CASE REPORT | renal cancer

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Multilocular Cystic Renal Neoplasm of Low Malignant Potential: Mimicker of Cystic Clear Cell Carcinoma – Urologist's Perspective

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Abstract

Introduction Multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) is a rare subtype of clear cell renal cell carcinoma (ccRCC) accounting for 2-4% of RCC. It is defined as a neoplasm that is composed entirely of numerous cysts surrounded by fibrous capsule and septa containing clear cells without expansile growth or mural nodules (WHO 2016). The purpose of this manuscript is to highlight that it is imperative to identify this entity by strict histological criteria and distinguish this entity from cystic ccRCC due to its low malignant potential, excellent prognosis with no recurrence or metastasis.

Case report A 46-year-old male presented with continuous mild loin pain for a month. There were no lower tract urinary symptoms. Ultrasound abdomen showed left lower pole renal mass. CECT-KUB was done as a definitive investigation which showed a solitary left lower pole renal cystic lesion with enhancement of size 3.8x3.6cm (Bosniak IV). As per CT findings, the patient underwent Laparoscopic partial nephrectomy. Histopathological examination showed multiple cysts with thin septal walls possessing clear cells with low-grade nuclei. 2 years of follow-up postoperatively with imaging studies revealed no recurrence or metastasis.

Conclusions The purpose of this report is to emphasize the need to identify this entity by strict histological criteria as per WHO guidelines, as imaging studies were more often inconclusive. Urologists should have an adequate understanding such an entity. Almost all cases are amenable to partial nephrectomy irrespective of size and no documented evidence of recurrence and metastasis which mandates less stringent follow up postoperatively as compared to ccRCC.

Key words kidney, tumour, nephroma, cystic carcinoma, nephrectomy

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Introduction

Multilocular cystic renal cell carcinoma (MCRCC) is a very rare subtype of clear cell renal cell carcinoma (CCRCC) accounting for 2-4% of CCRCC. It is a purely cystic kidney tumour that has cellular features and cytogenetic alterations (3p mutation, VHL) that are virtually identical to that of CCRCC [1, 2].

Recently, the International Society of Urological Pathology (ISUP 2013) and the World Health Organization (WHO 2016) redesignated the classification of tumours of the kidney [3-5]. Because of distinct pathological patterns and no incidence of recurrence and metastasis, MCRCC was redesignated as Multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) [6].

WHO proposed relatively strict diagnostic criteria and defined MCRNLMP as "a neoplasm that is composed entirely of numerous cysts surrounded by a fibrous capsule and septa that contains clear cells without expansile growth or mural nodules" (WHO 2016). These tumours are morphologically and radiologically indistinguishable from low-grade cystic CCRCC.

ISUP (2013) replaced the term “carcinoma” to low malignant potential [7, 8]. Tretiakova et al., [9] summarized from all similar sources available in the literature and concluded that MCRNLMP patients with atleast five-year follow-up had no recurrence or metastasis. The purpose of this manuscript is to emphasize the importance of identifying these entities by strict histological criteria as defined by WHO (2016) and making the urologists aware of this potentially curable condition. These lesions fall under the lower risk category, irrespective of TNM staging. On long term follow-up, as compared to CCRCC, there are no documented cases of recurrence or metastasis noted after complete resection by either radical or partial nephrectomy [10].

Case report

A 46-year-old non-smoker male presented with continuous dull aching left loin pain for one-month duration. He did not have any bothersome lower urinary tract symptom or any medical comorbidities. His blood biochemical investigations, renal and liver function tests were normal.

Ultrasonography of the whole abdomen showed a left lower pole cystic renal mass. Contrast-enhanced computed tomography (CECT KUB) scan showed a well defined, solitary, partially exophytic mass that was multicystic with solid components within them (Bosniak Category – IV). It was heterogeneously enhancing left lower pole renal mass, measuring 3.8X3.6cm (**Figure 1**). The patient underwent laparoscopic partial nephrectomy. Postoperative period was uneventful.

