

Case Report

Multilocular Cystic Renal Cell Carcinoma: A Rare, Unique Entity and Diagnostic Challenge

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Abstract

Multilocular cystic renal cell carcinoma (MCRCC) is a rare tumor with an excellent prognosis. We report a case of MCRCC in a 33-year-old male who presented with vague discomfort in the right flank for the last 1.5 years. Computed tomography scan revealed a multiseptate cystic mass in the upper pole of the right kidney. Surgically resected well-circumscribed cystic mass was formed entirely by thin-walled non-communicating cysts of variable size separated from surrounding renal parenchyma by a distinct fibrous wall. On histopathological examination, clear cells with prominent cytoplasmic border and low nucleocytoplasmic ratio were present in the lining epithelium as well as in the intervening septa. No solid area was appreciated in the cystic mass. Finally, after corroboration with the imprint cytology findings, the tumor was diagnosed as MCRCC with TNM staging and Fuhrman nuclear grading of T1bN0M0 and grade 1, respectively.

Keywords: Clear cell, cystic tumor, low-grade carcinoma, multilocular cystic renal cell carcinoma

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Introduction

Multilocular cystic renal cell carcinoma (MCRCC) is a rare cystic tumor of the kidney, occurring in the age range of 20 to 76 years, composed entirely of multiple cysts with clear cells in the septa and indistinguishable from grade 1 clear cell carcinoma. It has an excellent prognosis with no reports of recurrence or metastasis. It constitutes less than 5% of all renal cell carcinomas (RCCs). It must be distinguished from morphologic mimickers like benign multicystic nephroma (MCN) as well as from aggressive cystic clear cell carcinoma (cRCC).¹ However, the true incidence of MCRCC before the application of strict criteria of Eble and Bonsib² is unknown.³ Most of the MCRCC cases were discovered incidentally as overt symptoms of renal mass were usually absent.⁴

Case Report

A 33-year-old non-smoker male presented with vague discomfort in the right flank, off and on during the last 1.5 years, unrelieved by medical treatment in a rural hospital. There was no history of acute exacerbation of abdominal pain, weight loss, fatigability, fever, or urinary complaints including hematuria. The clinical examination revealed mild pallor, right-sided abdominal fullness and mild tenderness in the right flank. There was no palpable lymph node. A well demarcated multiseptate cystic space-occupying lesion in the upper pole of the right kidney without any solid area or calcification was detected on abdominal contrast-enhanced computed tomography (CECT) scan (Figure 1a).

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Features of hydronephrosis and hilar or para-aortic lymphadenopathy were not found. Routine preoperative examinations were otherwise normal. On surgical exploration, the entire multicystic mass, along with a portion of adjacent kidney tissue, was excised and sent for frozen section study. The imprint cytology of fresh tissue displayed a moderately cellular smear comprising sheets of cells with round nuclei having minimal atypia, inconspicuous nucleoli, vacuolated to clear moderate amount of cytoplasm in a hemorrhagic background (Figure 1b). Grossly, the well-circumscribed cystic mass was formed entirely by thin-walled non-communicating cysts of variable size, containing hemorrhagic fluid and separated from surrounding renal parenchyma by a distinct fibrous wall (Figure 1c). The mass measured $5.8 \times 5.2 \times 4$ cm. The frozen section histology revealed a multicystic lesion lined with monolayered and occasionally multilayered epithelium without any solid component (Figure 1d and 2a). The lining cells had conspicuous amounts of clear to pale eosinophilic cytoplasm and hyperchromatic nuclei with mild pleomorphism (Figure 2b). Thin vascular channels with or without adherent lining epithelium were also noted. Correlating the findings of imprint cytology and frozen section histology, a provisional diagnosis of MCRCC was made and a partial nephrectomy followed. Histopathological examination of formalin-fixed, paraffin-embedded, hematoxylin and eosin (H and E) stained tissue sections demonstrated a multiloculated cystic mass consisting of variably-sized, often hemorrhagic cysts, mostly lined with low cuboidal epithelium and occasionally forming small papillary fronds (Figure 2c and 2d). Tumor cells infiltrated within the thin fibrous septa in between the cysts in singles and small clusters but without forming any solid expansile nodules (Figure 3a and 3b). Most of the cells had small hyperchromatic lymphocyte-like nuclei, inconspicuous nucleoli, prominent cytoplasmic border, clear cytoplasm and low nucleocytoplasmic ratio (Figure 3c). The tumor-free adjacent renal parenchyma (Figure 3d) was otherwise unremarkable. The renal capsule, vessels, adrenal gland and perinephric fat were found to be tumor-free.

