PEDIATRIC RENAL NEOPLASMS

Sarangarajan Ranganathan, MD

KEYWORDS

• Wilms' tumor • Nephrogenic rests • Mesoblastic nephroma • Metanephric tumors
• Clear cell sarcoma • Malignant rhabdoid tumor • Translocation carcinomas

ABSTRACT

Renal tumors in childhood consist of a diverse group of tumors ranging from the most common Wilms' tumor, to the uncommon and often fatal rhabdoid tumor. Diagnosis is based on morphologic features and aided by ancillary techniques such as immunohistochemistry and cytogenetics. Molecular techniques have helped identify a group of pediatric renal cell carcinomas that have specific translocations, called translocation-associated carcinomas. Differential diagnosis of the various tumors is discussed. Pathogenesis and nephroblastomatosis, the precursor lesions of Wilms' tumor, also are discussed briefly, as are the handling of these tumor specimens and prognostic factors.

PEDIATRIC KIDNEY NEOPLASMS: OVERVIEW

Childhood renal tumors are an enigmatic group of tumors characterized by their uniqueness in being exclusive to the pediatric age group. They present various challenges to diagnostic pathologists because of their morphologic diversity and overlap with precursor lesions. The unique embryology of the kidney plays an important role in the development of Wilms' tumors (WTs) and their precursors. Pediatric renal tumors constitute the sixth commonest group of tumors in this age group. The majority of these tumors occur in the first decade of life with the exception of a few carcinomas that mimic their adult counterparts. This group of tumors also is the most extensively studied because of the enormous work contributed by the National Wilms Tumor Study Group (NWTS) that has resulted in the identification, classification, treatment, and extensive follow-up of children who have these tumors.[1–3]

The classification of renal tumors in infancy and childhood is shown in **Box 1**. The most common tumor encountered in practice is WT, which constitutes almost 80% of all genitourinary tumors in children.[2] The other renal tumors include congenital mesoblastic nephroma (CMN), renal rhabdoid tumor, and clear cell sarcoma of the kidney (CCSK). Although initially believed to represent a small group of pediatric renal tumors, renal cell carcinomas (RCCs) now are known to constitute almost 5% of pediatric tumors and are among the more extensively studied tumors because of their cytogenetic abnormalities. The rarity of these tumors makes their diagnosis a challenge for general surgical pathologists.

NEPHROBLASTOMA (WILMS' TUMOR)

NEPHROBLASTOMA/WILMS' TUMOR: GENERAL FEATURES

Wilms' tumors are defined as embryonal tumors of the kidney believed to arise by genetic events from precursor lesions called nephrogenic rests (NR).[1,4,5] WT is the sixth most common cancer in the pediatric age group. WTs have an incidence of approximately 1 in 8000 children and most of them (>98%) occur in the first decade of life and of these more than 90% occur in the first 4 years of life. Rare cases are reported in adults.[2] They have a slight female preponderance and can be unilateral or bilateral, with the latter associated more often with genetic syndromes, such as the Beckwith-Wiedemann syndrome and hemihypertrophy.[6] They usually present in early childhood with an abdominal mass most often noticed by parents. They rarely manifest with symptoms associated with aggressive and metastatic tumors.

Department of Pathology, Children's Hospital of Pittsburgh of UPMC, 3705 Fifth Avenue, Pittsburgh, PA 15213, USA
E-mail address: sarangarajan.ranganathan@chp.edu

Surgical Pathology 2 (2009) 27–60
doi:10.1016/j.path.2008.07.006
1875-9181/08/$ – see front matter

Key Features
Wilms' Tumor

1. Unilateral or bilateral
2. Single or multifocal
3. Large, round, fleshy, hemorrhagic, and necrotic mass
4. Blastema identified by solid aggregates, nests, serpentine or trabecular arrangement of small blue, angulated to ovoid cells
5. Tubules seen as primitive embryonal structures
6. Stroma can be hypocellular to cellular and show smooth muscle, rhabdomyoblastic, chondroid, osseus, and neural metaplasia
7. Anaplasia may be focal or diffuse
8. Renal sinus invasion, capsular rupture, renal vein invasion common
9. Metastasis to lymph nodes, liver, lungs commonly
10. Age, weight, loss of heterozygosity (LOH), stage, and anaplasia influence prognosis

Hematuria, hypertension, and abdominal pain also may be presenting symptoms. Rare cases of extrarenal WTs are reported in the sacrococcygeal, retroperitoneal, and pelvic locations. Epidemiologic variations between ethnic groups also are described.[7,8]

Approximately 10% of nephroblastomas occur as part of other syndromes that include the Wilms–aniridia–genital abnormalities–mental retardation [WAGR] syndrome, with defects in the 11p13 locus involving the WT1 gene; the Denys-Drash syndrome, involving the same WT1 locus; the Beckwith-Wiedemann syndrome of hemihypertrophy with bilateral nephroblastoma and nephroblastomatosis involving the WT2 gene at 11p15.5; familial WTs; or others, such as neurofibromatosis, Bloom syndrome, trisomy 18, Frasier syndrome, Perlman syndrome, and neurofibromatosis.[2,3,6]

NEPHROBLASTOMA / WILMS' TUMOR: GROSS FEATURES

WTs are large, spherical, pale gray to tan, soft, friable masses located at either pole of the kidney and often distorting the renal parenchyma by their size (**Fig. 1**A). The friable nature of the tumor makes it difficult to handle specimens and extreme precaution is necessary to prevent surgical knife

Box 1
Renal neoplasms that occur in the pediatric age group

Tumors of nephroblastic origin

Wilms' Tumor (WT)
- Favorable histology
- Anaplastic (unfavorable histology) WT

Variants of WT
- Rhabdomyomatous WT
- WT with heterologous elements (teratoid)

Nephroblastomatosis
- Perilobar nephrogenic rests (PLNR)
- Intralobar NR (ILNR)

Cystic nephroma and cystic partially differentiated nephroblastoma (CPDN)

Metanephric tumors
- Metanephric adenoma (MA)
- Metanephric adenofibroma (MAF)
- Metanephric stromal tumor (MST)

Stromal tumors of the kidney

Mesonephric origin
- Congenital mesoblastic nephroma (CMN)
- Classic
- Mixed
- Cellular (infantile fibrosarcoma-like)

Clear cell sarcoma of kidney (CCSK)

Malignant rhabdoid tumor (MRT)

Anaplastic sarcoma of the kidney

Primitive neuroectodermal tumor (PNET)

Synovial sarcoma

Desmoplastic small round cell sarcoma

Rhabdomyosarcoma

Others

Renal cell carcinoma (RCC)

Translocation carcinomas
- Xp11.2 carcinomas
- T(6;11) carcinomas

Papillary RCC (PRCC)

Classic (adult-type) RCC

Renal medullary carcinoma

Oncocytoid postneuroblastoma carcinoma