

A CASE OF MULTILOCULAR CYSTIC NEPHROMA: CLINICAL, HISTOLOGICAL AND IMMUNOHISTOCHEMICAL ASPECTS

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ABSTRACT

Multilocular cystic nephroma is uncommon tumor that supposedly lies at the benign end of the spectrum of adult cystic renal neoplasms.

We present a 54-year-old female that underwent a left-sided nephrectomy following incidentally found on CT scan tumor renal mass. Grossly, the specimen from nephrectomy included renal parenchyma bearing tumor formation measuring 9 × 6 cm. The cut section was multiloculated, cystic. Microscopic examination demonstrated a cystic neoplasm with multiple variable-sized cysts lined by flattened to low cuboidal epithelium with dense regular nuclei and variable amount of cytoplasm with some degree of clearing. These cysts were separated by septae containing fibrocollagenous stroma enriched by smooth muscle bundles; occasional foci of calcification were encountered. The diagnosis of multilocular cystic nephroma was established and additional immunohistochemical (IHC) investigation with a panel of antibodies was performed (all provided by DAKO), adhering to the manufacturer's instructions.

The epithelial lining expressed both CKAE1-AE3 and CK19, was invariably positive for Vimentin and for unexplained reasons, showed weak to moderate expression of CD99. The stromal component consistently expressed SMA in fascicular fashion, while Desmin was expressed in a definitely patchy, dot-like manner. Epithelial cells did not express CD10 and CD15, lacked ER and PR. Similar negative profile was seen in the stromal cells within the septae. The same set of IHC markers was applied to the singular case of MCRCC we had. The only difference noted was weaker CK19 expression. We concluded that IHC is of little help when we are faced with distinguishing this neoplasm from the main diagnostic problem – multilocular cystic renal cell carcinoma.

Key words: multilocular cystic nephroma, histology, immunohistochemistry.

INTRODUCTION

Cystic adenoma of the kidney was the first name given at the end of the 19 century by Walter Edmunds (5), to a rare benign, non-hereditary condition with a wide spectrum of histological findings, uncertain pathogenesis, multiple names in medical literature, and bimodal age distribution. Approximately 200 cases of multilocular cystic nephroma (MLCN) have been described in the literature to date but this number should be regarded with caution because of the variety of terms used to describe this entity. Some of the synonyms used in medical literature include: multilocular cystic renal tumor, cystic nephroma, multilocular benign cystic nephroma, multilocular cyst, polycystic nephroblastoma to name a few.

MLCN could be both congenital, affecting predominantly infant males (male to female ratio of 3:1), as well acquired affecting predominantly middle-aged females (male to female ratio of 1:9), (4, 8). The exact etiology of congenital and adult form is unresolved, while the classification is

controversial. According to Eble and Bonsib, MLCN stands at the one end of a spectrum of renal cystic diseases of the childhood that includes pure MLCN, cystic – partially differentiated nephroblastoma, multilocular cysts with nodules of Wilms tumor and Wilms tumors (4). Despite being denied formal individual existence, in adults, the spectrum of renal neoplasms with cysts presented throughout tumor tissue includes MLCN, mixed epithelial and stromal tumor (MEST), multilocular cystic renal cell carcinoma (MCRCC), and renal cell carcinoma with cystic change. These cystic tumors are extremely difficult to distinguish on clinical, radiological, and gross features and are a cause of diagnostic dilemma.

CASE PRESENTATION

A 54-year-old female with previous history of cholecystectomy and hysterectomy for benign reasons, underwent a left-sided nephrectomy following incidentally found on CT scan tumor renal mass. CT examination showed a heterogeneously enhancing, partially calcified, well-defined mass lesion in the upper pole of the left kidney. The patient's general physical examination was unremarkable. Blood, renal function tests and urinalysis were within normal limits. Grossly, the specimen from nephrectomy measured 15 × 6 × 7 cm and included renal parenchyma bearing tumor formation (Fig. 1A). The tumor was well-circumscribed, measuring 9 × 6 cm. The cut section was multiloculated, cystic. The cysts ranged from 0.2 cm to 4.5 cm, septal thickness did not exceed 0.3 cm. The content of the cyst included pale yellowish gelatinous material and occasional clots. The surface of the cysts was smooth and no solid masses or papillary projections were identified. No connection was seen between the cysts and the renal pelvis. Microscopic examination demonstrated a cystic neoplasm with multiple variable-sized cysts lined by flattened to low cuboidal epithelium with dense regular nuclei and variable amount of cytoplasm with some degree of clearing (Fig. 1B, C). These cysts were separated by septae containing fibrocollagenous stroma enriched by smooth muscle bundles (Fig. 1D); occasional foci of calcification were encountered. Renal capsule, vessels, adrenal gland and perinephric fat were free of tumor invasion. The diagnosis of MLCN was established and additional immunohistochemical (IHC) investigation with a panel of antibodies was performed (all provided by DAKO), adhering to the manufacturer's instructions.

