of Urothelial Carcinoma of Bladder-A Rare Case

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Abstract:

Introduction:

Sarcomatoid variant of Urothelial Bladder Carcinoma is a rare form and is estimated to account for 0.1-0.3% of all urothelial cancers. It is a biphasic malignant neoplasm with morphological and immunohistochemical evidence of both epithelial and mesenchymal differentiation. It is most common in 45-82yrs males.

Aim and Objective:

To Report an unusual case of Sarcomatoid Variant of Urothelial Carcinoma of Bladder in a 64yr male.

Methods:

Multiple bits of grey brown tissue was received, fixed, and processed in our histopathology lab and H&E stain was done. For further confirmation on the diagnosis we did IHC with Vimentin, SMA, CK7, SMA-100 and ALK1.

Result:

Histopathology: Revealed predominantly areas of necrosis and lesional component of spindle cells exhibiting moderate pleomorphism, high N/C ratio, and increased mitotic activity. The lesion was infiltrating the muscle fibers.

Summary: Though Urothelial bladder carcinoma is a common finding in histopathological lab, its sarcomatoid variant is a very rare occurrence with <1% incidence. These are highly aggressive tumors with overall 1 and 2year survivals of 50% and 25% respectively.

Microscopically it is characterized by areas of atypical spindle cells that are morphologically indistinguishable from a sarcoma. The spindle cells are usually closely packed but, at some places they are separated by collagen fibers or lie in a loose, myxoid stroma. Clinico-imagiologically they may present with gross hematuria, flank pain, abdominal mass ,and hydronephrosis. It is complicated with tendency of rapid growth and to metastasized affecting the prognostic outcomes. Thus we are hereby reporting a rare case of sarcomatoid variant of urothelial carcinoma of urinary bladder which is characterized by difficulty in diagnosis and bad prognostic outcome due to potentiality of rapid growth and metastasize.

Conclusions:

Sarcomatoid Bladder Cancer is associated with poor prognosis. Multimodality therapy may improve these patient's outcome.

Keywords:

Sarcomatoid, Hydronephrosis, Multimodality Therapy

An Unusual Etiology of Gross Hematuria: Primary Extranodal Marginal Zone Lymphoma of the Bladder

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Abstract:

Background & Objectives:

Lymphoma of the urinary bladder (LUB) is rare, amounting to 0.2% of bladder cancers. Here, we present a case of primary extra nodal marginal zone lymphoma of the bladder presenting as a hematuria in a young male.

Case Report:

A 45-year-old male presented to the outpatient department with complaints of painless, gross hematuria. His medical history included urethral stricture repair 20 years ago following a road traffic accident. MRI revealed diffuse, well-defined thickening of the bladder mucosa. A transurethral bladder biopsy was subsequently performed.

Haematoxylin and eosin-stained slides revealed a tumour composed of sheets of small to intermediate-sized, monomorphic lymphoid cells with cleaved nuclei and moderate pale eosinophilic cytoplasm. Immunohistochemistry showed that these cells were diffusely positive for CD20, CD43, and focally for BCL2, while negative for cytokeratin, GATA3, CD10, BCL6, CD3, and CD5. The dendritic meshwork was highlighted by CD23 immunostaining. The Ki-67 labelling index was low. Based on these findings, a diagnosis of primary extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) was made. A bone marrow biopsy was also performed, which revealed hematopoietic elements from all three cell lineages, with no evidence of malignancy in the examined sections.

Conclusion:

Primary extranodal marginal zone lymphoma of the urinary bladder is a rare condition, and its diagnostic characteristics may not be familiar to clinicians who are less accustomed to it. There is a risk of misdiagnosis as poorly differentiated urothelial carcinoma or chronic cystitis. Accurate diagnosis relies on a thorough immunohistochemical and molecular workup.

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Young-Onset Penile Squamous Cell Carcinoma: A Case Report

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Abstract:

Penile squamous cell carcinoma (SCC) is an uncommon malignancy, particularly in men under 45 years, with an incidence of 0.1-0.8 per 100,000. This case report highlights a 36-year-old uncircumcised male with a history of chronic tobacco use presenting with a 6-month history of a growing lesion on the glans penis and delayed consultation due to socio-economic constraints. Clinical examination revealed a lesion covering the entire glans, and biopsy confirmed SCC. Radiological imaging identified enlarged inguinal lymph nodes, suggestive of metastasis. The patient underwent partial penectomy with bilateral pelvic lymph node dissection.

Histopathological analysis revealed well-differentiated SCC (G1) with no lymphovascular or perineural invasion and uninvolved surgical margins. Examination of 11 dissected lymph nodes showed no malignant invasion, only reactive changes. The tumor was staged as pT1 N0 Mx.

This case underscores the significance of tobacco use, smoking, and poor hygiene as major risk factors for penile SCC, especially in uncircumcised individuals. It highlights the critical role of radiological imaging in staging and guiding surgical management, as well as the importance of histopathological evaluation for accurate diagnosis and staging. Additionally, it emphasizes the need for early detection and timely intervention to improve outcomes. Addressing socioeconomic barriers is essential to minimize diagnostic delays and enhance patient prognosis in rare malignancies like penile SCC.

Keywords:

Penile Squamous Cell Carcinoma, Tobacco Use, Young-Onset Cancer, Uncircumcised, Histopathology, Socio-Economic Barriers

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An Atypical Presentation of Extragastrointestinal Stromal Tumor: A Case Report

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Abstract:

Introduction:

This report presents a rare case of bladder extragastrointestinal stromal tumor, which manifested as a leiomyoma on imaging studies in a patient experiencing recurrent postmenopausal bleeding. This case represents the fifth such instance documented in the literature.

Clinical presentation:

A 58-year-old woman sought medical attention at the outpatient clinic of a government medical center, complaining of repeated postmenopausal bleeding episodes. Upon physical assessment, her vital signs were found to be within standard ranges. On abdominal examination, a firm solid mass was felt. The ultrasound report mentioned a 13×12.7×10.8 cm well-defined hypoechogenic lesion arising from the anterior wall of the uterus. Contrast-enhanced computerized tomography was reported as a subserosal fibroid. The patient was planned for hysterectomy in view of a large fibroid. A 15×14 cm yellowish-firm mass with areas of cystic degeneration and necrosis was seen on the right side, which appeared to be arising from the bladder. A hysterectomy with bilateral salpingo-oophorectomy was done. A tumor was seen arising from the posterior wall of the bladder. A complete resection of the tumor was done and the bladder was repaired in two layers. Metastasis and primary foci were ruled out. On immunohistochemistry, the tumor was positive for CD117, desmin, and DOG1. The final impression was a gastrointestinal stromal tumor of the urinary bladder.

Keywords:

Extragastrointestinal tumor, Immunohistochemistry, Leiomyoma, Postmenopausal bleeding, Urinary bladder

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Jejunal Diffuse Large B-Cell Lymphoma: A Rare Extranodal Challenge

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Abstract:

Introduction:

Primary gastrointestinal lymphoma is a rare tumor, accounting for less than 5% of all gastrointestinal cancers. Non-Hodgkin lymphoma (NHL), which represents about 2.7% of global cancer cases, frequently involves extranodal sites, particularly the gastrointestinal (GI) tract. Among these, diffuse large B-cell lymphoma (DLBCL) is the most common subtype. However, unlike more typical sites such as the stomach or ileum, the jejunum is a rare location for primary extranodal lymphomas due to the limited presence of lymphoid tissue.

Case Report:

A 47-year-old male presented with 3 months of intermittent fever, vomiting, colicky abdominal pain, and a 10 kg weight loss. Examination revealed an 8x6 cm palpable mass in the right iliac fossa. Imaging (USG and CECT) showed circumferential thickening of the distal ileum, loss of mural stratification, perilesional fat stranding, and enlarged lymph nodes, suggesting malignancy with metastatic lymphadenopathy. Diagnostic laparoscopy revealed a 15x15x3 cm jejunal mass with mesenteric lymphadenopathy. Biopsies were obtained, and immunohistochemical staining revealed tumor cells expressing CD20, with CD45 positive, CD3 in background cells, Ki67 at 80%, BCL6, and MUM-1 positive. Other markers were negative, confirming the diagnosis of diffuse large B-cell lymphoma (DLBCL) of the jejunum.

Conclusion:

This case emphasizes the diagnostic challenge of primary intestinal DLBCL in the jejunum, presenting with nonspecific symptoms. Awareness, histopathology, and IHC correlation are key for accurate diagnosis and early treatment. Further research is needed for improved management.

Keywords:

Extranodal lymphoma, Non-Hodgkin lymphoma, Diffuse large B-cell lymphoma, Immunohistochemistry

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Neoplasms Arising in Renal Allograft: Report of Two Rare Cases

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Abstract:

Neoplasms arising in renal allografts is a rare entity. Cancer is one of the leading causes of death in kidney transplant recipients. De novo Renal cell carcinoma (RCC) in allograft kidney is extremely rare and increased risk occur due to immunosuppression. RCC is often asymptomatic and can be an incidental finding on routine examination. Here we discuss 2 cases -a benign and a malignant neoplasm arising in renal allograft.

A 30 year old female with history of CKD underwent kidney transplant with mother as donor and was on immunosuppression. She presented with history of generalised weakness and fatiguability since 3-4 months. On evaluation was found to have anemia, pure red cell aplasia with parvo B19 infection. CMV positive. Her creatinine was elevated to 2.3. On allograft USG and doppler a mass was detected at upper pole of graft kidney. HPE suggestive of clear cell carcinoma. Graft tissue however did not show any evidence of rejection. Partial nephrectomy was done.

A 66 year old female, asymptomatic, marginal kidney donor, underwent donor nephrectomy for renal allograft transplant. On graft kidney a 1x1 cm fat containing lesion over upper pole was detected. Histopathologic examination showed renal parenchyma along with tumor with features of angiomyolipoma

Conclusion:

Tumors in a kidney allograft is rare. This observation reiterates the necessity of imaging and histopathologic examination of the graft.

Keywords:

Renal Allograft, Clear Cell Carcinoma, Angiomyolipoma

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Impact of Gleason Grade Group on Margin Status in Radical Prostatectomies

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Abstract:

Positive surgical margins following radical prostatectomy is an adverse prognostic factor associated with increased mortality, higher rate of biochemical recurrence, local progression and metastasis. This retrospective audit aims to evaluate the margin positivity prevalence in radical prostatectomy specimens and correlate the significance of Gleason grade group and other histopathological parameters in predicting margin positivity status. The study included 206 consecutive cases over a 11 year period, from March 2013 to November 2024. Robotic surgeries included 106 (51.5%) cases, while the rest were non-robotic (48.5%). The final Gleason score was 6, 7, 8, 9 and 10 in 18 (12.9%), 106 (76.25%), 9 (6.47%), 7 (5.03%) and 1 (<0.005%) cases. One hundred and five cases (50.9%) showed involved margins. Margin involvement was seen almost equally in robot-assisted (54 (51.9%)) and non-robot assisted (50 (48.15%)) prostatectomies. The most common site was apex (in 89 (85.5%)) followed by base (35 cases). Multifocal involvement was present in 33 (31.7%) cases. The most common Gleason's pattern at the site of margin involvement was pattern 3 (in 43.2%). Intra-prostatic (incisional) involvement (83.5%) vastly outnumbered extra-prostatic margin involvement.

Keywords:

Prostate, Margin, Gleason's, Robot Assisted

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Atrophic Kidney Like Lesion (AKLL): Report of a Provisional Entity with Brief Review of Literature

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Abstract:

Introduction:

Atrophic kidney-like lesion (AKLL) is a provisional renal entity with distinct morphological and immunohistochemical features. Less than ten cases of AKLL have been reported in the literature. We are hereby describing the clinicopathological features of AKLL in a 38-year-old man. The case is being presented because of its rarity and novelty.

Case Report:

A 38 year old man presented with an incidentally detected left renal mass. CECT abdomen showed an exophytic hypodense mass with foci of calcification arising from the upper pole of the left kidney measuring 6.5x6x5cm with no evidence of any thyroid mass. PET-CT did not show any lesion anywhere in the body including thyroid gland.

Radical nephrectomy performed revealed a circumscribed grey white tumor (6.5x6x5cm) in the upper pole of kidney without any haemorrhage or necrosis.

