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Distinguishing common epithelial tumors that arise in the kidney has significant implications, in terms of therapy and prognosis. We reviewed the expression of different immunohistochemical markers reported in the literature on renal neoplasms to develop an immunohistochemical panel as an adjunct to histologic examination. Particular emphasis is placed on the distinction between clear cell renal cell carcinoma and chromophobe renal cell carcinoma, and between the eosinophilic variant of chromophobe renal cell carcinoma and renal oncocytoma.

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Renal cell carcinoma (RCC) represents a group of clinically and genetically diverse diseases. Familial RCC syndromes, although rare, provide an invaluable model to study the molecular mechanisms of renal carcinogenesis. Many oncogenes and tumor suppressor genes have been identified as responsible for several forms of familial RCC syndromes. Understanding of the molecular pathways of these genes will have significant impact on the diagnosis and treatment of familial and sporadic RCCs.

Application of Molecular Diagnostic Techniques to Renal Epithelial Neoplasms 279

Timothy D. Jones, John N. Eble, and Liang Cheng

Molecular and cytogenetic techniques have been used extensively to study the genetics of renal epithelial neoplasia. Several genes and chromosomal aberrations have been identified that play important roles in the development and progression of kidney tumors. Each histologic type of renal neoplasm is characterized by specific types of genetic alterations, a finding that can aid in making correct diagnoses in difficult cases. In addition, molecular genetic research in renal cell tumors continues to: (1) assist in our understanding of the nature and causes of tumorigenesis and tumor progression, (2) further the assessment of prognosis, (3) facilitate early detection, (4) lead to advances in therapy, and (5) help guide treatment.

Clear Cell Renal Cell Carcinoma 305

David J. Grignon and Mingxin Che

Clear cell renal cell carcinoma is the most common epithelial malignancy of the kidney, and overall, has the worst prognosis of the common epithelial tumors in adults. Recognition of the diverse morphologic features is important for proper classification. Pathologic stage and nuclear grade are the most important prognostic parameters for this tumor.

Oncocytic Renal Neoplasms: Diagnostic Considerations 317

Neil A. Abrahams and Pheroze Tamboli

Advances in our understanding of renal neoplasia have resulted in recognition of numerous tumors that are composed predominantly of cells with abundant eosinophilic cytoplasm. This article discusses the features of renal oncocytoma (including oncocytosis), chromophobe renal cell carcinoma (RCC), and clear cell RCC; explores the relationship between renal oncocytoma and chromophobe RCC; briefly discusses other tumors with abundant eosinophilic cytoplasm; and emphasizes the differential diagnosis of such tumors.

Nephroblastic Neoplasms 341

Joseph D. Khoury

Nephroblastoma, or Wilms tumor, is a malignant embryonal neoplasm that is derived from nephrogenic blastemal cells, with variable recapitulation of renal embryogenesis. The pathogenesis of nephroblastoma is complex and has been linked to alterations of several genomic loci, including *WT1*, *WT2*, *FWT1*, and *FWT2*. Generally, nephroblastoma is composed of variable proportions of blastema, epithelium, and stroma, each of which may exhibit a wide spectrum of morphologic variations. Distinguishing nephroblastoma with favorable histology from tumors that exhibit anaplasia is an

integral component of histologic assessment because of its prognostic and therapeutic implications. Nephrogenic rests and a special variant of nephroblastoma, cystic partially differentiated nephroblastoma, also are discussed.

Translocation Carcinomas of the Kidney

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Pedram Argani and Marc Ladanyi

Renal carcinomas with chromosome translocations that involve Xp11.2 and resulting gene fusions that involve the *TFE3* transcription factor gene are newly recognized entities in the 2004 World Health Organization renal tumor classification. One distinctive subtype bears a t(X;17)(p11;q25), which results in the identical *ASPL-TFE3* gene fusion that was identified initially in alveolar soft part sarcoma. Another distinctive type of renal neoplasm bears a t(6;11)(p21;q12) that was shown to result in a fusion of the intronless, untranslated *Alpha* gene with *TFEB*. Although the t(6;11) neoplasm features a distinctive dimorphic cytology and labels for melanocytic markers immunohistochemically, it shares morphologic, immunohistochemical, and molecular features with the Xp11 translocation carcinomas; therefore, we propose to group them under the broader category of "MiTF/TFE translocation carcinomas."

Metanephric Neoplasms: The Hyperdifferentiated, Benign End of the Wilms Tumor Spectrum?

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Pedram Argani

The family of metanephric neoplasms of the kidney includes a pure epithelial lesion (metanephric adenoma), a purely stromal lesion (metanephric stromal tumor), and a mixed epithelial-stromal lesion (metanephric adenofibroma). These neoplasms likely represent the hyperdifferentiated end of the Wilms tumor spectrum. Metanephric adenoma typically occurs in women, often is associated with polycythemia, and must be distinguished from the solid variant of papillary renal cell carcinoma and epithelial-predominant Wilms tumor. Metanephric stromal tumor is a bland spindle cell tumor that usually affects young children; features intratumoral and occasional extratumoral angiodysplasia, juxtaglomerular cell hyperplasia, and concentric peritubular growth; and must be distinguished from congenital mesoblastic nephroma and clear cell sarcoma of the kidney. Metanephric adenofibroma is a composite neoplasm with features of metanephric adenoma and metanephric stromal tumor.

Tubulocystic Carcinoma, Mucinous Tubular and Spindle Cell Carcinoma, and Other Recently Described Rare Renal Tumors

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Gregory T. MacLennan and David G. Bostwick

In the recent past, the list of distinctive neoplasms that arise in the kidney has grown remarkably, aided by clinical and pathologic

observation, and by the development of new ancillary diagnostic techniques. This article discusses several rare tumors. Two neoplasms (mixed epithelial and stromal tumors of kidney, and primitive neuroectodermal tumor of kidney) were identified 30 years ago, but have been studied extensively and characterized better recently. The other lesions that are discussed—mucinous tubular and spindle cell carcinoma, tubulocystic carcinoma, epithelioid angio-myolipoma, and primary renal synovial sarcoma—have been described only in the past 10 to 15 years, and delineation of their characteristics continues.

Handling and Reporting of Tumor-Containing Kidney Specimens

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Mingxin Che and David J. Grignon

The pathologic features of renal cell carcinoma are the most valuable factors in predicting prognosis and planning surveillance and treatment protocols. Urologists and pathologists should optimize approaches in handling tumor-containing kidney specimens to allow for their best evaluation and reporting.

A Review of Prognostic Pathologic Features and Algorithms for Patients Treated Surgically for Renal Cell Carcinoma

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Christine M. Lohse and John C. Cheville

Pathologic features that are important in outcome prediction for patients who are treated surgically for renal cell carcinoma are reviewed, including histologic subtype, sarcomatoid differentiation, the TNM classification, primary tumor size, nuclear grade, and histologic tumor necrosis. How these pathologic features have been incorporated into prognostic algorithms that were developed by Memorial Sloan-Kettering Cancer Center, University of California Los Angeles, and Mayo Clinic are examined.

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