CYSTIC TUMORS OF THE KIDNEY

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CYSTIC NEPHROMA

Cystic nephromas are benign neoplasms occurring predominantly in women and have as their principal differential diagnostic considerations, cystic partially differentiated nephroblastoma and multilocular cystic renal cell carcinoma.

Clinical Features of Cystic Nephroma

Cystic nephroma often is found incidentally by radiological examinations for other conditions, but may present as a palpable mass in the flank. or with pain or hematuria. Rarely, cystic nephroma is bilateral. Nephrectomy and partial nephrectomy are curative but incomplete excision has been followed by recurrence. Sarcoma has arisen in cystic nephroma in eight cases. Women predominate over men by approximately 8 : 1.

Diagnostic Criteria for Cystic Nephroma

Adult patient
Expansile mass surrounded by fibrous pseudocapsule
Interior entirely composed of cysts and septa with no expansile solid nodules
Cysts lined by flattened, hobnail, or cuboidal epithelium
Septa may contain epithelial structures resembling mature renal tubules
Septa may not contain epithelial cells with clear cytoplasm
Septa may not contain skeletal muscle fibers

Pathology of Cystic Nephroma

Cystic nephromas are well demarcated from the surrounding kidney by a thick fibrous pseudocapsule. The tumors vary widely in size (mean = 9 cm). Cystic nephroma commonly herniates into the renal sinus or may bulge from the convexity of the renal cortex. The tumor is completely cystic and there are no solid nodules. The cysts contain clear or hemorrhagic fluid and range in size from microscopic to 5 cm or greater. The septa are thin (typically <5 mm), translucent, and uniform. Necrosis and hemorrhage are rare except when the tumor has herniated into the renal pelvis. The septa may become calcified.

The cysts are lined by flattened, cuboidal, or hobnail epithelium. Occasionally, the lining cells have clear cytoplasm. Mitotic figures are not visible or are very rare. Many tumors have areas of cystic surface which lack epithelium.

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The septa are thin and correspond to the outlines of the cysts, without expansile nodules . The septal stroma consists of fibrous tissue which varies from myxoid to collagenous and occasionally it is cellular and has a wavy appearance resembling ovarian stroma. Skeletal muscle, fat, and smooth muscle have not been found in cystic nephroma. The septa of cystic nephroma often contain small cysts lined by bland cuboidal epithelial cells resembling renal tubules cut in cross section.

CYSTIC PARTIALLY DIFFERENTIATED NEPHROBLASTOMA

Cysts are common in Wilms tumor and range in size from microscopic to several centimeters in diameter. Usually, the cysts are present as a minor feature accompanying the blastema, stroma, and epithelial elements typical of Wilms tumor. Rarely, otherwise typical Wilms tumor may have substantial areas essentially indistinguishable from cystic nephroma. At this extreme end of the spectrum, Wilms tumor fulfills all of the criteria for cystic nephroma, lacking expansile nodules and consisting only of cysts with delicate septa. However, within the septa are small foci of blastema, immature-appearing proliferating stromal cells, and primitive or immature epithelium.

Diagnostic Criteria for Cystic Partially Differentiated Nephroblastoma

Expansile mass surrounded by fibrous pseudocapsule
Interior entirely composed of cysts and septa with no expansile solid nodules
Cysts lined by flattened, hobnail, or cuboidal epithelium
Septa may contain epithelial structures resembling mature renal tubules
Septa may contain blastema, with or without embryonal stromal or epithelial elements

Clinical Features of Cystic Partially Differentiated Nephroblastoma

Cystic partially differentiated nephroblastoma, is exceptional after the first 24 months of life. Among 5,100 patients enrolled in the NWTS, there were 21 cystic partially differentiated nephroblastomas. The mean age was 16 months and oldest was 44 months. There is a 3 : 1 predominance of males. Surgery, or surgery and chemotherapy have been curative in all NWTS cases but Joshi and Beckwith did report one recurrence, presumably a complication of incomplete resection. Cystic partially differentiated nephroblastoma occurs with equal frequency in boys and girls.

Pathology of Cystic Partially Differentiated Nephroblastoma

The tumors often are large, particularly considering the patient's age, ranging up to 180 mm in diameter. On gross inspection, cystic partially differentiated nephroblastoma is indistinguishable from cystic nephroma.

The cysts in cystic partially differentiated nephroblastoma have a lining similar to cystic nephroma with flattened, cuboidal, or hobnail epithelium, or with segments which lack lining cells. The defining characteristic of cystic partially differentiated

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nephroblastoma
occurs in the septa which are variably cellular and contain undifferentiated and differentiated mesenchyme, blastema, and nephroblastomatous epithelial elements. Skeletal muscle and myxoid mesenchyme are present in the septa of most tumors. Focally, the septal elements may protrude into the cysts in microscopic papillary folds. The epithelial components consist mainly of mature and immature microscopic cysts resembling cross sections of tubules and glomeruloid bodies.

That cystic nephroma and cystic partially differentiated nephroblastoma are different diseases is supported by these facts:

1) Cystic nephroma in adults occurs with an 8 : 1 predominance of women while cystic partially differentiated nephroblastoma occurs with equal frequency in boys and girls.

2) Cystic nephroma in adults is exceptional before the age of 30, while cystic partially differentiated nephroblastoma is exceptional above the age of 2 years.