Microscopically, the tumor consisted of variably sized thyroid like follicles lined by cuboidal to columnar cells with moderate amount of eosinophilic cytoplasm, round to oval nuclei with fine chromatin, inconspicuous nucleoli filled with homogeneous eosinophilic colloid like material. No areas of conventional renal cell carcinoma were seen.

Immunohistochemically, the tumor cells showed immunopositivity for cytokeratin, CK7, CD10, PAX8, vimentin, AMACR(focally) and were negative for TTF1, Thyroglobulin, HMB45 and SMA.

Conclusion:

Atrophic kidney like lesion is a very rare entity with distinct histomorphology and immunohistochemical features. Radiology cannot differentiate between conventional RCC and AKLL. Thus, pathological examination with supporting immunohistochemistry is a must for confirming the diagnosis.

Keywords:

Atrophic Kidney Like Lesion, Renal Mass, Conventional Renal Cell Carcinoma

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Seminal Vesicle Adenocarcinoma Mimicking Papillary RCC: A Diagnostic Conundrum in a 13-Year-Old Boy with Zinner Syndrome

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Abstract:

Introduction:

Zinner Syndrome (ZS) is a developmental disorder of the mesonephric ducts usually presenting at later stages of life. Occasional cases of Primary Seminal Vesicle Adenocarcinoma (PSVA) have been reported in ZS in older adults. However, none have been described in the paediatric age group. Herein, we present a case of PSVA mimicking papillary renal cell carcinoma (PRCC) in a 13-year-old boy with ZS.

Case Presentation:

A 13-year-old boy presented with gross haematuria and passage of clots for five months. The imaging (USG, CECT, MRI) revealed a solid-cystic lesion with papillary projection, abutting posterior wall of bladder and absence of left kidney. A biopsy performed outside (prior to evaluation at AIIMS) gave a diagnosis of papillary renal cell carcinoma. At AIIMS, the patient underwent resection of the cyst and lymph node dissection with a possible diagnosis of a carcinoma.

Histopathology showed a tumor with morphological features of an adenocarcinoma along with overlapping features of PRCC. A battery of immunohistochemistry and extensive work up with radiologists and urologists was done to arrive at a final diagnosis of PSVA and to rule out PRCC. The patient is currently in close follow-up and doing well after resection.

Conclusion:

This case highlights the diagnostic dilemma in cases of pelvic cysts with overlapping immunohistochemistry, and highlights the need to perform extensive evaluation and preserve a broad list of differentials for proper evaluation and precise diagnosis.

Keywords:

Zinner Syndrome, Primary Seminal Vesicle Adenocarcinoma, Papillary RCC, Pelvic Cystic Mass

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Urachal Carcinoma: A Short Case Series in a Tertiary Care Hospital

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Abstract:

Introduction:

Urachal carcinoma is a rare urological disease. The shortage of data about diagnosis and surgical treatment in literature makes it hard for clinicians to make a decision. Indeed, urachal carcinoma is an aggressive disease that requires prompt staging and treatment to ensure the best outcome for patients. We reviewed the last evidence about the management of urachal carcinoma to provide an easy-to-use guide for clinical practice.

Aim:

The aim of our study is to conduct a study regarding the histomorphological and immunohistochemical patterns of urachal carcinomas, along with its clinical and radiological features.

Materials and Methods:

Institutional retrospective record based study done for a period of two years, from December 2022 to December 2024.

Results and Discussion:

Two cases were found in the last two years, which showed the mean age incidence in the 5th to 6th decade. Computed tomography (CT) findings solid and cystic mass and punctate calcification, along with thickened bladder dome and anterior wall and urachal area. Both of the cases showed positivity for CK 7, CK 20, CDX 2, CEA, and negative for GATA- 3 and AMACR.

Keywords:

Immunohistochemistry, Solid and Cystic Areas on Computed Tomography

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Primary Amenorrhea: Unpuzzled Phenotype with Puzzling Histotype

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Abstract:

Androgen insensitivity syndrome (AIS) is an X linked inherited disorder caused by a mutation in the androgen receptor gene which prevents the body's cells from recognizing and responding to androgens. Generally, AIS is subcategorised into complete and incomplete AIS based on the severity of the mutation. Complete AIS clinically presents as male pseudo hermaphroditism, where they are phenotypically female with the male genotype.

We present an interesting case of a 22-year female who came with the complaints of primary amenorrhea to gynecology outpatient department. She underwent a serological screening for hormone imbalance and a routine ultrasound abdomen. Surprising, there was a rudimentary uterus and a pair of undescended testes located in bilateral inguinal canal region. Serological findings showed very high levels of serum testosterone (969.200 ng/dl), slightly elevated antimullerian hormone levels (23 ng/dl), elevated serum estradiol level 39.340 ng/dl and normal serum cortisol levels.

Subsequently bilateral gonadal structures were removed and sent for histopathological examination. Gross examination of both the gonadal structures appear grey brown with focal grey white areas with one of the gonad showing a tubal like structure. Microscopic examination revealed the presence of seminiferous tubules like structure along with the adjacent area showing the cross section of fallopian tube. Immunohistochemistry for inhibin confirmed the sertoli cells and there was no evidence of spermatogenesis. We present this case due to its rarity of occurrence and for the mixed serological and histopathological findings.

Keywords:

Androgen Insensitivity Syndrome, Deficient Androgen Receptor, Male Pseudo Hermaphroditism, Karyotype

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The Urethral Enigma – Two Faces of Prostatic Urethral Adenocarcinoma

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Abstract:

Primary urethral carcinoma is a rare but aggressive genitourinary malignancy that leads to urethral obstruction. It usually presents late symptomatically with varied histomorphological patterns, resulting in poor prognosis and delayed treatment. Approximately half of these cases involve the proximal urethra in both men and women. Here, we present 2 rare cases of prostatic urethral adenocarcinoma.

Case 1: A 35-year-old male patient presented to the OPD with complaints of on and off hematuria for five months, and was associated with dysuria, colicky abdominal pain and burning micturition. Radiological findings showed a papillary growth measuring 5x2x2cm in the trigone of the bladder, involving bilateral vesicoureteric junctions and the base of the prostate, while colonoscopy was unremarkable. Radical cystoprostatectomy with ileal conduit was then performed, and histopathological evaluation revealed an infiltrating gelatinous lesion in the bladder, extending into the deep muscle and prostatic tissue. Microscopic evaluation revealed a poorly differentiated malignancy with signet cell morphology.

Case 2: A 58-year-old male patient presented to the OPD with difficulty in micturition infrequently since 3 months. He is a known smoker since 10 years. Per rectal examination revealed grade 2 BPH. Following this, he underwent transurethral resection of prostate (TURP) and was submitted for histopathological examination, which revealed a mucinous lesion of the prostatic urethra.

IHC workup of both tumours in case 1 and 2 show that the tumour cells are positive CK7, CK20 and CEA, suggestive of a prostatic urethral origin while being negative for NKX 3.1 and GATA-3 ruling out prostate and bladder origin respectively.

Keywords:

Prostatic urethra, Signet ring cell, Urethral carcinoma, Poorly differentiated carcinoma

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Suspicious Urinary Bladder Mass Masquerading the Urinary Bladder Carcinoma – Rare Case Report of Urinary Bladder Endometriosis

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Abstract:

Leiomyomas are common benign tumors of female genital tract presenting with dysfunctional uterine bleeding and abdominal discomfort. Due to their benign nature it is rare to see these tumors invading other tissues. Urinary bladder (UB) endometriosis is a uncommon condition in which endometrial tissue grows into the detrusor muscle of the bladder. Approximately 7% of all women present with endometriosis. We reported a case of 54 year old female presented with obstructive lower urinary tract symptoms (LUTS) and lower abdominal pain. MRI KUB with MR UROGRAPHY was done and it identified soft tissue lesion involving the vaginal vault at the floor of UB and invading the posterior bladder wall with intact mucosa. On cystoscopy, extra mucosal polypoidal lesion was seen at the right side of posterior bladder wall suspected as neoplastic lesion. Histopathological biopsy was done and reported as leiomyoma with Endometriosis urinary bladder. However no evidence of malignancy was identified.

Keywords:

Urinary Bladder Mass, Endometriosis, Leiomyoma, LUTS

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Rare But Favourable: A Case Report of Mucinous Tubular and Spindle Cell Renal Carcinoma

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Abstract:

Introduction:

Mucinous tubular and spindle cell renal carcinoma is a rare and unique subtype of renal cell carcinoma characterized by a combination of tubular structures, spindle cells, and mucinous stroma. It has a generally favourable prognosis compared to other renal cell carcinomas but remains poorly understood due to its rarity.

Case Presentation:

We report a case of a 52-year-old female who presented with hematuria and flank pain. Imaging studies revealed a 12.5 cm, hypodense lesion in the right kidney. A right open radical nephrectomy was performed. Grossly the tumor appeared well circumscribed and solid with few grey black areas. Histopathologically the tumor is composed of tightly packed elongated and anastomosing tubules lined by low grade cuboidal cells merging with bland spindle cells in a myxoid stroma containing basophilic extracellular mucin. Few interspersed foamy macrophages and tumour infiltrating lymphocytes are also noted. Tumour cells are of low grade with rare mitosis and few of them show clear cytoplasm. Nucleoli were conspicuous and eosinophilic at 400X magnification (ISUP Grade 2). Immunohistochemistry revealed strong positivity for CK7, PAX 8, focally for CD10 and a low Ki 67 labelling index, supporting the diagnosis of Mucinous Tubular and Spindle Cell renal Carcinoma.

Discussion:

Mucinous tubular and spindle cell renal carcinoma poses diagnostic challenges due to its overlapping histological features with other renal neoplasms, such as papillary RCC and sarcomatoid carcinoma. This case highlights the importance of integrating histopathology, immunohistochemistry, and clinical presentation for accurate diagnosis.

Conclusion:

While rare, Mucinous tubular and spindle cell renal carcinoma should be considered in the differential diagnosis of renal tumors. Early identification and surgical intervention ensure favourable outcomes.

Keywords:

Mucinous Tubular and Spindle Cell Renal Carcinoma, Immunohistochemistry, ISUP Grade

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Beyond the Benign: A Case of Squamous Cell Carcinoma Arising Within an Epidermoid Cyst

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Abstract:

Epidermoid cysts, benign lesions of hair follicle origin composed of stratified squamous epithelium and keratin, are typically asymptomatic but may become inflamed or infected. Malignant transformation is rare.

We present a case of a 36-year-old woman with a 10-year history of recurrent, painless perianal swelling, which had spontaneously resolved three months before presentation. Physical examination revealed a non-tender, perianal mass without signs of inflammation. Magnetic resonance imaging (MRI) demonstrated a cystic lesion adjacent to the anal canal, suggestive of an epidermoid cyst, benign. The lesion was subsequently excised for histopathological analysis.

Gross examination of the excised specimen revealed a skin-covered, soft tissue mass upon incision, grey-white, pultaceous material was expressed. We found a suspicious firm, solid, grey-white area.

Microscopic examination of skin with underlying cyst lined by stratified squamous epithelium and filled with flakes of keratin. Sections from the suspicious area show a transition to high-grade dysplasia and an invasive neoplasm exhibiting increased pigment-laden cells. Immunohistochemical staining for HMB45 was performed to exclude melanoma, and the tumour cells demonstrated positive staining for p40, confirming the diagnosis of poorly differentiated squamous cell carcinoma.

The rarity of squamous cell carcinoma (SCC) arising from epidermoid cysts obscures its clinical and pathological features, hindering optimal management. Early detection and prompt intervention are therefore essential for positive patient outcomes.

Keywords:

Epidermal Cyst, Inclusion Cyst, Cutaneous Cyst, Squamous Cell Carcinoma, Malignant Transformation

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Beyond Surgery: The Lurking Battle - A Case Report

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Abstract:

Introduction:

TFE3-rearranged renal cell carcinoma (RCC) is an uncommon emerging histological subtype that belongs to MiT family translocation of tumours, primarily affecting young adults. It is characterized by specific genetic alterations involving the TFE3 gene on chromosome X. These rearrangements, typically translocations, lead to the formation of fusion genes that drive uncontrolled cell growth and tumor development.

Case Presentation:

A 52 year old male, came with complaints of right side loin pain and hematuria for past one month. He was further evaluated with radiological imaging and his CT urogram showed a well defined endo-exophytic heterogenous enhancing lesion seen arsing from upper and midpole of the right kidney measuring 7.3x6.4x7.9cm. The lesion also showed tumour thrombosis invading through right renal vein and suprarenal segment of IVC. Right radical nephrectomy was performed for the above on 31/05/2022.