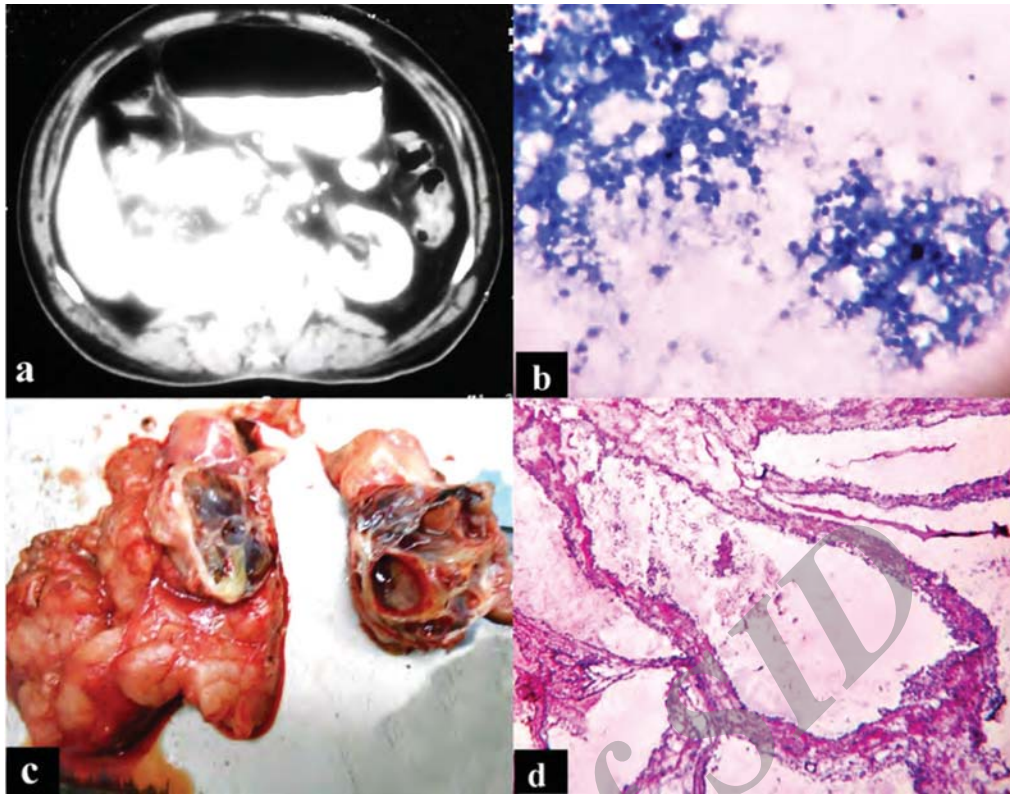


Figure 1. (a) Axial view of CECT of abdomen showing a well-defined multiseptate cystic mass in the upper pole of right kidney; (b) Photomicrograph of imprint smear of the resected cystic mass (Giemsa, $\times 400$); (c) Resected specimen of multiseptate cystic mass of right kidney; (d) Photomicrograph of frozen section showing a multiseptate mass lined mostly with cuboidal to flattened epithelium (H and E, $\times 40$).

Finally, the tumor was diagnosed as MCRCC with TNM staging and Fuhrman nuclear grading of T1bN0M0 and grade 1, respectively. On follow-up after six months of surgical resection, the patient was asymptomatic with no evidence of recurrence or metastasis.

Discussion

MCRCC appears to be a neoplasm with an intrinsically cystic growth pattern, and no, or at the most little, malignant potential. The first MCRCC was reported by Robinson⁵ in 1957, the term “multilocular cystic renal adenocarcinoma” was introduced and accepted as a distinct entity in 1982⁶ and the strict criteria for the diagnosis of the same was suggested by Eble and Bonsib² in 1998. The present case met all the criteria of MCRCC,^{1,2} namely an expansile mass surrounded by a fibrous wall, tumor entirely composed of cysts and septa with no expansile solid nodules, and the septa containing aggregates of epithelial cells with clear cytoplasm.

Corica et al.,⁷ expanded the maximal acceptable percentage of solid tumor component from the 10% criterion of Murad et al.,⁸ to 25%, which was later applied by Nassir et al.,⁴ Conversely, the criteria proposed by Eble and Bonsib,² which was later accepted in the WHO classification,¹ clearly stated that MCRCC should have no expansile nodules in the septa. Hence, Cystic RCCs (cRCCs) were incorporated into the analysis in addition to true MCRCC in various studies, leading to some controversies concerning its malignant potential.³ Two major studies have been conducted by Suzigan et al.,³ and Halat et al.,⁹ applying the strict criteria: the

former revealed that most of the cases had stage T1 and Fuhrman grade 1 as in the present case, in addition to 5-year disease-specific survival rate of 100% and no evidence of recurrence on follow-up.