Gross examination of the specimen showed a single lesion of size 4.2x3 cm, encapsulated, purely multicystic possessing varying sizes of non-communicating cysts with clear serous or gelatinous material as content. There was no necrosis or solid nodules. Microscopic examination showed a multicystic lesion with thin septal walls of fibro-collagenous connective tissue containing single or occasionally multiple layers of clear cuboidal cells containing abundant cytoplasm (**Figure 2A, 2B**).These cells had small hyperchromatic nuclei with regular borders and inconspicuous or absent nucleoli (ISUP grade 1 - low grade). Mitotic figures were scarce. No expansile mural nodules, necrosis, vascular invasion, hyalinization or sarcomatoid changes were noted. Immunohistochemistry showed strong membrane positivity for vimentin and epithelial membrane antigen (EMA) (**Figure 3A, 3B**). Tumour falls under T1bN0M0 with ISUP nuclei grade 1. The patient is on regular follow-up with imaging studies and has a disease-free survival of more than three years.

Discussion

Renal cysts are one of the common findings that we come across during the screening ultrasound abdomen in our routine urological practice. Most of them are benign and asymptomatic. They become symptomatic when there is a secondary infection or bleeding within the cysts. The incidence of renal cysts increases with increase in age and seen in over 50% of patients above 50 years of age [11]. Hartman reported that up to 15 % of all renal cell carcinomas are cystic [12]. On the other hand, MCRNLMP represents only 2-4% of all CCRCC [13]. These tumours develop due to extensive cystic regression or growth within renal tubules, causing obstruction ultimately forming cysts.

The term MCRNLMP was first suggested by Suzigan et al. [14]

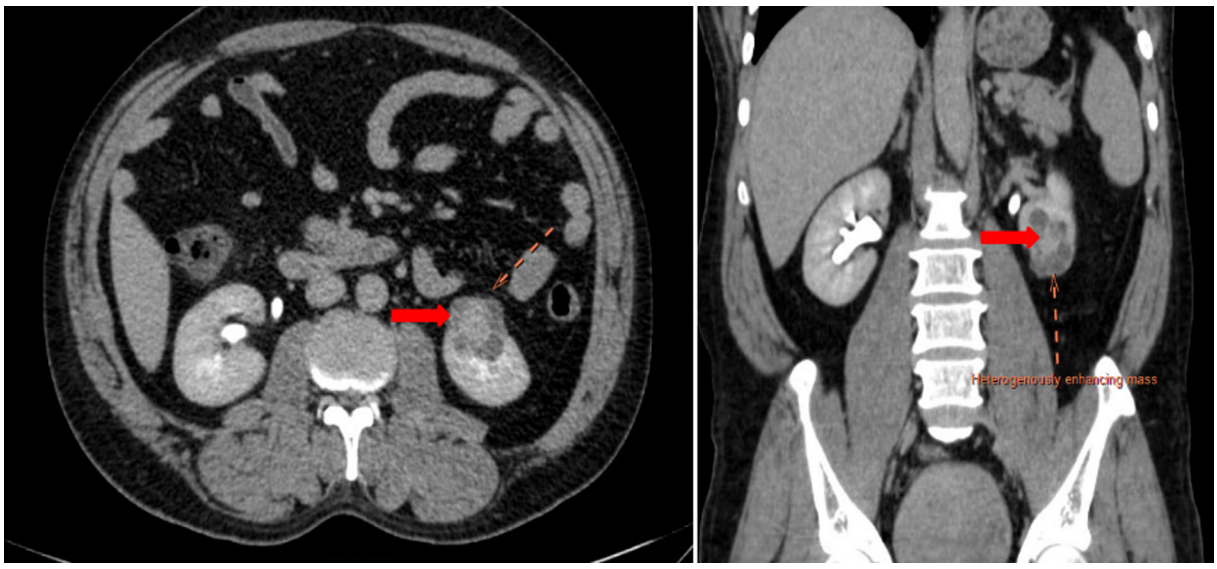

Figure 1. Contrast enhanced CT-KUB showing a well defined, solitary, partially exophytic, multicystic with solid component, heterogeneously enhancing left lower pole renal mass.