On histopathological examination, the tumour cells were arranged in papillary architecture with epithelioid clear cell morphology exhibiting nuclear pleomorphism. Ancillary studies were done and the tumour cells were TFE3 positive and CK7 negative by immunohistochemistry and a final diagnosis of TFE3 rearranged RCC was rendered.

Discussion:

TFE3 rearranged RCC is a rare subtype of renal cell carcinoma , accounting for only 1-5% of all RCC cases. It can metastasize to various sites, including the lungs, bones, and brain, scalp metastasis is likely even less common. Metastatic TFE3-rearranged RCC generally carries a poorer prognosis compared to localized disease. Early diagnosis and treatment are crucial to improve outcomes. In our case, his post-operative period was uneventful. After 2 years he presented to the out patient department in SRIHER with swelling in the scalp near the occipit for past 2 weeks. The swelling over the scalp was found, measuring approximately 2x2cm , tender and firm in consistency. Excision biopsy was performed on 06/01/2024 and scalp metastasis from TFE3 rearranged renal cell carcinoma was morphologically diagnosed. The patient was evaluated with PET-CT, identified with multiple metastasis and started on chemotherapy.

Conclusion:

Understanding the underlying genetic mechanisms, identifying at the earliest and developing effective treatment strategies for this challenging malignancy remain critical areas of research.

Keywords:

Renal Cell Carcinoma, Scalp Metastasis, Xp11.2 , Oncology, TFE3

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From Bladder to Kidney: A Squamous Odyssey in Urothelial Carcinoma

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Abstract:

Background:

Urothelial carcinoma with squamous differentiation involving both the bladder and kidney is an interesting oncological presentation. Squamous differentiation often signifies aggressive tumor biology and poor prognosis.

Case Presentation:

A 65-year-old man presented with hematuria and flank pain. Imaging revealed a heterogeneously enhancing lesion along the left ureter extending into the vesicoureteric junction (VUJ) with moderate upstream hydroureteronephrosis. Additionally, a lesion was noted in the left kidney. The patient underwent radical cystectomy with left nephroureterectomy. Gross pathology revealed solid, firm, pale-white tumors in the left posterolateral wall of ureter, distal VUJ and left kidney. Microscopy showed invasive urothelial carcinoma with extensive squamous differentiation in both sites.

Discussion:

Urothelial carcinoma with squamous differentiation in bladder and kidney represents a theranostic challenge. Squamous differentiation correlates with more aggressive behavior, requiring multimodal treatment. While urothelial carcinoma of the bladder is well-documented, concurrent renal involvement with squamous differentiation remains exceptionally rare.

Conclusion:

This case underscores an intriguing presentation of squamous differentiation in urothelial carcinoma in the ureter, VUJ and kidney.

Keywords:

Urothelial Carcinoma, Squamous Differentiation, Bladder Cancer, Renal Carcinoma, Radical Cystectomy, Nephroureterectomy

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Testicular Yolk Sac Tumor Solid variant -A Rare Case Report

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Abstract:

Introduction:

A rare solid variant of testicular yolk sac tumor histological subtype of germ cell tumor distinguished by solid growth pattern.Unlike other variants of yolk sac tumor which may exhibit more mixed of cystic pattern, solid variant of yolk sac is composed predominantly solid sheets of tumor cells.

Case Presentation:

4 years 8 months male present with painless right inguinal scrotal swelling since one month with previous past history of wilm's tumor. The histopathology specimen of right testis sent to the department for further evaluation. The section shows solid sheets of cell with clear cytoplasm and eccentric placed nuclei, some cell shows eosinophilic cytoplasm and centrally placed nuclei and minimal amount of fibrocollagenous tissue. The characteristics structure schiller duvel bodies present in solid variant of yolk sac tumor.

Discussion:

In summary this can be more challenging to diagnose and treat the yolk sac solid variant. Early diagnosis and early treatment will show very good impact.

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Angioleiomyoma of Urethra- A Rare Case with a Review

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Abstract:

Background:

Angioleiomyoma of the urethral is an uncommon benign neoplasm that arises from vascular smooth muscle cells. It has many histopathological mimickers.

Case Details:

A 68-year-old man presented with hematuria. EUM showed a 1x1cm pulsating bulbar urethral mass at proximal bulbar urethra and induration present at Bulbar urethra measuring 3x3cm. Excision of the urethral mass done. Grossly it showed two grey/brown tissue, measuring 3 cm, and 3.5 cm. The microscopic examination showed a tumor arranged in vague nodular pattern and hapazardly arranged fascicles. The tumor cells were spindle shaped with moderate to abundant fibrillary cytoplasm, round to elongated nuclei, fine chromatin and inconspicuous nucleoli. These spindle cells surround many slit like thin walled blood vessels and thick walled blood vessels as well. Areas of myxoid stromal change was also evident. These tumor cells were also seen infiltrating adjacent skeletal muscle bundles and adipose tissue. There are no areas of necrosis. Mitosis: 0-1/10 HPF. On immunohistochemistry (IHC), the tumor cells were strong and diffuse positive for SMA and desmin, weak focal positive for EMA while negative for CD34. CD34 highlighted the blood vessels within the tumor.

Conclusion:

We report this additional case of angioleiomyoma of the urethra. The differential diagnoses of this entity are myopericytoma, angiomyofibroblastoma, angiofibroma, plexiform angiomyxoma, and perivascular epithelioid cell tumor. We report this case due to its rarity and discuss the diagnostic approach.

Keywords:

Angioleiomyoma, Urethra, Desmin, Angiofibroma, Myopericytoma, SMA

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Unusual Urinary Bladder Tumour of Pink Cell Morphology: A Case Report

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Abstract:

Background:

Neuroendocrine tumors (NETs) of the urinary tract are rare, constituting less than 1% of urothelial neoplasms. These tumors are broadly classified into well-differentiated tumors, small-cell neuroendocrine carcinoma (SCNEC), and large-cell neuroendocrine carcinoma (LCNEC). Paragangliomas are also included under the classification of genitourinary NETs.

Case Report:

A 17-year-old male presented with pain abdomen, haematuria and difficulties in urination. Cystoscopy revealed a growth in the urinary bladder. Transurethral resection of bladder tumor (TURBT) was performed and TURBT chips were received for histopathological examination. Microsections showed tumor cells arranged in lobules and sheets, composed of large cells with abundant eosinophilic cytoplasm and round nuclei. Areas of necrosis or mitosis were not identified. Immunohistochemistry showed positivity for S100, Synaptophysin, Chromogranin, CD56, NSE, GATA3 while negative for PanCK, CK7, CK20, EMA, P63, TTF1, Calretinin, Inhibin, TFE3, SOX10, SMA, Desmin and NKX3.1.

Discussion:

Neuroendocrine tumors of the urinary bladder are uncommon and can mimic other malignancies both histologically and clinically. The NETs exhibit varied morphology including small cell NET, large cell NET and rare oncocytic NET variant. While NETs commonly exhibit cytokeratin positivity, cytokeratin-negative cases are exceedingly rare, presenting diagnostic challenges.

Keywords:

Neuroendocrine Tumor, Immunohistochemistry, Urinary Bladder

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A Curious Case f Adenoid Cystic Carcinoma Metastasizing To Kidney Masquerading As Renal Cell Carcinoma

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Abstract:

Introduction:

Adenoid cystic carcinoma accounts less than 1% of all head and neck malignancies with extremely rare incidence of metastasis to kidney.

Materials and Methods:

USG guided FNA of right kidney was done. It was fixed with ethanol (95%) and stained with papanicolaou stain for cytopathological examination.

Results:

A 32-year-old female presented with back pain since 1 month duration. Ultrasonography revealed a well defined hypoechoic smoothly marginated lesion measuring 34x37mm in mid and lower pole of the right kidney. No para aortic nodes identified. No peritoneal collections seen. HRCT of thorax revealed multiple variable sized soft tissue nodules in bilateral lung parenchyma. The patient underwent USG guided fine needle aspiration cytology of the renal lesion, smears show high cellularity, with clusters of cohesive small uniform epithelial cells arranged around good number of hyaline globules, solid fragments of tumor cells also seen with dispersed bare nuclei. The cells have minimal cytoplasm with small uniform nucleus and distinct nucleoli. On further evaluation the patient gave previous history of left submandibular gland tumor 4 yrs back for which the patient underwent excision and histopathologically reported as Adenoid cystic carcinoma.

Discussion:

The metastasis from Adenoid cystic carcinoma is known to occur late, even after many years after primary tumor has been removed. However renal metastasis of ACC is extremely rare with only few case reports in the literature.

Keywords:

Adenoid Cystic Carcinoma, Kidney, Metastasis, FNAC, Salivary Gland

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Testicular Sertoli Cell Tumor in an Elderly Male- A Case Report

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Abstract:

Introduction:

Sertoli cell tumors of testis are rare neoplasm originate from sex cord and interstitial stromal cell of testis. It accounts for <1% of all testicular tumors. It can present at any age, but they are most common in adult male.

Materials and Methods:

Left orchidectomy specimen was received for histopathological examination. Immunohistochemistry was performed on tissue block.

Results:

65-year male presented with painless left testicular mass since 1-year and with recent enlargement of mass. Ultrasound shows hypoechoic intra testicular lesion. Serum tumor markers including LDH, AFP and HCG were with in normal limit. Gross examination revealed thickened tunica vaginalis testis with multiple polypoid projections in the sac. Microsections show a neoplasm, composed of tumor cells arranged in tubules,cords or small nests lined with cuboidal cells showing moderate nuclear pleomorphism, nuclear hyperchromasia and moderate eosinophilic cytoplasm. Immunohistochemistry showed positive for Calretinin, inhibin, CK, Beta catenin, AR, Vimentin and negative for PAX8, SALL4, PLAP, OCT4, CD30, alpha fetoprotein. On the basis of histomorphology and IHC final diagnosis was Sertoli cell tumor.

Discussion:

Most of the Sertoli cell tumors are benign. They can be of diagnostic challenge due to over lapping clinical and histomorphological features with others testicular tumors.

Keywords:

Sertoli Cell Tumor, Testis, Immunohistochemistry

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Paratesticular Dedifferentiated Liposarcoma presenting as Inguinal Hernia

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Abstract:

Introduction:

Paratesticular liposarcoma is a rare tumour of the genitourinary tract and its dedifferentiated variant is an even rarer form of the tumour (10% of liposarcoma cases). Clinically, patients usually present with findings similar to that of an inguinal hernia. Here, we are presenting a rare case of paratesticular dedifferentiated liposarcoma (DDL).

Case Report:

A 74-year-old male came with complaints of left inguinoscrotal swelling for 1.5 years, which was gradually progressing in size. The swelling was irreducible and was not associated with pain, nausea or vomiting. A provisional diagnosis of left irreducible hernia was made. However, ultrasound of the swelling was suggestive of a spermatic malignancy. Left high orchidectomy with tumour excision was done. Grossly, we received a globular structure with an attached spermatic cord and an atrophic testis. The tumour was seen abutting the atrophic testis. Microscopy revealed, a poorly circumscribed lipogenic tumour along with a non-lipogenic component. The lipogenic component showed a well differentiated area with an abrupt transition to a dedifferentiated non-lipogenic spindle cell component. Diagnosis of grade 3 dedifferentiated liposarcoma was made which was further confirmed by MDM2 positivity on IHC.

Keywords:

Paratesticular Tumor, Dedifferentiated Liposarcoma, MDM2, Inguinal Hernia

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A Rare Case of Gonadal Dysgenesis with Gonadoblastoma

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Abstract:

Introduction:

Gonadal Dysgenesis (GD) is a type of Differences in Sexual Development (DSD) characterized by asymmetrical gonadal development with one or more gonads being poorly developed, resulting in streak gonads or dysgenetic testes. Gonadal dysgenesis can be pure 46XX, 46XY or mosaic karyotype (commonly 46XY, 45XO). Germ cell neoplasia in situ and gonadoblastoma may develop in the dysgenetic gonad. Here we are presenting a case of gonadal dysgenesis with gonadoblastoma.

