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Benign Mimickers of Prostate Adenocarcinoma on Needle Biopsy and Transurethral Resection **1**

George J. Netto and Jonathan I. Epstein

Prostate needle biopsy currently is the gold standard method for the diagnosis, management, and prognosis of prostate cancer. Obtaining an accurate diagnosis is crucial for pursuing proper patient management. This article discusses histologic mimickers of prostate carcinoma highlighting microscopic features that are helpful to reach a correct diagnosis and emphasizing potential diagnostic pitfalls.

Prostatic Adenocarcinoma, Prostatic Intraepithelial Neoplasia, and Intraductal Carcinoma **43**

Ming Zhou and Cristina Magi-Galluzzi

Prostate carcinoma (PCa) exhibits a wide range of architectural and cytological features. Gleason grading remains one of the most powerful histological prognostic parameters. However, it has evolved considerably. High-grade prostatic intraepithelial neoplasia (high-grade PIN) is accepted as a precursor lesion of PCa. Its detection in prostate biopsy is also considered as a risk factor for detecting cancer in subsequent biopsies. Such risk, however, has significantly decreased in recent studies. Intraductal carcinoma of the prostate (IDC-P) represents the intraductal spread of invasive cancer and constitutes a poor histologic parameter. This article reviews the key histological features of PCa, high-grade PIN and IDC-P, as well as the Gleason grading system that was most recently updated in 2005.

Variants and Unusual Patterns of Prostate Cancer **77**

Samson W. Fine

Beyond the typical acinar morphology observed in most prostatic adenocarcinoma, a spectrum of morphologic variants and prostate cancer subtypes exists. These unusual entities may be further classified into (1) cancer morphologies arising by divergent differentiation of prostatic ductal, acinar, or basal cells and associated with unique clinical features or therapeutic approaches, and (2) histologies occurring in the context of usual prostatic adenocarcinoma that may result in diagnostic misinterpretation or difficulties in Gleason grade assignment, especially in limited samples. This article details several variants, with emphasis on diagnostic criteria, differential diagnoses, and clinical significance.

Mesenchymal Tumors of the Prostate

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Donna E. Hansel, George J. Netto, Elizabeth A. Montgomery, and Jonathan I. Epstein

Prostatic mesenchymal tumors encompass various benign and malignant neoplasms that may derived from the intrinsic prostatic stroma or from associated elements including muscle, connective tissue, blood vessels, and neural structures. The differential diagnosis of these tumors is broad and encompasses prostatic epithelial processes that demonstrate prominent spindle cell morphology, as well as mesenchymal tumors that secondarily involve the prostate. Careful morphologic examination, clinical history, and judicious use of a limited panel of immunohistochemical markers and molecular tests aid in the proper diagnosis of these lesions. This article provides a structured guide for the analysis and diagnosis of both benign and malignant prostatic mesenchymal lesions and highlights key features that distinguish these entities within the differential diagnosis of prostatic spindle cell lesions.

Benign Diseases of the Bladder

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Joshua F. Coleman and Donna E. Hansel

Benign diseases of the bladder often present diagnostic challenges to practicing pathologists due to their diverse nature and ability to mimic a variety of epithelial or mesenchymal neoplasms. Categories of benign bladder disease include infectious cystitis, noninfectious cystitis, reactive proliferative processes, and benign processes that secondarily involve the bladder. An understanding of the key clinical and morphologic features of these lesions and the useful ancillary techniques specific for these entities is critical to the correct diagnosis of these lesions. This article reviews the key features of these benign bladder diseases and highlights methods to distinguish these lesions from other benign and malignant processes involving the bladder.

Urothelial Carcinoma and its Variants

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Cristina Magi-Galluzzi, Sara M. Falzarano, and Ming Zhou

Bladder cancer is the ninth most common cancer worldwide, and the most common malignancy affecting the urinary tract, with approximately 330,000 new cases and more than 130,000 deaths per year. Bladder cancer is primarily attributable to smoking, which accounts for 65% of male and 30% of female cases in some developed countries. Other major risk factors include analgesic abuse, some types of chemotherapy, occupational exposure to chemicals, and in Egypt and some Asian regions, endemic infection with *Schistosoma haematobium*. Approximately 90% of bladder tumors are classified as urothelial carcinoma (UC), also referred to as transitional cell carcinoma, and are believed to originate from transformation of the normal urothelium. UCs often exhibit elements of squamous or glandular differentiation. The spectrum of microscopic forms of urothelial carcinoma has been expanded recently to include several histologic variants, the recognition of which is important to avoid diagnostic misinterpretation, to predict outcome, and to guide the selection of the most appropriate therapeutic approach. This article reviews characteristic pathologic features and key clinical aspects of UC and its most common variants.

Molecular Pathology of the Genitourinary Tract: Prostate and Bladder

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S. Joseph Sirintrapun and Anil V. Parwani

The knowledge of cellular mechanisms in tumors of the prostate and bladder has grown exponentially. Molecular technologies have led to the discovery of *TMPRSS2*

in prostate cancer and the molecular pathways distinguishing low- and high-grade urothelial neoplasms. Techniques such as fluorescence in situ hybridization are already being used as an adjunct to cytologic diagnosis of urothelial neoplasms. This trend portends the future in which classification and diagnosis of tumors of the prostate and bladder through morphologic analysis will be supplemented by molecular information correlating with prognosis and targeted therapy. This article outlines tumor molecular pathology of the prostate and bladder encompassing current genomic, epigenomic, and proteomic findings.