The differential diagnosis of MCRCC includes other cystic lesions of the kidney, primarily cystic nephroma, extensively cystic clear cell RCC (cRCC), clear cell variant of papillary RCC, cystic necrosis in RCC and tubulocystic carcinoma.⁹ Cystic nephroma cannot be differentiated confidently from MCRCC grossly or radiologically. Literature available on the role of cytologic diagnosis of the cystic renal lesions is inadequate and often controversial. However, unlike cystic nephroma, which has a paucicellular smear with scattered epithelial cell with moderate atypia, multicystic renal cell carcinoma shows moderate epithelial cellularity with no or mild nuclear atypia.¹⁰ This is very similar to the imprint cytology findings in the present case. In our case, although aspiration cytology was not done, imprint cytology proved to be an invaluable tool in making a correct frozen section diagnosis along with histologic correlation.

Histologically, distinguishing features of cystic nephroma are focally distributed clear cells in the lining of the septa, hobnail epithelium, ovarian-like stroma, mature tubules in the septa and absence of clear cells in the fibrous walls. Grossly evident solid areas in cystic mass or expansile nodules of clear cells under microscope are features favoring clear cell cRCCs. Although the immunoprofiles of MCRCCs and clear cell RCCs are not identical, careful and meticulous application of light microscopic morphologic criteria remains the most important diagnostic tool. Furthermore, MCRCCs may show focal and small papillary fronds but

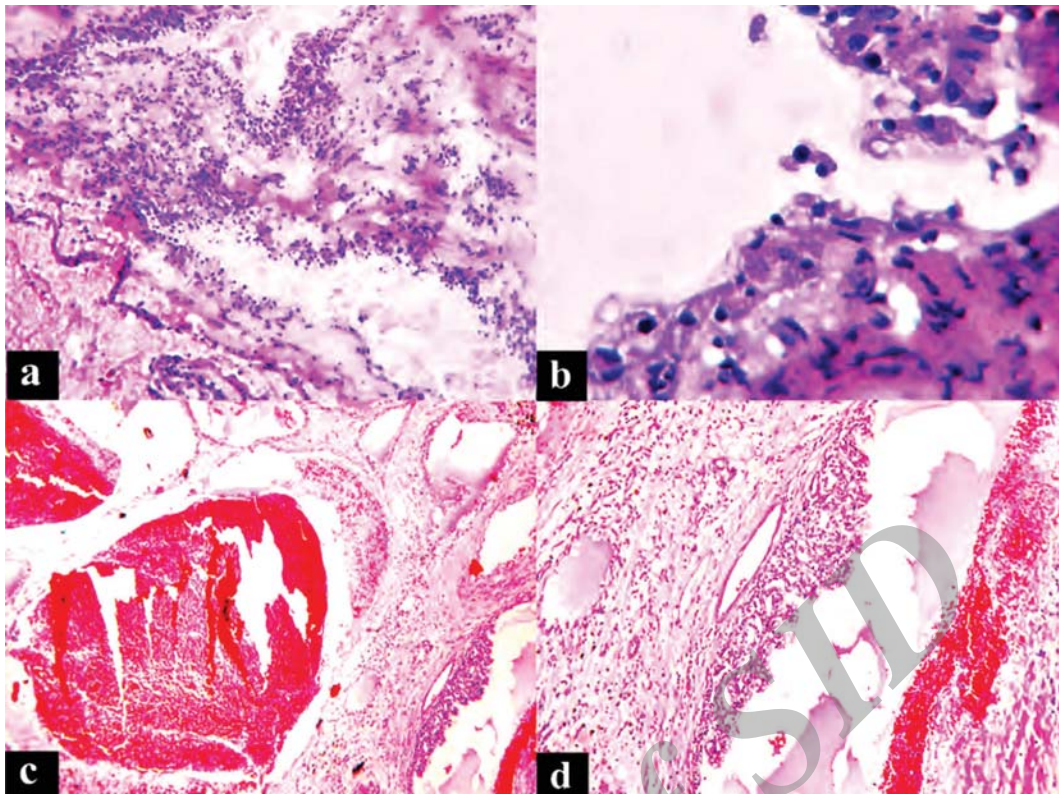


Figure 2. (a) Photomicrograph of frozen section showing monolayered and multilayered epithelium lining the cystic mass and thin vascular channels (H and E, $\times 100$); (b) Frozen section showing multilayered epithelium having clear to pale eosinophilic cytoplasm with hyperchromatic nuclei (H and E, $\times 400$); (c) Photomicrograph of multiloculated hemorrhagic cyst lined with flattened epithelium and small papillary fronds (H and E, $\times 40$); (d) Photomicrograph showing papillary fronds lined with clear cells (H and E, $\times 100$).