Case Report:

15/M presented with complaint of ambiguous gentialia since birth with micro penis and hypospadias with bilateral undescended testis. O/E bilateral testes were absent in the scrotum, centrally located penis with hypospadias. Hormone profile shows S. LH-19.62 Miu/ml, Estradiol-39.03 pg/ml, S. FSH-57.28mIU/ml, Testosterone, Total-4.16 ng/ml. USG Abdomen- Cystic lesion in pelvis posterior to urinary bladder – likely remnant of mullerian duct with left undescended testis in left iliac fossa, with right testis possibly in right lumbar region. Excision of rudimentary uterus, bilateral gonads done. Histopathology was suggestive of Gonadal dysgenesis with gonadoblastoma. Germ cells were positive for SALL-4 and PLAP and sex cord cells which were positive for inhibin and WT1.

Conclusion:

Gonadoblastoma can be seen in patients with gonadal dysgenesis with Y chromosome material. Because of high risk for malignant transformation gonadectomy of streak gonad or gonadectomy of dysgenetic testicle should be performed at early age.

Keywords:

Gonadal Dysgenesis, Gonadoblastoma

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Metachronus Metastasis of Renal Cell Carcinoma in Urinary Bladder

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Abstract:

Introduction:

RCC tends to metastasize to a variety of distant organs, the most common of which are the lungs, bones, and lymph nodes. Urinary bladder is one of the least common site of renal cell carcinoma metastasis. Here we are reporting a case of metachronus metastasis of clear cell RCC to urinary bladder.

Case Report:

A 61-year-old male patient, a follow up case of left clear cell RCC post left radical nephrectomy with bladder cuffing, presented with difficulty in breathing, dry cough for 2 months. Straw colored pleural fluid was aspirated and sent for cell block. Cell block is negative for malignancy. USG abdomen shows Urinary bladder(UB) mass in left postero-lateral wall- likely neoplastic. CT abdomen revealed a well-defined enhancing polypoidal extra luminal lesion arising from postero-inferior wall of UB. Transurethral bladder tissue from superficial and deep bladder tissue sent for histopathological study. It showed tumor having features of Clear Cell Renal cell carcinoma. Tumor cells are strongly positive for Vimentin, CD10, moderate positivity for PAX8 and negative for P63, CK7, CK20, and GATA3.

Conclusion:

The urinary bladder is one of the rarest sites of RCC metastasis. Metachronus metastasis is more common than synchronous metastasis.

Keywords:

Clear Cell Rcc, Urinary Bladder Metastasis, Metastasis

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Prostate Rhabdomyosarcoma – A Rare Case Report

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Abstract:

Introduction:

Prostatic rhabdomyosarcoma is a very rare malignant mesenchymal tumor in adults, which accounts for less than 1% of all prostatic tumors among adults. Because of its rapid growth & consequent local growth it leads to renal failure due to bladder outlet obstruction & also has systemic spread to lungs, liver & bones. We report a rare case of rhabdomyosarcoma of prostate in a young male

Case Report:

A 27 years old male presented with complaints of difficulty in micturition for last 1 month and constipation for last 3 days. There was no associated comorbidity. On digital rectal examination, a mass was palpated in the anterior aspect however anal sphincter & mucosa were normal. Serum PSA level was 1.14ng/ml. CEMRI of pelvis revealed grossly enlarged prostate with peripheral enhancement & internal necrosis. TRU CUT biopsy of left lower lobe of prostate revealed tumor cells arranged in sheets. The cells were round to polygonal with hyperchromatic to vesicular nuclei. Good number of tumor giant cells, typical and atypical mitoses & extensive tumor necrosis noted. Possibility of a primary malignant mesenchymal tumor of prostate was made from histopathological analysis. TRUCUT biopsies from rest of the lobes of prostate revealed normal prostatic tissue only. Immunohistochemistry was positive for Myo D1, Desmin and Vimentin and negative for Pan CK, SMA, S100 and CD 117. Final diagnosis of Rhabdomyosarcoma of prostate was made.

Conclusion:

Due to its nonspecific symptoms in the early stage, it can lead to late detection and is associated with very poor prognosis and metastasis to distant organs. A high index of suspicion alone will help in detecting rhabdomyosarcoma of the prostate before complications occur.

Keywords:

Rhabdomyosarcoma, IHC, Prostate

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Surgical Management of MEN 2A Syndrome: Bilateral Laparoscopic Adrenalectomy and the Role of Genetic Counselling

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Abstract:

Evaluation:

Patients with classic clinical manifestations of MEN2 are evaluated for two main reasons:
1. To screen for other associated common tumors to decrease overall morbidity and mortality.
2. To screen for genetic mutation so that other family members should be tested and provided adequate prophylactic medical and surgical care such as prophylactic thyroidectomy.

Method:

A 54 year old male patient named Umar came to urology OPD with C/O of suprapubic pain since 4 months, which was dull aching and occasional, was associated with palpitation, pain was not associated with food intake or any other factors. He was a C/O DM, HTN since 2016. Patient had a history of total thyroidectomy in 2008 and biopsy showed MCT . Patient's sister underwent total thyroidectomy and bilateral adrenalectomy in 2018.

Surgical Management:

Procedure: Bilateral Laparoscopic Adrenalectomy
Indications: Presence of pheochromocytomas, typically bilateral in MEN 2A patients.
Surgical Steps: *Patient Preparation*: General anesthesia and appropriate positioning, right lateral position for left adrenal tumour and left lateral for right adrenal tumour.
Port Placement: Insertion of laparoscopic ports for instruments and camera.

Genetic Testing and Counselling:

- The genetic testing for RET proto-oncogene is employed to diagnose and identify a specific type of mutation present in an index patient (the first affected member of the family) such as high-risk, moderate-risk or low-risk mutations.
- For an index patient with suspected MEN2A, evaluation beginws with testing for the most common mutated codons in exons 10 and 11, and if negative, we move on to look for other common mutations in descending order.
- Other cases in which genetic testing can be considered:
- First-degree relatives of a patient with proven germline RET mutation
- Parents whose infants or young children have the clinical characteristics of MEN 2B

Who Should Be Tested: All first-degree relatives of patients with MEN 2A.
RET Mutation Testing: Confirming the specific mutation allows for tailored surveillance and management.

Counselling Objectives:

- Educate patients and families about the genetic nature of MEN 2A.
- Discuss the implications of genetic testing results.
- Provide psychological support.

Surveillance Strategies:

- Regular biochemical and imaging screenings for early detection of associated tumors.
- Prophylactic thyroidectomy in mutation carriers to prevent MTC.
- Patients with CLA
- Families whose infants or young children have Hirschsprung disease
- Only a small blood sample is required for RET genotyping; therefore, it can be performed at or soon after birth. At the latest, genotyping should be done before time so that prophylactic thyroidectomy could be performed in the event of a positive result.

Conclusion:

- Effective Management: Bilateral laparoscopic adrenalectomy is effective in managing adrenal pheochromocytomas in MEN 2A patients.
- Essential Role of Genetic Counselling: Critical for early diagnosis, management, and psychological support of patients and at-risk family members.
- Multidisciplinary Approach: Combining surgical intervention with genetic counselling ensures comprehensive care and improved quality of life for MEN 2A patients.

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Cephalic and Podalic presentation in Obstetrics Uro-Oncology - An Unusual Renal Cell Carcinoma Metastasis

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Abstract:

Renal cell carcinoma constitutes 2-3% of all adult malignancies and often diagnosed incidentally.Therefore the classical RCC triad such as hematuria, flank pain and palpable mass is more of the exception rather than the rule. Renal malignancy have a strong tendency to metastasize hematogenously following occasionally unpredictable patterns of spread.Typically, RCC spreads to the liver, lungs or bones but seldom metastasizes to muscles or soft tissues.

Here, we discuss two upfront and unique presentations of RCC, two different soft tissue metastatic sites (scalp and gluteus), oncological behavior and a therapeutic conundrum.

Cephalic presentation- A 52-year-old woman presented with painful enlarging ulcerative nodule over the left scalp. PET-CT scan revealed a soft tissue nodule measuring (2× 1.5 cm) located subcutaneously on left parietal scalp region. Patient underwent palliative electron radiation therapy to scalp lesion and systemic therapy with lenvatinib to control progression of disease.

Podalic presentation- A 72-year-old male patient reported with a painful mass on the right buttock, as the first and unique signs of a previously undetected advanced RCC. MRI showed infiltrating enlarged mass (4.7 × 2.6 cm) in the right gluteus maximus with restriction diffusion. Due to the

clinical conditions, the patient underwent palliative radiation therapy delivered to the hemipelvis with the scope to relieve pain; subsequently started systemic therapy with pazopanib.

Scalp and Gluteus metastasis from RCC is an exceedingly infrequent phenomenon. The complexity of presentation underscores the need for vigilant approach from the oncologist to identify and manage this uncommon entity.

Keywords:

Renal Cell Carcinoma, Soft Tissue Seedling, Gluteus Metastasis, Scalp Metastasis, Palliative Radiotherapy

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Pleomorphic Sarcoma of Prostate – A Rare Case Report

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Abstract:

Introduction:

Primary sarcoma of the prostate is an extremely rare malignancy, accounting for less than 0.1% of all primary prostate cancers. Pleomorphic sarcoma of the prostate is even rarer. We present this case due to its exceptional rarity

Case History:

A 53-year-old diabetic male presented with fever, pain, hematuria, and urinary retention for three months. Contrast-enhanced CT of the pelvis revealed an enlarged prostate (240 cc). The patient underwent transurethral resection of the prostate. Histopathological examination of TURP specimen showed spindle cell proliferation with marked nuclear pleomorphism, hyperchromasia, pleomorphic tumor cells, and multinucleated giant cells, with increased mitotic figures. Immunohistochemistry revealed tumor cells strongly positive for Vimentin and a MIB1 index of 30%, while negative for CK, LCA, S100, HMB45, GATA-3, SMA, and Desmin, confirming the diagnosis of undifferentiated high-grade pleomorphic sarcoma of the prostate.

Post-TURP contrast-enhanced MRI pelvis showed a markedly enlarged prostate (10×10×13 cm) projecting into the bladder, involving seminal vesicles, and abutting the mesorectal fascia. Serum PSA was 1.28. The patient received neoadjuvant radiotherapy (50 Gy in 25 fractions via VMAT to the prostate). Post-radiotherapy CE-MRI showed residual solid-cystic lesion (7.5×5.8×5 cm), still abutting the bladder and invading seminal vesicles. Then he received 6 cycles of chemotherapy (Doxorubicin 20 mg/m^2 D1-D3 and Ifosfamide 1500 mg/m^2 D1 to D4). Post chemo CE-MRI pelvis showed markedly reduced size of prostate (52cc) with residual lesion not invading seminal vesicles and urinary bladder. The patient declined surgery and was subsequently started on metronomic chemotherapy (Etoposide 50 mg OD for 21 days in 28-day cycles). After four cycles, prostate size was reduced to 34 cc, with complete response at primary.

Discussion:

A literature review identified only one prior case of pleomorphic sarcoma of the prostate (Iwahashi Y et al., IJU Case Reports, 2020). Although surgery is typically the preferred treatment, this case was managed with radiotherapy and chemotherapy, demonstrating potential for non-surgical management.

Conclusion:

Pleomorphic sarcoma of the prostate is an aggressive and rare malignancy. Accurate diagnosis requires advanced imaging and histopathology. This case underscores the importance of considering pleomorphic sarcoma in differential diagnoses of prostate tumors and highlights the potential efficacy of non-surgical treatment approaches.

Keywords:

Pleomorphic, Prostate, Sarcoma

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Urachal Adenocarcinoma at Dome of UB by Robot Assisted Partial Cystectomy in a Elderly Female

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Abstract:

Aim:

To clinical of a urachal adenocarcinoma at dome of UB it is diagnostic workup & surgical management by robot assisted partial cystectomy.

Method:

A 70yrs old female presented our OPD with complaints of Urgency, Frequency & Nocturia since 01yrs. Associated with hematuria 01yrs with pedal edema of 01yrs duration. H/o hypertension & diabetes. H/o TUR Biopsy 24/07/2024.

USG:

Approximately 20x28x28mm polypoidal mass in anterior wall of UB with extension into adjacent bowel wall.

CECT:

Show lobulated mildly enhancing mass lesion involving midline anterior wall measuring 4x4cm & projecting in the anterior perivesical fat region. Slight extension in bladder lumen ---- ? Urachal Carcinoma.