The epithelial lining expressed both CKAE1-AE3 and CK19, was invariably positive for Vimentin and for unexplained reasons, showed weak to moderate expression of CD99. The stromal component consistently expressed SMA in fascicular fashion, while Desmin was expressed in a definitely patchy, dot-like manner. Epithelial cells did not express CD10 and CD15, lacked ER and PR. Similar negative profile was seen in the stromal cells within the septae. The same set of IHC markers was applied to the singular case of MCRCC we had. The only difference noted was weaker CK19 expression.

DISCUSSION

MLCN is an uncommon, non-heritable, mostly unilateral renal tumor which has a female predominance in adults with mean age about 50 years (8, 10). MLCN presents with non-specific symptoms such as abdominal or flank pain, urinary tract infection symptoms, hematuria and hypertension (1). These tumors are commonly found incidentally on imaging studies or may present as an abdominal mass found on routine physical examination. Distinct radiographic features have been described, but are not universally present in all cases (9). Ultrasound is often the first investigation used in evaluating abdominal masses, confirmed by CT scan. The sonographic findings depend on the amount of stromal tissue and size of empty-appearing spaces. Cysts usually show up as hypoechoic lesions delineated by hyperechoic septae and this feature can be suggestive of MLCN but not diagnostic. The mass is often easily demonstrable at ultrasound, with an average diameter of approximately 10 cm. Calcification has been described varying from rare to presented in up to 46 % of cases (10) feature of MLCN, and curvilinear calcifications may be seen on ultrasound within the septa.

The nonspecific clinical findings and the poor contribution of imaging studies make it impossible to make a definitive preoperative diagnosis. Various pathological criteria have been proposed in the past to differentiate and classify this entity. Powell et al. (7) established eight diagnostic criteria for these lesions: unilateral involvement; solitary lesion; multilocular lesion; non-communication with the renal pelvis; non-communication of the cysts with each other; loculi lined by epithelium; intralocular septa devoid of renal parenchyma; and if residual renal tissue were present, it should be normal. Of these criteria, one was modified by Boggs and Kimmelstiel (2), several years later to include the presence of immature renal tissue in the intervening septa. Following the 2004 World Health Organization (WHO) classification of renal neoplasms, MLCN is defined as a tumor composed of large cysts, microcysts, and tubules with stroma consisting of variably cellular spindle cells, the dividing septae being less than 5 mm (3, 4). The cells lining cysts may be flat, cuboidal or hobnail. Most epithelial cells had scant amphophilic cytoplasm, however Turbiner et al. described that 5 out of 20 investigated cases had clear vacuolated cells (8). The differential diagnosis with MCRCC is only in the septae containing small groups of clear cells indistinguishable from low-grade clear cell carcinoma.

Marked overlapping morphologic characteristics are identified comparing MLCN and MEST. In contrast to MLCN, the epithelial and stromal elements of MEST are more complex with thicker cystic septae that may expand to form solid areas. MLCN and MEST are considered as two distinct entities and are categorized as “mixed mesenchymal and epithelial tumors” in the 2004 WHO classification (3). Based on the clinical, morphological and genetic overlap some authors believe that these tumors should be grouped together as a single entity and proposed the unifying term “renal epithelial and stromal tumor” (REST), (8, 10).

There are a few large studies exploring IHC expression of different markers in the epithelium and stroma of MLCN (6, 8, 10). Albeit minor discordances, neoplastic epithelial cells have been shown to express CK 19, whereas the stromal component was frequently positive for ER and PrR especially in cases with ovarian-like stroma. As exemplified in our cases, accounting for all case reports up to date, IHC is of little help when we are faced with distinguishing this neoplasm from the main diagnostic problem – MCRCC.