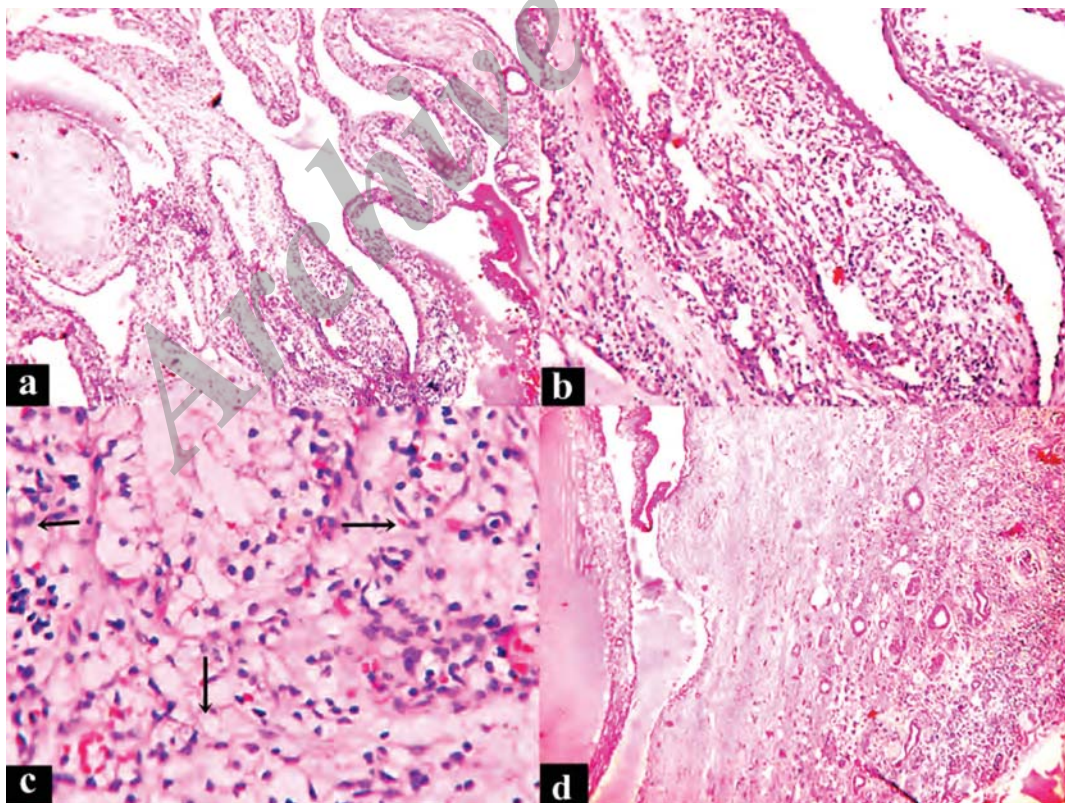


Figure 3. (a) Photomicrograph of multilocular cystic mass showing fibrous septa infiltrated by clear cells (H and E, $\times 40$); (b) Clear cells in singles and in clusters in the intervening fibrous septa under low power microscopic field (H and E, $\times 100$); (c) Photomicrograph showing clear cells with low N:C, small hyperchromatic nuclei and prominent cell border infiltrating the surrounding fibrous septa (in the direction of the arrow) from the lining epithelium (H and E, $\times 400$); (d) Photomicrograph showing adjacent renal parenchyma (right) free from tumor (left) mass (H and E, $\times 40$).

the extensive papillary structures of the clear cell variant of papillary RCC are usually absent in MCRCC.^{3,9,11}

As MCRCCs are tumors of low grade and stage with low malignant potential, they can be cured by surgical resection, either by simple nephrectomy or nephron sparing surgery, such as partial nephrectomy as in the present case.^{3,7} Our case is thus unique as it fulfills the above-mentioned strict criteria and depicts the corroborative role of imprint cytology and histology in diagnosing this rare neoplasm.

Conflict of interest: None

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