Preface
Towards Precision Genitourinary Pathology

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Editor

Precision medicine requires precision pathology, that is, precise and clinically relevant histopathologic classification, grading, staging, and reporting of cancer. Genitourinary Pathology Society (GUPS), an international organization aiming to advance the science and practice of urologic pathology, recently convened experts to review new and evolving concepts and controversial topics in prostate, bladder, and kidney cancer pathology in an effort to advance precision genitourinary pathology. Six position papers ensued.[1-6] Many of the recommendations were incorporated in the recently published World Health Organization (WHO) Classifications of Tumors of the Urinary System and Male Genital Organs.[7] It is imperative for pathologists to keep abreast of these changes in order to generate diagnoses and reports that meet contemporary patient management needs.

Grading continues to play a critical role in prostate cancer (PCa) management and therapy planning. Baraban and Epstein provided an overview of recent updates and key concepts related to Gleason grading and Grade Groups and discussed both common and unusual morphologic challenges with each Gleason pattern and strategies for addressing them. Malignant cribriform lesions, including cribriform cancer and intraductal carcinoma, have emerged recently as one of the most important morphologic patterns for PCa management. Cai and Shah presented a contemporary diagnostic approach to cribriform lesions and addressed the controversies pertaining to whether intraductal carcinoma should be graded. New diagnostic tools, including MR imaging and targeted biopsies, genomic testing, and artificial intelligence-enabled diagnostic algorithms, have significantly reshaped pathologists' roles in PCa diagnosis. Coiner and colleagues reviewed the benefits of MR imaging and targeted biopsies and recommendations for reporting such biopsies. Molecular tumor profiling has gained relevance in personalized clinical management and precision oncology treatment of localized and metastatic PCa. Akhoundova and colleagues reviewed the role of gene expression assays for genomic risk stratification to support decision algorithm regarding active surveillance or indication of intensification of therapy in localized cancer, and tumor molecular characterization by next-generation sequencing as well as by assays assessing HRD and MSI status to predict benefit from molecularly targeted therapies. Patel and colleagues summarized the recent breakthroughs in clinical artificial intelligence, especially in the deployment in the diagnosis of PCa, and laid out the prospects for a future with artificial intelligence–driven assistive solutions in genitourinary pathology.

Regarding urothelial neoplasia, there has been continuous debate and discussion on the classification of papillary and flat neoplasia. Comperat and colleagues presented the recent reporting recommendations by GUPS on "flat and papillary urothelial neoplasia" and offered diagnostic tips for such lesions. Gandhi and colleagues highlighted the histologic characteristics of subtype histology and divergent differentiation recognized by the WHO classification, with updates on their

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molecular and clinical features. Aron and Zhou argued for additional modifications of the pTNM staging, including T1 and T2 substaging, for better risk stratification. Not yet used in clinical practice, the molecular classification of bladder cancer, however, has gained momentum. Guo and Czerniak emphasized the distinct molecular alterations underlying the diverse clinical behaviors of bladder cancer that have led to novel molecular classifications, and have improved diagnosis and treatment of this complex disease. They also discussed biomarkers to aid the selection of patients for immune checkpoint therapy that has changed the therapeutic landscape of bladder cancer.

The classification of renal neoplasia has changed significantly in the WHO classification, 5th edition, with new entities added, including several oncocytic tumors (eosinophilic, solid, and cystic renal cell carcinoma). Several tumors with distinct morphology and molecular changes, such as low-grade oncocytic tumors and eosinophilic vacuolated tumor, were also included as emerging entities. Much of the credit goes to GUPS renal neoplasia working groups, who published two position papers, one on new developments in the existing WHO kidney tumor entities and one on new and emerging kidney tumor entities. These topics were reviewed by Akgul and Williamson, and Siadat and colleagues, respectively.

The classification and staging of testicular germ cell neoplasms have not changed significantly. However, the nuance of classification and staging that are important for clinical management may not be fully comprehended due to the infrequency of these tumors in the clinical practice. Dashora and colleagues reviewed the recent advances and potential future changes in the classification of testicular germ cell and sex cord stromal tumors, with a discussion on practical approaches to difficult diagnostic areas and pitfalls, along with utility of ancillary investigations. Al-Obaidy and colleagues summarized the current AJCC staging of the germ cell tumors, highlighted essential concepts, and provided insight into the most important parameters of testicular tumors staging.

I am very fortunate to have assembled a panel of renowned genitourinary pathologists to review and bring to you the most recent updates, which are important for the precision and personalized management of prostate, bladder, kidney, and testis tumors. It is my hope that the changes outlined in these reviews will bring us a step closer to precision genitourinary pathology.

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