

August 2016 IAP Case of the Month

A 60 year old woman incidentally found to have a complex left renal cyst.

Contributed by:



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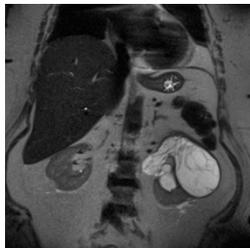


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Clinical History:

The patient is a 60 year old woman with a known BRCA1 mutation and a history of stage IIIC high-grade serous ovarian carcinoma. She completed treatment in April 2011 with no evidence of residual disease. During her treatment, she was noted on imaging to have a pancreatic cyst. She underwent follow-up MRCP in March 2015. Imaging demonstrated stability of the pancreatic cyst, but incidentally revealed a 9.3 cm left superior pole renal cyst. Six month follow up imaging demonstrated growth of the cyst to 11.0 cm with thick internal septations and medial extension of the cyst into the renal pelvis causing hydronephrosis (figure 1). The patient subsequently underwent an adrenal-sparing nephrectomy.

Figure 1. T2-weighted coronal MRI demonstrating a Bosniak type III left renal cyst with internal septations.



Gross Examination:

Gross examination of the specimen revealed a cystic, multiloculated tumor surrounded by a pseudocapsule filled with clear, serous fluid (figure 2). The tumor was well-circumscribed and tan to yellow. It involved the upper and mid portions of the kidney with extension into the collecting system and measured 12.5 x 10.3 x 6.5 cm.

Figure 2. Gross photograph demonstrating a well-circumscribed multiloculated cystic tumor with medial extension into the collecting system.



Microscopic Examination:

Histologic sections demonstrated a well-demarcated multiloculated cystic neoplasm (figure 3). The cyst walls were remarkable for a single layer of epithelial cells ranging from flat to hobnail in appearance while the intervening stromal septae ranged from paucicellular to ovarian-like stroma (Figure 4).

Figure 3. Low-power photomicrograph demonstrating a well-demarcated multiloculated cystic neoplasm.

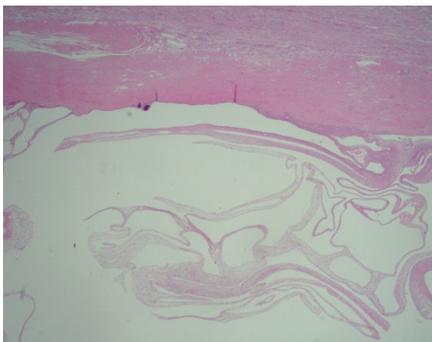


Figure 4. High-power photomicrograph demonstrating a single layer of epithelial cells ranging from flat to hobnail in appearance and intervening stromal septae ranging from paucicellular to ovarian-like stroma.



Final Diagnosis:

Cystic Nephroma

Discussion:

Cystic nephroma is considered a cystic neoplasm of the kidney, which are defined as isolated cystic tumors without cystic changes being present in the remainder of the renal parenchyma (1). Other diagnoses in the category of cystic neoplasms in adults include: mixed epithelial and stromal tumor, multilocular cystic renal neoplasm of low malignant potential (formerly called multilocular cystic clear cell renal cell carcinoma), and tubulocystic renal cell carcinoma. There has been much controversy and confusion over the classification of these tumors, particularly in the case of cystic nephromas and mixed epithelial and stromal tumors because of the various names they have been given in the past and their somewhat similar and overlapping morphologic features.

Cystic nephroma in particular has had several different names since being first described in 1892 including: multilocular cystic tumor, renal multilocular cyst, renal cystadenoma, and partial polycystic kidney (1). Possible explanations for the pathogenesis of cystic nephromas have also varied greatly ranging from developmental to dysplastic to neoplastic with malignant potential (2).

Patients with cystic nephromas may present with a palpable abdominal mass, flank pain, or hematuria, but most tumors are detected incidentally on imaging. Cystic nephromas cannot be distinguished from other cystic neoplasms on imaging (3).