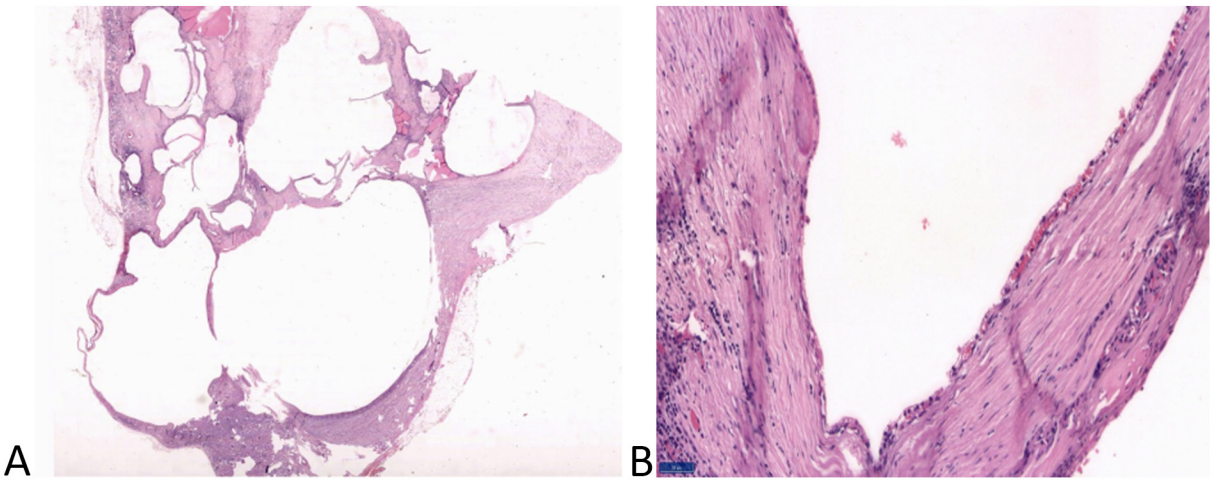

Figure 2. Haematoxylin & Eosin staining of the cystic lesion. (A) Multiple cystically dilated spaces separated by thin fibrous septae (20X); (B) Cystic spaces are lined by a single layer of low cuboidal epithelial cells with clear cytoplasm (100X).

in 2006, where they revisited 2004 WHO classification of renal tumours. In his study on 45 patients with multilocular cystic RCC, they observed that the condition carried an excellent prognosis and the five-year disease-specific survival rate was 100%. They observed that 82% of their cases in were T1 stage and the low nuclear grade was found in 100% cases (G1-62% and G2-38%). In their series, none of the patients had any evidence of disease after surgery.

The term MCRCC was renamed as MCRNLMP by ISUP in 2013. The WHO Classification of 2016 as well subsequently accepted this change in terminology. MCRNLMP is defined as a multilocular cystic tumour lined by low ISUP grade (1-2) clear cells, immunohistochemically and molecularly not different from CCRCC [15].

It would be of some clinical significance, had any of the imaging studies given guidelines to differentiate atypical renal cysts, partially cystic RCC and MCRNLMP [16]. All three conditions look similar in imaging that prevents a Urologist or Radiologist in diagnosing this condition pre-operatively. However, histopathological examination could clearly distinguish between the three types. The gross features included well-encapsulated multilocular non-communicating cysts containing clear serous or gelatinous fluid or rarely hemorrhagic debris but absent solid nodules or tumour necrosis [17]. The microscopic features include cysts with septae lined by clear cuboidal cells with low-grade nuclei either as a single layer or in aggregates. A lack of expansile growth or solid nodules is a characteristic finding in such conditions [18]. Immunohistochemistry is positive for CD10, EMA and vimentin.

Other primary differential diagnoses include cystic nephroma, cystic clear cell papillary RCC and tubulocystic RCC [19]. Cystic nephroma is seen predominantly in females, and the presence of ovarian type stroma is a distinguishing factor. Cystic clear cell papillary RCC also contains clear cells with low-grade nuclei, but differentiating feature is the presence of papillary architecture. Tubulocystic RCC lining cells have eosinophilic cytoplasm with