TUR Biopsy:

Was done under LA on 24/07/2024 showed columnar epithelium, poorly prepaired specimen, repeat biopsy was advised.

Surgical Management:

- Robot assisted partial cystectomy as urachal adenocarcinoma was suspected after clinical & radiological picture.
- Partial cystectomy was performed with adequate bladder wall margins upto the umbilicus.

HPE:

Papillary carcinoma with mucus differentiation (High grade), tumor invaded superficial & deep muscularis propria.

Discussion:

- During the first trimester of prenatal development, urine drains from the fetal bladder through the allantois that exits the umbilicus.
- This channel closes at the umbilical end during the second trimester to form a remnant hollow tube between the bladder and the umbilicus, known as the urachus.
- Typically, the urachus closes and elongates to form a fibrous cordlike structure running along the retropubic space, connecting the apex of the bladder to the umbilicus.

Conclusion:

- Urachal carcinoma is a rare and aggressive malignancy.
- The low incidence of the disease results in limited large-scale clinical trials that could provide standardized guidelines for its diagnosis and management.
- Despite this obstacle, physicians can derive insight from the available case studies and large-scale case series that provide data on this rare disease.
- Although the criteria for urachal carcinoma diagnosis are controversial, diagnoses typically involve cystoscopy and a CT urogram to characterize the localization of the tumor, other necessary imaging studies to rule out the possibility of other primary adenocarcinoma, and transurethral biopsy for pathologic examination.

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Synchronous Papillary Renal Cell Carcinoma and Gastrointestinal Stromal Tumor: A Rare Case Report

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Abstract:

Introduction:

Renal cell carcinoma (RCC) is a common tumor in kidney, accounts for 2-3% of all adult malignancies. Gastrointestinal stromal tumor (GIST) originate from intestinal cell and commonly arises from stomach, incidence 10-15 cases/ million. They seldom occur simultaneously in sporadic cases, incidence 2.2%. Such association is supported by common genetic and molecular pathways involving tyrosine kinase. Here we present a unusual case of synchronous RCC & GIST of stomach and for documentation.

Case History:

A 63 years old male clinically presented with pain abdomen and vomiting for 1 month. CECT abdomen (20.01.2024) showed a heterogenous lesion arising from lower pole of left kidney, size 12*9.2*9.1cm. He undergone Left Radical Nephrectomy with Retroperitoneal lymph node dissection on 23.01.2024. Post-op histology was Papillary renal carcinoma, grade 3 with stage pT3aN0M0.

Again presented with pain abdomen and dyspepsia for 1 month, 3 months of after surgery. CECT abdomen (10.05.2024) showed exophytic mass from gastric body, size 3.8*3.8*3cm. UGIE showed ?GIST and biopsy revealed spindle cell neoplasm + GIST. He undergone Explaratory laparotomy + sub-total gastrectomy + omentectomy + resection anastomosis on 30.05.2024. Post-op histology showed GIST. NGS showed positive c-KIT and p53 mutation.

PET-CT (17.10.2024) showed lung and vertebral metastasis for which received palliative RT of dose 30gy/10# from 11.11.2024 to 22.11.2024.

Discussion:

Occurrence of simultaneous papillary RCC and GIST is unusual. Both are related to mutation in proto-oncogenes c-MET & c-KIT in familial tumors. Surgery is mainstay of treatment. Both tumors well respond to tyrosine kinase inhibitors.

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Enfortumab Vedotin: Use of EV in Advanced Bladder Cancer – A Single Centre Experience

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Abstract:

Background:

Enfortumab vedotin(EV), is an antibody-drug conjugate used for the treatment of urothelial cancer. It is a nectin-4-directed antibody and microtubule inhibitor conjugate. Enfortumab refers to the monoclonal antibody part, and vedotin refers to the payload drug (MMAE) and the linker. It is approved for usage in locally advanced or metastatic Urothelial cancer as a single agent or in combination with Pembrolizumab.

Materials – Methods and Results:

Case 1: 58year male, presented to the urologist with obstructive LUTS with hematuria. Evaluated to have urinary bladder mass, underwent TURBT – incomplete resection i/v/o high volume disease with muscle invading HGUC so he underwent RC post ileal conduit with no adjuvant therapy. 1.5 years later, recurrence with Liver & bony metastasis, received ddMVAC, NGS showed Exon 8 mutation of TP53, he was started on Avelumab. But progression on avelumab with an increase in liver metastases with deranged LFT, he was started on EV, as 2nd line maintenance despite Jaundice - reduced dose and then gradually increased to the recommended dose, as it was thought mainly due to Liver metastasis. During EV, LFT improved with no further jaundice, and bony metastases also responded. Best response – PR.

Case 2: 67year male, who was diagnosed c/o UTUC, post Radical Nephroureterectomy and adjuvant Gem-Carbo developed CKD so stopped therapy. Presented to our department with recurrence & metastases to omentum/peritoneum. NGS showed TP53 Exon 8 mutation & FANCA Exon 14 mutation-positive, he was started on Pembrolizumab. But progressed post 4 cycles, so he was started on single agent EV at 1.25mg/kg, but developed EV-induced Vesico-bullous lesion involving >50% of the BSA post 1st cycle D15, which ended in fatality.

Conclusion:

This case series depicts in spite of good response for EV, but the fatal AE probably due to changes in population dynamics/ethnicity. So a larger population-based study on the Indian population is necessary to further comment on its efficacy and adverse events in our setting.

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Management of Bilateral Renal Angiomyolipoma in a Tuberous Sclerosis Complex Patient: Two Case Reports

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Abstract:

Introduction:

Renal angiomyolipoma represents an uncommon benign renal neoplasm frequently linked to tuberous sclerosis complex (TSC), a genetic condition characterized by hamartomas affecting various organs. Here, we present two patients with clinically proven tuberous sclerosis with bilateral renal angiomyolipoma, due to its rarety and documentation.

Case No. 1: A 44-year old male who presented with adenoma sebaceum at the age of 3 years, with no notable neurological or developmental deficits. However, at age 42 years, he began experiencing abdominal discomfort, prompting imaging studies that revealed bilateral renal angiomyolipoma. A right nephrectomy was performed at an external facility for an unknown reason. Histopathological and immunohistochemical analysis confirmed as angiomyolipoma, and subsequent evaluations indicated progression of the tumour in the left kidney. To manage the left renal angiomyolipoma and preserve renal function, patient was initiated on everolimus, an mTOR pathway inhibitor. Follow-up examinations have demonstrated a marked decrease in tumour size alongside stable renal function.

Case No. 2: A 22-year old female who presented with adenoma sebaceum at age 4 years, with café au lait spot. At the age of 21, she complained abdominal pain, for which she underwent imaging, and subsequent histopathology confirmed the patient as bilateral renal angiomyolipoma. She was advised tablet Evorlimus, but she was lost to follow up.

Discussion:

Tuberous sclerosis is associated with mutation of TCS 1/2 genes releases Hamartin and Tuberin, those are responsible for m-TOR pathway. It is associated with benign tumours of brain, subependymal gaint cell astrocytoma, bilateral angiomyolipoma of kidney, Rhabdomyoma of kidney, lymphangiomyomatosis of lung. The prevalence of renal angiomyolipoma is 0.2-0.6% with a 20% association with TSC.

These two cases we report here due to its rarity and documentation.

Keywords:

Tuberous Sclerosis Complex, Renal Angiomyolipoma, Adenoma Sebaceum, Everolimus, Nephrectomy

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Primary Urinary Bladder Endometriosis: An Atypical clinical Presentation in a 35-Year-Old Female

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Abstract:

Introduction:

- Endometriosis a painful condition that affects up to 10% of women of reproductive age and occurs when cells similar to those that line the uterus grows elsewhere in the body. One of the types of endometriosis is urinary tract endometriosis (UTE). It affects 0.3 to 12% of all endometriosis patients. Although the bladder is the most common site of UTE, bladder endometriosis, in general, is rare.
- Bladder endometriosis can be superficial (only found on the surface of the bladder), or deeper and found on the inside of the bladder wall. Rarely, it can also affect the ureter, which is the muscular tube that connects the kidney to the bladder. Bladder endometriosis can also be either primary (occurring spontaneously) or secondary (occurring after pelvic surgery).

Causes of bladder endometriosis:

- The exact cause of bladder endometriosis is still not clear. Researchers developed several theories to explain the cause of the disease. One of these includes the migratory or metastatic theory. It proposes that retrograde menstruation causes products of the period to "go back" into the pelvis and implant in the bladder wall. This kickstarts the process of inflammation and adhesion with scarring that leads to endometriosis.

Symptoms of bladder endometriosis

- As the location and size of bladder endometriosis can vary considerably from patient to patient, so do the symptoms.
- A significant proportion of patients present with so-called urinary storage symptoms when first diagnosed. These can include bladder irritation, urgency, frequency, and painful symptoms when the bladder is full. Less commonly, patients report blood in the urine.
- Importantly, the symptoms tend to occur cyclically with the menstrual cycle and are usually worse in the days leading to the period. As Dr. Seckin has stated, "if the symptoms are overlapping the periods, menstruation, before, during and after, certainly bladder endometriosis should be suspected."

Method:

- 35 yrs female presented with dysuria, increased frequeny since last 4 months Dysmenorrhea and Chronic pelvic pain since last 4 months no h/o any hematuria, lithauria, or any other urinary symptons

Pathophysiology:

- Endometrial tissue infiltrates the bladder wall, causing cyclical hematuria and bladder irritation.
- Hormonal influence during the menstrual cycle exacerbates symptoms.

Management:

- Nonsteroidal anti-inflammatory drugs (NSAIDs) can temporarily relieve pelvic pain and inflammation. In addition to medication, physical therapy may play a role in managing bladder endometriosis. Pelvic floor physical therapy aims to improve muscle function and reduce pain in the pelvic regions with other types of endometriosis, the treatment of bladder endometriosis will depend on several factors. These include the patient's age, fertility status and family planning preferences, the severity of the disease, the severity of urinary symptoms, and menstrual function.

Conclusion:

- Urinary bladder endometriosis should be considered in females with unexplained urinary symptoms, especially if they coincide with menstrual cycles.
- Early diagnosis and intervention can significantly improve quality of life and prevent complications.

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A Case Report on Renal Cell Carcinoma with IVC Thrombus: A Life-Threatening Complication

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Dr. Panda S
KIMS, Bhubaneswar, India

Abstract:

Background:

Introduction: Renal cell carcinoma (RCC) is the seventh most common cancer in males, and the tenth most common cancer in females. RCC can manifest as fatigue, fever, hematuria, backache, hypercalcemia, high blood pressure, or weight loss, constituting 2% of all diagnosed malignancies [1,2]. The etiology of RCC is multifactorial, and smoking and drug exposure are among the most common causes of RCC [2]. RCC invades the inferior vena cava IVC and develops a venous tumor thrombus (VTT) in 4-10% of patients [2] The extension of the thrombus could reach the right atrium in less than 20% of the cases (8). According to Neves and Zincke, the level of the IVC thrombus was classified as Level I when it is limited to the renal vein (RV), Level II when it is below the hepatic vein, Level III when it is above the hepatic vein but below the diaphragm, and Level IV when the thrombus extends above the diaphragm or into the right atrium (9). The level of the thrombus dictates the surgical approach which could include total nephrectomy, limited or extensive IVC dissection, or vascular or cardiopulmonary bypass (10). A higher level of the thrombus in the IVC did not affect the long-term survival; nevertheless, it was associated with a higher rate of surgical complications and hospital stay especially with Level III and IV thrombus (12). Here we report a case of RCC with IVC thrombus, a rare life threatening complication, in a 49 year old female who was operated in our centre.