Soon to be published data of the largest series of cystic nephromas in adults performed at Indiana University will further define the clinicopathologic spectrum of cystic nephromas (4). Grossly, cystic nephromas are multiloculated cystic mass often delineated from the surrounding renal parenchyma by a

pseudocapsule. The cystic spaces are lined by PAX8-positive flat, cuboidal, or hobnail epithelium that may occasionally show nuclear atypia or demonstrate clear cytoplasm with apical eosinophilic granules. Rarely there may be multiple epithelial layers or small blunt papillae protruding into the cysts.

The stroma is variable, ranging from hypocellular and collagenous to hypercellular with wavy spindle cells (4). The stromal cells are positive for smooth muscle actin in all studied cases and are positive for progesterone and estrogen in 85% and 50% of tumors, respectively. The hypercellular wavy spindle cell stroma is more prevalent in younger patients while the hypocellular collagenized stroma tends to be present in older patients suggesting that the stroma matures overtime.

The stroma may demonstrate additional findings including hyalinized acellular structures with well-defined rounded contours resembling corpora albicantia (4). Another possible stromal feature is polygonal or rarely spindle cells adjacent to the epithelial-lined cysts that are immunohistochemically positive for inhibin, SF1, and melan-A suggesting a possible steroidogenic role. There may also be embedded epithelial elements ranging from small clusters of cells with no lumen to tiny cysts. The embedded epithelial cells demonstrate similar nuclei to the spindle cells of the stroma. As such, it is hypothesized that cystic nephromas result from a stromal proliferation and the epithelial component arises from a stromal-epithelial transition which initially forms the epithelial elements embedded within the stroma and eventually progress to form large cysts.

The differential diagnosis for cystic nephroma includes the aforementioned entities: mixed epithelial and stromal tumor, cystic renal neoplasm of low malignant potential, and tubulocystic renal cell carcinoma. Mixed epithelial and stromal tumor is the primary differential with cystic nephroma, but usually, cystic nephroma can readily be differentiated from mixed epithelial and stromal tumor by the absence of solid stromal areas and the complex epithelial elements characteristic of the latter. Multilocular cystic renal neoplasm of low malignant potential is defined by the presence of nests of clear cells within the septae and an absence of a solid clear cell component. Tubulocystic renal cell carcinoma has variably sized structures ranging from small tubules to large cysts lined by cells with amphophilic cytoplasm and large nuclei with prominent nucleoli.

In terms of epidemiology, cystic nephromas are extremely rare with only approximately 200 cases reported in the literature (2). Although there are tumors in pediatric patients that also carry the designation of “cystic nephroma” it is now accepted that these are unrelated entities.

There has been considerable controversy in the literature regarding the relationship between cystic nephroma and mixed epithelial and stromal tumor. Because of the overlapping epidemiologic features and immunohistochemical profiles, the unifying term “renal epithelial and stromal tumor” was proposed (1). In the 2012 ISUP “Vancouver classification” of renal tumors, the consensus was that these represents two ends of a spectrum and so these were considered to be the same lesion for classification purposes (5). This is the approach that has been adopted in the 2016 WHO classification with the adoption of the “mixed epithelial and stromal tumour family” (3). It should be noted that not all kidney tumor authorities are in agreement. Drs. Grignon and Eble have long considered these to be distinct

entities. Two recent studies from Indiana University have presented data in support of that position (4 & 6). Both tumors are benign, so from a pragmatic perspective the distinction at this point does not have known clinical significance.

List of References:

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4. Calió A, Eble JN, Grignon DJ, Delahunt B. Cystic Nephroma in Adults: A Clinicopathological Study of 46 Cases. *Am J Surg Pathol* (in press).
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6. Calio A, Eble JN, Grignon DJ, Delahunt B. Mixed Epithelial and Stromal Tumor of the Kidney: A Clinicopathologic Study of 53 Cases. Under review.