3) Skeletal muscle fibers are common in cystic partially differentiated nephroblastoma but are not present in cystic nephroma. If cystic nephroma in adults were a terminally differentiated variant of cystic partially differentiated nephroblastoma, it would be remarkable that the skeletal muscle should disappear along with the immature elements.

MULTILOCULAR CYSTIC RENAL CELL CARCINOMA

Clear cell renal cell carcinomas often contain microscopic and macroscopic cysts. Rarely, the cystic architecture dominates and appears to represent the inherent growth pattern of the tumor. The population of carcinoma cells in such tumors is small and recognizing them as variants of renal cell carcinoma can be challenging.

Diagnostic Criteria for Multilocular Renal Cell Carcinoma

Expansile mass surrounded by fibrous pseudocapsule

Interior of tumor entirely composed of cysts and septa with no expansile solid nodules

Septa contain aggregates of epithelial cells with clear cytoplasm

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Approximately 40 cases have been described.

Clinical Features of Multilocular Cystic Renal Cell Carcinoma

Multilocular cystic renal cell carcinoma is uncommon there is a predominance of males over females of approximately 3 : 1. All have been diagnosed in adults (age range 20 to 76 years, mean = 51 years). Although in most instances the reported follow up is brief, no patient has suffered recurrence or progression of the tumor.

Pathology of Multilocular Cystic Renal Cell Carcinoma

Multilocular cystic clear cell renal cell carcinoma grossly resembles cystic nephroma and cystic partially differentiated nephroblastoma. The greatest diameters of the tumors have ranged from 25 mm to 130 mm (mean, approximately 60 mm). The cysts vary in size and contain fluid which ranges from serous to hemorrhagic. The septa are thin and expansile nodules are not present. Calcification is present in the septa of more than 20% of tumors and osseous metaplasia occasionally occurs.

The cysts are lined for the most part by a single layer of epithelial cells or the epithelial lining is absent. The lining cells may be flat and atrophic or somewhat plumper cells with cytoplasm ranging from clear to pale. In some cysts the lining may consist of multiple layers of cells. Occasionally, there are small papillae covered by the same cells with clear cytoplasm. The nuclei almost always are small, spherical, and have dense chromatin.

The septa consist of fibrous tissue, which often is densely collagenous. In all tumors, there is a population of epithelial cells with clear cytoplasm within the septa. This may be a focal finding. The clear cells form small collections but do not form macroscopic nodules. These epithelial cells may be confused with histiocytes, or with lymphocytes surrounded by retraction artifacts. Increased vascularity within the cell clusters is a clue to their epithelial. These epithelial cells resemble those lining the cysts and have small dark nuclei in all but a few tumors. Immunohistochemistry can be helpful in confirming the epithelial nature of the cells within the septa. Similar to the conventional clear cell renal cell carcinoma, they frequently decorate strongly with antibodies to cytokeratins and epithelial membrane antigen.

MIXED EPITHELIAL AND STROMAL TUMOR OF THE KIDNEY

In 1993, Pawade et al. described three cases of a novel cystic renal tumor which they termed “cystic hamartoma of the renal pelvis.” Additional cases have been reported as “mesoblastic nephroma of adults” and as “mixed epithelial and stromal tumor of the kidney.” The last terminology is preferred since these tumors clearly have no relationship to mesoblastic nephroma of infants and since they appear to be mixtures of neoplastic epithelial components and spindle cells, the term “hamartoma” is inappropriate.

Clinical Features of Mixed Epithelial and Stromal Tumor of the Kidney

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There is a strong predominance of women, often perimenopausal. Pain in the loin or flank was the most common presenting complaint. This tumor has not been reported in a child. No patient has had a recurrence..

Pathology of Mixed Epithelial and Stromal Tumor of the Kidney

Most of these tumors appear to arise centrally in the kidney and to grow as expansile masses. Most have been large and the precise anatomic site of origin has been obscure. The frequency of herniation into the renal pelvic cavity lends support to the idea of origin from the renal medulla. The tumors lack a thick fibrous wall but compressed renal tissue usually forms a pseudocapsule in the larger tumors. The tumors are grossly composed of multiple cysts and solid areas. The solid areas may be extensive. The septa of the cysts are thicker than is typical of cystic nephroma, cystic partially differentiated nephroblastoma, and multilocular cystic clear cell renal cell carcinoma.

These are complex tumors composed of large cysts, microcysts, and tubules. The largest cysts are lined by columnar and cuboidal epithelium which sometimes forms small papillary tufts. Urothelium, which may be hyperplastic, may also line some of the cysts. The microcysts and tubules are lined by flattened, cuboidal, or columnar cells. Their cytoplasm ranges from clear, to pale, to eosinophilic, or is vacuolated. The architecture of the microcysts is varied and ranges from simple microcysts with abundant stroma between them to densely packed clusters of microcysts, to complex branching channels which may be dilated. These varied elements often are present intermingled in the same area of the tumor. The stroma consists of a variably cellular population of spindle cells with plump nuclei and abundant cytoplasm. Areas of myxoid stroma and fascicles of smooth muscle cells may be prominent. Blood vessels with thick walls may be present. Fat cells may be present. Mitotic figures and atypical nuclei have not been reported. The spindle cells often decorate with antibodies to smooth muscle markers. HMB-45 is not present in these tumors.

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