Case presentation: A 49 year old female with a past medical history of hypertension presented with a chief complaint of left flank pain for last 6months. The pain was gradual in onset, progressive, and non-radiating without vomiting, hematuria, fever. But it was asso. with anorexia and fatigue. She had no H/O smoking or any kind of addiction. On examination she was afebrile and hemodynamically stable with average built. Her abdomen was mildly tender, without any palpable mass and the rest of the local and systemic examination was unremarkable. Her hemoglobin was 9.4gm%, calcium 8.2 mg/dl, vit D3 15ng/ml otherwise all blood parameters were WNL. on USG whole abdomen she was diagnosed with left renal mass and was further evaluated. On CECT KUB Left kidney shows well defined heterogenously enhancing SOL of size 66 x 51 mm showing extension of left renal vein reaching upto IVC (stage 3a robson's staging) (fig 1). Renal doppler study suggested a heterogeneously hypoechoic mass lesion in upper pole of left kidney with extension into left renal vein and IVC and is seen over a length of 5-6 cm with in IVC and approximately 3.5 cm below intrahepatic IVC suggestive of neoplastic etiology. -Left main renal artery and left upper segment artery not visualised. - Small accessory renal artery in upper pole of left kidney. - Normal right renal doppler study

Open left radical nephrectomy with IVC thrombectomy was planned, chevron incision was made (fig 2), Left Upper Pole renal dissection done followed by lower pole dissection done. Gonadal vein, lumbar veins & ureter identified & dissected till hilum. Large left renal vein is seen with thrombus extending into IVC, Kocherisation done & IVC dissected from up. IVC cleared 5cm above & below renal vein. Right renal vein identified and hooked. Serial clamping of infrarenal IVC, right renal vein and suprarenal IVC done. IVC opened & thrombus retrieved followed by closure of IVC with 5-0 prolene. Left renal vein & artery tied & cut. Left kidney retrieved.

The nephrectomy specimen revealed that the tumour was protruding from superior pole of left kidney (fig 3) Histopathology of the specimen showed malignant cells with clear cytoplasm and distinct membranes. Cells were uniform, round, irregular, and vesicular nuclei with small nucleoli i.e Clear cell renal cell carcinoma. It is a unifocal, 6cm (maximum dimension). Grade- 1(WHO/ ISUP grade) upper pole Tumour without involving renal capsule, perinephric fat, fascia of gerota, sinus pad of fat, adrenal gland, ureter, renal artery. Tumour embolus is seen in lumen of renal vein but vein wall is free. Sarcomatoid features, Rhabdoid

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features, Tumour necrosis were not identified. Lymphovascular Invasion also not identified. Pathological staging: pT3a pN (not submitted) pM (not applicable). The patient responded well to treatment and was discharged with outpatient follow-up at six months with CT Scan and then yearly.

Conclusion: RCC with metastases to IVC leads to a poor prognosis. While CT scans can delineate the renal tumor margins, doppler is more efficient in detecting IVC invasion. Mayo staging helps in classifying the thrombotic mass in IVC. Management to date is difficult, as surgical excision is the only curative option. Our case highlights the importance of standard preoperative CT scan and doppler imaging to assess IVC invasion and its morphologic features, including vessel breach or complete occlusion of the IVC.

Keywords:

Renal Cell Cancer, IVC Extension, Venous Thrombus

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Persistent Mullerian Duct Syndrome With Undescended Testis and Testicular Seminoma - A Rare Case

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Abstract:

Persistent Mullerian duct syndrome (PMDS) is a rare type of male pseudohermaphroditism caused by a deficiency in anti-Müllerian hormone (AMH) or a defect in its type II receptor. In total, there have been ~150 cases of PMDS reported in adults, the majority in the US, Europe and the Middle East. Medline/Pubmed search retrieved 44 articles (49 patients) of testicular tumors associated with PMDS, majority(59%) presenting with a large abdominal mass. Our case is a 22 year old male patient with PMDS with abdominal mass diagnosed as seminoma testis. Our aim of this case presentation is rarity of case (PMDS with testicular tumour) and association of undescended testis increases the likelihood of developing testicular tumour in PMDS. The clinicians should be aware of rare entity while dealing with the cryptorchidism with inguinal hernia and necessary management should be done to offer proper treatment.

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Synchronous Primary Lobular Breast Cancer and Renal Cell Carcinoma: A Rare Case Report

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Dr. Diptirani Samanta
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Dr. Biren Banerjee
IMS & SUM Hospital, Bhubaneswar, India

Dr. Smarak Senapati
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Abstract:

Introduction:

Synchronous malignancies have been commonly associated with kidney cancer. Bladder, prostate, colorectal and lung cancer are mostly associated with Renal cell carcinoma (RCC). Breast cancer often co-occurs with colorectal, endometrial, and ovarian cancers. But the synchronous presentation of invasive lobular breast carcinoma and clear cell renal cancer is rare.

Case Presentation:

A 55-year-old postmenopausal woman presented with lump in right breast. Biopsy was invasive lobular carcinoma of breast. PET-CT revealed right breast mass of size 1.7 x 0.9 cm (SUVmax 7.2) in lower outer quadrant,2.4 x 1.7 cm (SUVmax 3.3) in upper inner quadrant, right level 1 axillary node of size 1.4 x 1.1 cm (SUVmax4.7) along with a mass of heterogenous density in right mid and lower pole of kidney of size 8.1 x9.0 cm (SUVmax4.1) with no pericapsular invasion, no renal vein and IVC or any lymphnode involvement. She underwent right Modified Radical Mastectomy and right Radical Nephrectomy. Post-op histopathology for MRM specimen was invasive lobular carcinoma PT3PN1CM0, ER+, PR+, GCDFP15+, loss of E-CADHERIN, PAX-8 and HER2NEU negative, KI67 12% and for right nephrectomy specimen was clear cell carcinoma, no pericapsular invasion, negative margin PT2CN0CM0 with CD10+, GCDFP15- and PAX8 non-contributory. She received 8 cycles chemotherapy followed by Radiotherapy for breast carcinoma, which concluded in November 2024. Close observation was planned in Tumour Board for RCC as peri-op & radiological findings showed negative perirenal nodes. The patient is asymptomatic now and taking anastrozole 1mg once daily.

Clinical Discussion:

The coexistence of breast carcinoma with RCC is uncommon. Most reported cases involve metastatic tumours or metachronous breast malignancy with RCC. The etiology of synchronous malignancy is complex, and treatment options usually include a combination of surgery and/or adjuvant therapy. We tried to find out any common pathway for such occurrence and did PTEN and Tp53 mutation analysis through NGS. Both came positive, so possibility of COWDEN syndrome was established. COWDEN Syndrome also known as PTEN hamartomatous tumour is a rare genetic disorder caused by mutations of PTEN gene. In COWDEN Syndrome ,life time risk of breast cancer is 85% and of kidney cancer is 15-35% and typically presents later in life (40s-50s).

Conclusion:

This case report contributes valuable insights to the limited literature on synchronous breast cancer with renal cell carcinoma. Incidence of COWDEN syndrome is 1 in 200000 individuals in general population but might be underestimated due to underdiagnosis or misdiagnosis. This case is being reported due to its rarity and for documentation.

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Primary Diffuse Large B -Cell Lymphoma of Ureter: A Case Report

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Dr. Dipti Rani Samanta
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Dr. Tapan Kumar Sahoo
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Dr Krushna Ch Pani
Acharya Harihar Regional Cancer Research Centre, Cuttack, India

Abstract:

Background:

Around 30% of all non-Hodgkin lymphoma (NHL) cases arise from extra nodal sites which requires site-specific strategies either for diagnosis or therapy. Gastrointestinal (GI) tract, skin, bone, and brain are the most common sites of extra nodal lymphoma. If the ureters are involved, it is typically due to extrinsic compression from bulky lymphadenopathy. Urinary tract and male genital organ lymphoid neoplasms are uncommon, accounting for less than 5% of all primary extra nodal lymphomas. Primary involvement of the ureter is rare, with few cases reported.

Case Report:

A 40-year-old male patient presented with increasing symptoms of urinary frequency, and left flank pain. An ultrasound (USG) of the abdomen and pelvis revealed moderate hydro nephrosis of the left kidney without cortical thinning, and a hypoechoic lesion of size 6cm in left ureter with irregular margins raising a suspicion for neoplastic lesion. CT urography confirmed the presence of left upper ureteric mass mostly at pelvi-ureteric junction with associated hydronephrosis. The patient underwent a left nephroureterectomy with a cuff of the bladder. Histopathology revealed consistent Diffuse Large B-cell Lymphoma (DLBCL). Immunohistochemistry showed CD45, and CD20 positivity, and CD3 negativity, confirming the diagnosis of DLBCL. The proliferation index (Ki-67) was notably high at 70%. The patient received systemic chemotherapy with 6 cycles of R-CHOP regimen last on 20th March 2024. A follow-up PETCT showed no evidence of metabolically active residual lesion with Deauville score of 1 indicating favourable complete response to the treatment.

Conclusion:

This case highlights the complexity of diagnosing and managing primary ureteric lymphoma, underscoring the importance of a multidisciplinary treatment approach in such rare presentations of DLBCL. The present case needs to be reported due to its rarity.

Keywords:

DLBCL, Nephroureterectomy, Ureter primary

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Treatment of Metastatic Renal Cell Carcinoma with Nivolumab and Cabozantinib: Case Scenarios

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Abstract:

Introduction:

Metastatic Renal cell carcinoma (RCC) is a therapeutic challenge to clinicians since it shows significant resistance to chemotherapy and radiotherapy. With the introduction of Immuno Oncology (IO) drugs and Tyrosine Kinase Inhibitors (TKI), the treatment paradigm of RCC has evolved. In recent years they have shown improved response rate and favorable toxicity profile.

Case History 1:

A 45 year old male presented with complain of hematuria for 6 months and cough for 1 month. CECT Abdomen (03/09/2024) showed a large a heterogeneously enhancing solid mass of size 17.5cm*14.5cm*12.5 cm in the mid and lower pole of left kidney extending to proximal part of left renal vein with multiple enlarged pre and para aortic Lymphadenopathy.

Renal Biopsy suggestive of Clear cell carcinoma and IHC revealed CD10 positive

PETCT Scan of Whole Body suggestive of large necrotic mass with low grade metabolic activity arising from lower and mid pole kidney lesion with multiple abdominal, mediastenal nodal metastasis and lung metastasis

Patient received Injection Nivolumab 240mg 2weekly for 5 cycles and Tablet Cabozantinib 40mg 1 tablet once daily for 3 months

On evaluation PETCT scan of whole body suggestive of favourable response in comparison to pre-therapy scans.

Case History 2:

50 year old male presented with complain of low backcache for 1 month, he is a known case of RCC of left kidney post op

On examination there was a cutaneous nodule in the chin. On metastatic work up CECT Abdomen and Pelvis revealed multiple vertebral metstasis. MRI screening of whole spine and MRI of DorsoLumbar Spine revealed multiple vertebral metastasis. Also FNAC from the lesion revealed poorly differentiated carcinoma.

Patient treated with Nivolumab for 5 cycles, Cabozatinib for 2and half months and Denosumab 2 cycles

Complete clinical resolution of cutaneous nodule after therapy

Conclusion:

Nivolumab, a programmed Death-1 immune check point inhibitor (ICI) has become a standard treatment for metastatic RCC particularly after failure of TKIs. ChekMate 025, CheckMate 9ER, TiNivo-2, PROBE Trial and NCI-2023-07385 are the key clinical trials evaluating Nivolumab in the treatment of metastic RCC leads to improved Overall Survival (OS), Progression Free Survival (PFS) and Objective Response Rate (ORR).

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A Rare case of Carcinoma Nasopharynx with synchronous Renal Cell Carcinoma

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Acharya Harihar Regional Cancer Research Centre, Cuttack, India

Abstract:

Introduction:

The occurrence of nasopharyngeal cancer is notably influenced by geography and race. In the majority of the global population, it is a rare malignancy. Renal cell carcinoma (RCC) constitutes about 3% of all cancers, with the greatest incidence in Western nations.

However, the occurrence of both NPC and RCC at the same time is exceptionally rare.

Case Report:

Here we present a case of concurrent Renal cell carcinoma with carcinoma nasopharynx. A 68 years old male presented to our hospital with complaints of swelling in left side of neck for 3 months. On Contrast enhanced CT imaging of neck, a mass in nasopharynx with multiple ipsilateral neck nodes was found, which on histo-pathological examination found to be poorly differentiated squamous cell carcinoma. On FDG-PET CT scan, an low grade FDG avid exophytic lesion in left kidney was appreciated, for which the patient was undergone CT guided biopsy found to be clear cell RCC, WHO grade I.

Discussion:

Our patient had two distinct synchronous primary tumors, NPC and RCC. To our knowledge, this rare combination has been reported previously in only three patients two cases with concurrent NPC and RCC and one in which RCC was diagnosed 5 years after NPC.

Smoking is a common major risk factor for both NPC and RCC. It has been reported that the probability of developing RCC increases approximately twofold with cigarette smoking.