IN SUMMARY, we present a rare case of renal tumor that supposedly lies at the benign end of the spectrum of adult cystic renal neoplasms. At present, this spectrum encompasses different entities that bear little or no clinical implication – e.g. MEST or even MCRCC carcinoma, notable for excellent clinical prognosis.

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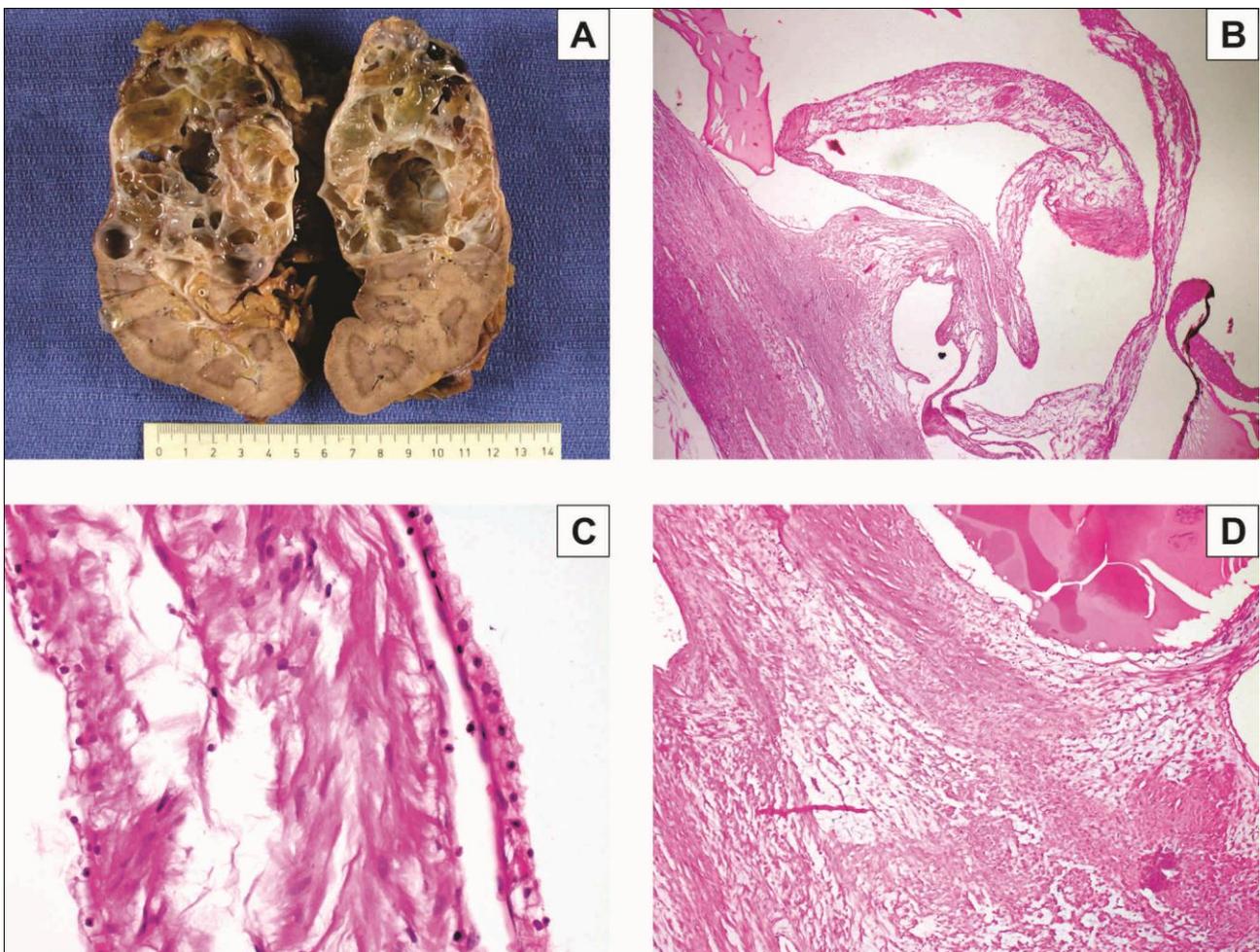


Fig. 1. A – Gross specimen. B, C – Hematoxylin&Eosin staining revealed multiple variable-sized cysts lined by flattened to low cuboidal epithelium, dense regular nuclei, variable amount of cytoplasm with some degree of clearing; D - septae consist of fibrocollagenous stroma with smooth muscle bundles.