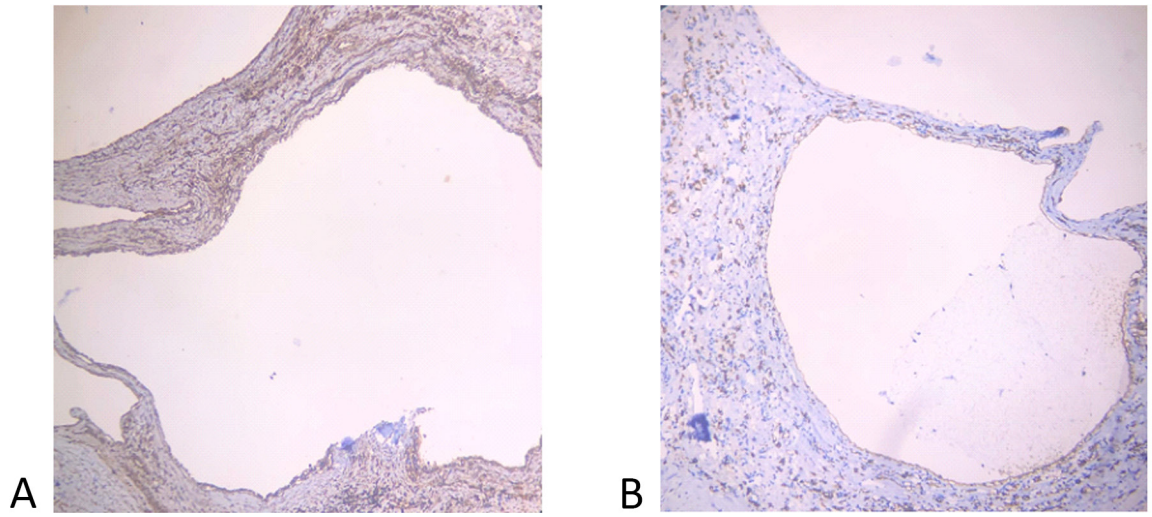

Figure 3. Immunohistochemistry of the tumour showing positivity for vimentin (A) and EMA (B) staining in the cystic lining cells (Immunostains, X100).

high-grade nuclei instead of clear cells. As described earlier, the differentiating factor for cystic CCRCC is the presence of expansile nodules.

Li et al., [20] in one of the most extensive reported case series of 76 patients concluded that these tumours were predominantly of a low nuclear grade irrespective of tumour size and TNM staging and suggested longer follow-up interval to minimize unnecessary investigations. Nassir et al. [21] defined MCRNLMP as a predominantly cystic lesion with neoplastic clear cells, probably a subtype of CCRCC having a benign clinical course.

Gong et al., [22] in their study on 31 patients, found that Multilocular cystic RCC had no tumour progression or metastasis and had excellent prognosis. Murad et al. [23] in one of the most extended follow-up of 6 cases of MCRNLMP observed neither recurrence nor metastasis concluding that these tumours are a low-grade variant of RCC with excellent prognosis.

A comparative study between MCRNLMP and predominantly cystic CCRCC by Tretiakova et al. [9] concluded MCRNLMP had uniformly good behavior and support ISUP recommendation for its non-carcinoma designation. They also concluded that predominantly cystic CCRCC had better prognosis as compared to solid or non-cystic CCRCC and the extent of the cystic component should be mentioned in the histopathology report by the reporting pathologist.

These studies confirmed that MCRNLMP is a low grade, well-defined tumour and most cases were amenable to partial nephrectomy with no recurrence and metastasis. In our case, on three years follow-up post partial nephrectomy with annual clinical examination and imaging studies, showed no recurrence or metastasis. Urologists should have an adequate understanding of this entity because we can adopt longer follow-up intervals for patients with this tumour to minimize unnecessary examinations and patient anxiety.

Conclusions

It is a rare subtype of CCRCC with low malignant potential and represents 2-4% of all CCRCC cases. Most cases were detected incidentally and cannot differentiate from other cystic lesions by imaging studies. Histopathology as per WHO guidelines helps in definitive identification. Irrespective of TNM stage, they fall under low risk, and no documented evidence of recurrence or metastasis after complete resection on follow up. Proper understanding of this entity by urologists helps in reducing patient anxiety by adopting longer follow-up intervals and avoiding cumbersome imaging studies.

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NIL

Ethical policy

Approval was taken from institutional ethical committee. The study was performed in accordance with the Declaration of Helsinki. Patients gave their informed consent for their participation.

Author contributions

All authors have equally contributed to the manuscript.

Competing interests

NIL

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