Interestingly, the biological similarity of in vitro NPC and RCC cell lines was implied by one comparative study, in which tumorigenicity was inhibited in both cell lines when chromosome 3 was transferred into the cells. Moreover, treatment of NPC and RCC cell lines with histone deacetylase inhibitors shows a similar pattern of alteration of gene expression.

Although little is known about this type of presentation, the similar in vitro behavior indicates a link between the NPC and RCC cell lines. Awareness of this simultaneous presentation and inclusion of the nasopharynx and kidneys in the screening and staging processes of RCC and NPC might result in detection of more analogous cases and help elucidate their clinical relevance.

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SCIENTIFIC AGENDA

Day 1 10/01/2025,Friday

Hall - A (Main Hall)

Breakfast (7:30 AM – 8:30 AM)

Tea, coffee, water along with refreshments will be served throughout the sessions and across the day in the auditorium.

Hot topics in Urologic Pathology
(8:30 AM - 9:40 AM, 30 Minutes Talk followed by 5 Minutes Q & A)

Chairpersons: **Dr. Nandita Kakkar, Dr. Samir K. Behera, Dr. Kaumudee Pattnaik, Dr. Sudipta Mohakud, Dr. Lity Mohanty**

Multiparametric MRI in Prostate Cancer Diagnosis and Management: Role of Pathologist – **Dr. Cristina Magi - Galluzzi (8:30 AM - 9:05 AM)**

Contemporary Update on Prostate Cancer Grading – **Dr. Ming Zhou (9:05 AM - 9:40 AM)**

Keynote Address (9:40 AM - 10:15 AM)

Chairpersons: **Dr. Sangeeta Desai, Dr. Nuzhat Husain, Dr. Lity Mohanty, Dr. Niharika Panda, Dr. Matthew O. Leavitt**

Applications of Digital and Computational Pathology and Artificial Intelligence in Genitourinary Pathology Diagnostics – **Dr. Mahul B. Amin**

Prostate cancer (10:15 AM - 10:50 AM)

Chairpersons: **Dr. T. S. Ganesan, Dr. Debahuti Mohapatra, Dr. Dipti Rani Samanta, Dr. Saroj K. Das Majumdar, Dr. Aiman Haider**

Prostate Surgery without histopathology proof in era of modern and molecular imaging **Dr. Makarand Khochikar (10:15 AM - 10:35 AM)**

Debate: PSMA PET - CT is the imaging of choice in Prostate Cancer **(10:35 AM - 10:50 AM)**
For: **Dr. Girish K. Parida**
Against: **Dr. Biswajit Sahoo**
Expert comment: **Dr. Makarand Khochikar**

Panel discussion (10:50 AM - 11:30 AM)

Localized prostate cancer - multimodality management

Chairpersons: **Dr. Anita Ramesh, Dr. Amit Joshi**

Moderator: **Dr. Surendra N. Senapati**

Panelist

Dr. Sandy Srinivas
Dr. Prasant K. Parida
Dr. Cristina Magi - Galluzi
Dr. Lucy Pattanayak
Dr. Amit Sehrawat

Dr. Animesh Saha
Dr. Sailendra Parida
Dr. Lalatendu Moharana

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SCIENTIFIC AGENDA

Keynote Address (11:30 AM - 12:05 PM)

Chairpersons: **Dr. Surendra N. Senapati, Dr. Anita Ramesh, Dr. Amit Joshi, Dr. Soumya S. Panda, Dr. Makarand Khochikar**

Oligometastatic prostate cancer: Current understanding and consensus on multi - modality management - **Dr. Sandy Srinivas**

Metastatic hormone sensitive prostate cancer : Choosing wisely - **Dr. Krishna Kumar Rathnam (12:05 PM - 12:25 PM)**

Industry Sponsored Session (12:25 PM - 1:25 PM)

Chairpersons: **Dr. Mahul B. Amin, Dr. Rajal B Shah, Dr. Cristina Magi - Galluzzi, Dr. Ghanashyam Biswas**

Guardant NGS in GU malignancies - **Dr. Soumya S. Panda (12:25 PM - 12:55 PM)** ***by Zydus Lifesciences***

Improving outcomes in prostate cancer care with AI - based risk stratification - **Dr. Uttara Joshi (12:55 PM - 1:25 PM)** ***by AIRA Matrix***

Lunch break (1:25 PM – 1:55 PM)

Industry Sponsored Session
Panel discussion (1:55 PM - 2:35 PM)

Castrate resistant prostate cancer - **by Intas Pharmaceuticals**

Chairpersons: **Dr. Kshitish C. Mishra , Dr. Santosh Menon, Dr. Sunil Agarwala**

Moderator: **Dr. Anita Ramesh**

Panelist

Dr. Ming Zhou
Dr. Sudatta Ray
Dr. Vijay K. Srinivasalu
Dr. Rajiv Tangri

Dr. Abhishek Raj
Dr. Aiman Haider
Dr. Saumya R. Mishra

Hot topics in Urologic Pathology
(2:35 PM - 4:20 PM, 30 Minutes Talk followed by 5 Minutes Q & A)

Chairpersons: **Dr. Kshitish C. Mishra , Dr. Santosh Menon, Dr. Sunil Agarwala, Dr. Preeti Diwaker, Dr. Sunayana Misra**

Divergent Differentiations and Variant Histologies of Bladder Cancer – **Dr. Gladell P. Paner (2:35 PM - 3:10 PM)**

Germ Cell Tumors of the Testis: Diagnoses that You Do Not Want to Miss – **Dr. Andres M. Acosta (3:10 PM – 3:45 PM)**

Chairpersons: **Dr. Ghanashyam Biswas, Dr. Santosh Menon, Dr. Manas R. Pradhan, Dr. Tanushree Mishra, Dr. Pritinanda Mishra**

Penile Cancer: A pathologist's perspective on current trends in diagnosis, staging, and treatment – **Dr. Jasreman Dhillon (3:45 PM -4:20 PM)**

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SCIENTIFIC AGENDA

Case-based discussions (4:20 PM - 5:35 PM)

Chairpersons: **Dr. Sandhya Sundaram, Dr. Sonia Badwal, Dr. Rajni Parmar, Dr. Anuradha Sekeran, Dr. Paromita Roy**

Treatment-related neuroendocrine carcinoma of the prostate - **Dr. Rajal B. Shah** (4:20 PM - 4:35 PM)

Molecularly defined renal cell carcinomas - **Dr. Rohit Mehra** (4:35 PM - 4:50 PM)

Ductal adenocarcinoma of the prostate - **Dr. Ming Zhou** (4:50 PM - 5:05 PM)

Endophytic tumors of the urinary tract - **Dr. Gladell P. Paner** (5:05 PM - 5:15 PM)

Non-epithelial tumors of the penis - **Dr. Jasreman Dhillon** (5:15 PM - 5:35 PM)

Industry Sponsored Session (5:35 PM - 6:15 PM)

Chairpersons: **Dr. Samarendra Dash, Dr. Sanjay Mishra, Dr. Goutam Panda, Dr. Rajan Arora**

Oral GnRH analogues: Recent updates - **Dr. Susanta K. Paikaray** (5:35 PM - 5:55 PM) ***by Zydus Lifesciences***

Evolving landscape in hormonal management of prostate cancer - **Dr. Amit Joshi** (5:55 PM - 6:15 PM) ***by AstraZeneca***

Cultural program (6:30 PM - 7:30 PM)

Faculty Dinner (7:00 PM Onwards)

Hall - B (Parallel Hall)

Judges: **Dr. Sangeeta Desai, Dr. Nandita Kakkar, Dr. Sandhya Sundaram, Dr. Nuzhat Husain, Dr. Seema Kaushal, Dr. Rajni Parmer, Dr. Santosh Menon, Dr. Sonal Sharma, Dr. Pritinanda Mishra, Dr. Anuradha Sekaran, Dr. Subhashis Mohanty, Dr. Meenakshi Swain, Dr. Murali Varma**

Pathology : Oral Presentations **(10:30 AM - 1:00 PM)**

Judges: **Dr. Lucy Pattanayak, Dr. Amit Sehrawat, Dr. Sharada Mailankody, Dr. Tanushree Satpathy, Dr. Abhishek Raj, Dr. Sthiti Das, Dr. Sunil Jaiswal**

Clinical : E - Poster Presentations **(2:30 PM - 3:45 PM)**

Day 2 11/01/2025,Saturday

Hall - A (Main Hall)

Breakfast (7:30 AM – 8:00 AM)

Tea, coffee, water along with refreshments will be served throughout the sessions and across the day in the auditorium.

Industry Sponsored Session (8:00 AM - 8:25 AM)

Chairperson: **Dr. Makarand Khochikar, Dr. Padmalaya Devi, Dr. Amitabh Jena, Dr. Soumya S. Panda, Dr. Sulata Choudhury**

Augmenting Prostate Cancer Diagnosis with AI: Real-World Insights, Challenges & Solutions - **Ms. Shriya Kumar** (8:00 AM - 8:25 AM) ***by Qritive***

Keynote Address (8:30 AM - 9:05 AM)

Role of HPV in the management of penile cancer: Where do we stand? - **Dr. Philip E. Spiess**

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SCIENTIFIC AGENDA

Hot Topics in Urologic Pathology
(9:05 AM - 10:50 AM, 30 Minutes Talk followed by 5 Minutes Q & A)

Chairpersons: **Dr. Prafulla K. Das, Dr. Susama Patra, Dr. Seema Kaushal, Dr. Sonal Sharma, Dr. Meenakshi Swain**

Large Gland Lesions of the Prostate – **Dr. Rajal B. Shah (9:05 AM – 9:40 AM)**

How New Developments Impact Diagnosis in Existing Renal Neoplasms – **Dr. Sean R. Williamson (9:40 AM - 10:15 AM)**

Pink Cell Tumors of the Kidney: Making Sense – **Dr. Rohit Mehra (10:15 AM – 10:50 AM)**

Case based discussion (10:50 AM - 11:30 AM)

Chairpersons: **Dr. Sandhya Sundaram, Dr. Seema Kaushal, Dr. Dilleswari Pradhan, Dr. Sagarika Samantaray, Dr. Poonam Elhence, Dr. Ruchi Mittal, Dr. Dilip K. Kar , Dr. Meenakshi Swain**

Clear cell and papillary tumors of the kidney - **Dr. Sean R. Williamson (10:50 AM - 11:05 AM)**

Sex cord-stromal tumors of the testis - **Dr. Andres M. Acosta (11:05 AM - 11:20 AM)**

An interesting Kidney tumor - **Dr. Jayaram N. Iyengar (11:20 AM - 11:30 AM)**

Industry Sponsored Session (11:30 AM - 12:25 PM)

Chairpersons: **Dr. Chira Ranjan Khadanga, Dr. Surendra N. Senapati, Dr. Sanjib Mishra, Dr. Debahuti Mohapatra, Dr. Seema Kaushal, Dr. Pranati Pradhan**

Management of Platinum ineligible advanced bladder cancer-
Dr. Chinmaya K. Pani (11:30 AM – 12:00 PM)

The Key Role Urology is Playing in Defining Pathology's Digital Future -
Dr. Matthew O. Leavitt (12:00 PM - 12:25 PM) ***by Lumea***

Lunch break (12:25 PM - 12:55 PM)

Clinical Uro - Oncology - Bladder cancer (12:55 PM - 1:25 PM)

Chairpersons: **Dr. Surendra N. Senapati, Dr. Swodeep Mohanty, Dr. Kunal Goutam, Dr. Ranajit Kar, Dr. Manas R. Baisakh, Dr. Subhashis Mohanty**

Non-muscle invasive bladder cancer: Management principles and recent advances-**Dr. Makarand Khochikar (12:55 PM - 1:10 PM)**

Debate: Bladder Preservation Strategies in Bladder Cancer - Combined modality treatment is preferred over Radical cystectomy in locally advanced bladder cancer **(1:10 PM - 1:25 PM)**

For: **Dr. Suman Das**

Against: **Dr. Sunil Agarwala**

Expert comment: **Dr. Siddhartha Nanda**

Industry Sponsored Session (1:25 AM - 1:50 PM)

Paradigm shift in management of muscle invasive bladder cancer -
Dr. Atul Batra (1:25 AM – 1:50 PM)

ISBN: 978-93-92106-53-8

SCIENTIFIC AGENDA

Panel discussion (1:50 PM - 2:30 PM)