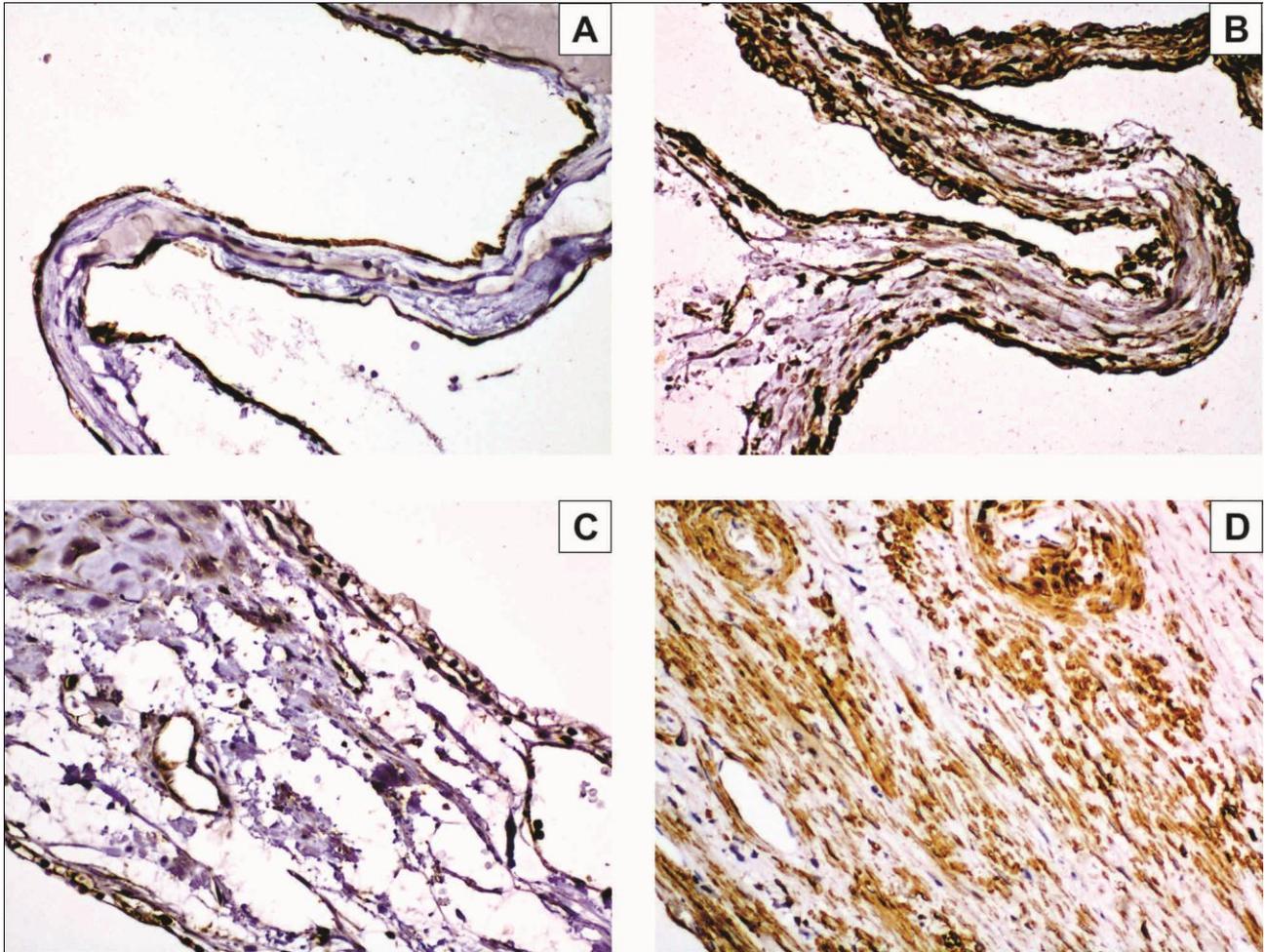


Fig. 2. IHC panel: A – CK19, B – Vimentin, C – CD99, D – SMA.