Neoadjuvant and adjuvant strategies in bladder cancer

Chairpersons: **Dr. Deepak Rautray, Dr. Makarand Khochikar, Dr. Nachiketa Mohaptra**

Moderator: **Dr. Dipti Rani Samanta**

Panelist

Dr. Soumya S. Panda
Dr. Atul Batra
Dr. Jogamaya Pattnaik
Dr. Seema Kaushal

Dr. Samarendra Dash
Dr. Sandip K. Barik
Dr. Rajeev Saini
Dr. Shailesh Soni

Dr. Ganesh C. Subudi
Dr. Prashant C. Das

Industry Sponsored Session (2:30 PM - 3:10 PM)

Role of Opdyta in Adjuvant Urothelial carcinoma **- Dr. Srigopal Mohanty (2:30 PM - 2:50 PM)**
by Bristol Myers Squibb (BMS)

Optimising treatment strategies in metastatic urothelial cancer - **Dr. Susanta K. Paikaray (2:50 PM - 3:10 PM)**
by Merck

Keynote Address (3:10 PM - 3:45 PM)

Chairpersons: **Dr. Gladell P. Paner, Dr. Murali Varma, Dr. Ming Zhou, Dr. Makarand Khochikar, Dr. Amit Joshi, Dr. Siddhartha Nanda**

Metastatic Urothelial Carcinoma: New Horizons with emphasis on Antibody Drug Conjugates:
Dr. Ajjai S. Alva (3:10 PM - 3:45 PM)

Clinical management of variant histologies of bladder cancer - **Dr. Bivas Biswas (3:45 PM - 4:00 PM)**

Industry Sponsored Session (4:00 PM - 5:35 PM)

Panel discussion (4:00 PM - 4:40 PM)

Improving Survival and Quality of Life in frontline advanced RCC with CTLA-4 & PD - 1 inhibition -
by Bristol Myers Squibb (BMS)
Moderator: **Dr. Bivas Biswas**

Panelist

Dr. Srigopal Mohanty
Dr. Ganesh C. Subudhi
Dr. Prasant K. Parida
Dr. Goutam Panda

Chairpersons: **Dr. Susama Patra, Dr. Rajan Arora, Dr. Mohini Rao, Dr. Indranil Chakrabarti**

Troubleshooting and QC in IHC - **Mr. Kamal Peddinti (4:40 PM - 5:00 PM)** ***by PathnSitu Biotechnologies***

Role of Denosumab in Prostrate Cancer - Preventive & Therapeutic Approach -
Dr. Sachin S. Biswal (5:00 PM - 5:15 PM) ***by Reliance Life Sciences***

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SCIENTIFIC AGENDA

Liquid Biopsy in Cancer Care: Real-World Applications and Understanding - **Dr. Safi Gowhar (5:15 PM - 5:35 PM)** ***by OneCell Diagnostics***

Inauguration & Cultural program (6:00 PM - 7:30 PM)

Banquet Dinner (7:30 PM Onwards)

Hall - B (Parallel Hall)

Judges: **Dr. T .S. Ganesan, Dr. Sandy Srinivas, Dr. Krishna K. Rathnam, Dr. Siddharth Nanda, Dr. Soumya S. Panda, Dr. Surendra N. Senapati, Dr. Sunil Agarwala, Dr. Sulagna Mohanty**

Clinical : Oral Presentations **(9:30 AM - 11:30 AM)**

Judges: **Dr. Rajiv Tangri, Dr. Bijal Kulkarni, Dr. Sankalp Sancheti, Dr. Rupanita Biswal, Dr. Shilpy Jha, Dr. Rashmi Patnaik, Dr. Preeti Diwaker, Dr. Rohan Sardana, Dr. Vikram Mathew, Dr. Shivani Gandhi, Dr. Reetika Menia, Dr. Pavithra A, Dr. Poonam Elhence, Dr. Shruti Sabnis, Dr. Aimen Haider, Dr. Rajan Arora, Dr. Sunayana Misra, Dr. Pallavi Bhuyan**

Pathology : E - Poster Presentations **(1:00 PM - 3:00 PM)**

Day 3 12/01/2025,Sunday

Hall - A (Main Hall)

Breakfast (7:30 AM – 8:00 AM)

Tea, coffee, water along with refreshments will be served throughout the sessions and across the day in the auditorium

Industry Sponsored Session (8:00 AM - 8:25 AM)

Chairperson: **Dr. Mahul B. Amin, Dr. Rajal B. Shah, Dr. Ajjai S. Alva, Dr. Rohit Mehra, Dr. Jasreman Dhillon**

The Dynamic Duo: CTC and ctDNA **- Dr. Jayant Khandare (8:00 AM - 8:25 AM)** ***by OneCell Diagnostics***

Chairperson: **Dr. Atul Sharma, Dr. Saroj K. Das Majumdar, Dr. Dipti Rani Samanta, Dr. Sanjukta Padhi, Dr. Manas R. Pradhan, Dr. Subhashis Mohanty**

Keynote Address (8:30 AM - 9:00 AM)

Communicating Pathology Results for Personalized Medicine: How Are the Surgical Members of the Society of Urologic Oncology Using Pathology Reports to Guide the Treatment of Prostate Cancer Patients? - **Dr. Murali Varma**

Genitourinary malignancies: Making sense of Indian data from low - and middle - income countries with emphasis on conducting collaborative research **- Dr. Atul Batra (9:00 AM - 9:15 AM)**

ISBN: 978-93-92106-53-8

SCIENTIFIC AGENDA

Panel discussion (9:15 AM - 9:55 AM)

Germ cell tumor

Chairperson: **Dr. Atul Sharma, Dr. Saroj K. Das Majumdar, Dr. Dipti Rani Samanta, Dr. Sanjukta Padhi, Dr. Manas R. Pradhan, Dr. Subhashis Mohanty**

Moderator: **Dr. Rejiv Rajendranath**

Panelist

Dr. Sandy Srinivas
Dr. Satyabrata Das
Dr. Soumya S. Panda
Dr. Abani K. Nanda
Dr. P. Sai Sradha Patro

Dr. Girish K. Parida
Dr. Susant K. Paikaray
Dr. Ranjan K. Patel
Dr. Phanindra K. Swain
Dr. Subrat K. Sahu
Dr. Sugyan N Mohanty

Beyond immunotherapy and TKI in Management of Renal Cell Carcinoma - **Dr. Aditya Sarin (9:55 AM - 10:10 AM)**

Chairperson: **Dr. Sean R. Williamson, Dr. Birendranath Banerjee, Dr. Krupasindhu Panda, Dr. T. S. Ganesan, Dr. Ravindra B. Sabnis, Dr. Sumit K. Panda**

Renal Cell Carcinoma (10:10 AM - 10:45 AM)

1. Debate RCC: Adjuvant immunotherapy is the current standard of care in RCC – **(10:10 AM - 10:25 AM)**

For**: Dr. Aditya Sarin**

Against**: Dr. Srigopal Mohanty**

Expert comments: **Dr. Rejiv Rajendranath**

2. Combining systemic therapy with local therapy (SBRT) in mRCC : **Dr. Lucy Pattanayak (10:25 AM - 10:45 AM)**

Panel discussion (10:45 AM - 11:25 AM)

Metastatic renal cell cancer second line and beyond

Moderator: **Dr. Atul Sharma**

Panelist

Dr. Philip E. Spiess
Dr. Ghanashyam Biswas
Dr. Kanhu C. Patro
Dr. Sean R. Williamson
Dr. B. H. Srinivas
Dr. Sharada Mailankody

Dr. Sangram K. Panda
Dr. Nitish R. Acharya
Dr. Gurudutt Gupta
Dr. Sulagna Mohanty
Dr. Garima Sarawgi

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SCIENTIFIC AGENDA

Industry Sponsored Session

Chairperson: **Dr. Sushil Giri, Dr. Jita Parija**

Panel discussion (11:25 AM - 12:05 PM)

Recent advances in advanced Endometrial Cancer **by AstraZeneca**

Moderator: **Dr. Ghanashyam Biswas**

Panelist

Dr. Siddhartha Nanda
Dr. Bhagyalakshmi Nayak
Dr. Deepak Das
Dr. Arya K. Banidutta
Dr. Priya P. Nayak
Dr. Sachin S. Biswal

Dr. Bijayalaxmi Sahoo
Dr. Nitish R. Acharya
Dr. Indranil Chakrabarti
Dr. Ushashree Das

Panel discussion: (12:05 PM - 12:45 PM)

Neuroendocrine carcinoma in urogenital tract: Multimodality management in case-based discussions

Chairperson: **Dr. Prafulla K. Das, Dr. Sean R. Williamson, Dr. Sambit K. Mohanty, Dr. Sumit K. Panda**

Moderator: **Dr. Sandy Srinivas**

Panelist

Dr. Atul Batra
Dr. Chinmaya K. Pani
Dr. Saroj K. Sahu
Dr. Sthiti Das
Dr. Nuzhat Husain
Dr. Manu Prasad

Dr. Dillip K. Muduly
Dr. Aditya Sarin
Dr. Santosh Menon
Dr. Jyoti R. Swain

Pathologic sub-staging of bladder cancer – updates, controversies, and guidelines - **Dr. Ankur Sangoi (12:45 PM - 1:15 PM)**

Benign mimics of urothelial carcinoma - **Dr. Ankur Sangoi (1:15 PM - 1:30 PM)**

Best practice recommendation for immunohistochemical markers in renal cell tumors - **Dr. Mahmut Akgul (1:30 PM – 2:00 PM)**

Mesenchymal lesions of the GU tract - **Dr. Mahmut Akgul (2:00 PM – 2:15 PM)**

Lunch break (2:15 PM - 2:45 PM)

Valedictory (2:45 PM - 3:15 PM)

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About Organizations

About GUPS

The Genitourinary Pathology Society (GUPS) is a global, non-profit organization dedicated to advancing the understanding and research in genitourinary pathology. Through collaboration, education, and research initiatives, GUPS brings together professionals in pathology, urology, and oncology to improve diagnostics and treatment approaches. The society is renowned for its scientific meetings, publications, and global networking opportunities that foster advancements in genitourinary disease research.

About IAIO

The International Association for Integrated Oncology (IAIO) is a prestigious, global platform dedicated to advancing oncology through education, research, and collaborative innovation. As a leading Organization, IAIO leverages cutting-edge technology to foster a globally connected cancer care community. With a focus on capacity building, clinical research, and knowledge dissemination, IAIO provides services ranging from cancer community management and global networking to scientific database management. By uniting professionals across medical, radiation, and surgical oncology, IAIO is shaping the future of integrated cancer care through impactful initiatives and transformative conferences

About KIMS

Kalinga Institute of Medical Sciences (KIMS), a constituent of KIIT University, is one of India's leading medical institutions. Offering world-class education and healthcare services, KIMS excels in providing multidisciplinary medical education and clinical training. Equipped with state-of-the-art facilities, KIMS focuses on producing skilled healthcare professionals while driving medical research that positively impacts society.

About AIIMS Bhubaneswar

AIIMS Bhubaneswar is a premier medical institution dedicated to advancing healthcare and medical education in India. As a center of excellence in health sciences, AIIMS Bhubaneswar fosters cutting-edge research, provides quality patient care, and nurtures the next generation of healthcare leaders. The institution is committed to addressing pressing public health challenges through innovative solutions and community outreach programs.

About Odisha Society of Oncology

The Odisha Society of Oncology is a regional organization dedicated to promoting cancer awareness, prevention, and treatment within the state of Odisha. The society brings together oncologists, healthcare professionals, and researchers to collaborate on improving cancer care outcomes. Through community education, medical training, and research initiatives, the society plays a crucial role in advancing oncology care in the region.

JOIN US !

INTERNATIONAL
ASSOCIATION FOR
INTEGRATED ONCOLOGY

International Association for Integrated Oncology(IAIO) is dedicated to promoting clinical care with diverse intervention strategies. By facilitating an integrated approach in collaboration with Oncologists, Healthcare Professionals, and Caregivers our organization engaged to enhance patient care. We believe that effective patient care extends beyond medical treatments; it necessitates a comprehensive approach where all stakeholders collaborate seamlessly.

Join as a Member !

Become a member of IAIO and unite to empower one another, exchanging and broadening our knowledge to advance innovative treatment techniques. Together, we can improve therapeutic approaches and create a lasting impact on patient outcomes.

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Conference Secretariat

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