Case Report

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Pathology Section

Rare Case of Multilocular Cystic Renal Neoplasm of Low Malignant Potential with Chronic Pyelonephritis

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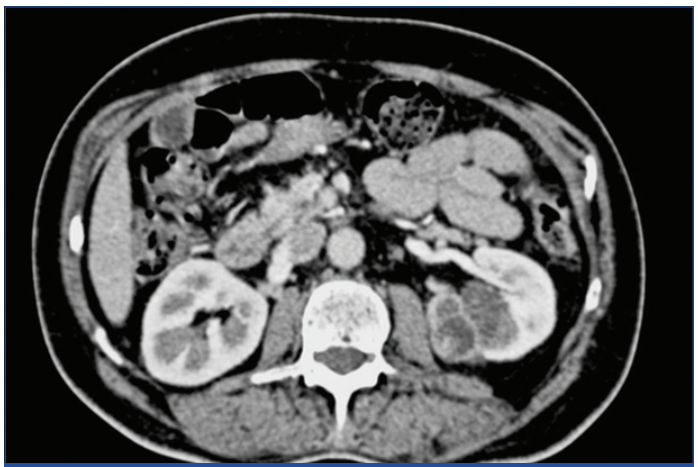
ABSTRACT

Multilocular Cystic Renal Neoplasm of Low Malignant Potential (MCRNLMP) represents a rare variant of clear cell (conventional) renal carcinoma. They constitute between 3-6% of clear cell Renal Cell Carcinoma (RCC). The RCC constitutes less than 1% of all renal tumours. The MCRNLMP has an excellent prognosis with no reports of recurrence or metastasis. Authors reported a case of 67-year-old male patient on account of its rarity, co-existing pyelonephritis and incidental detection of MCRNLMP. Differentiation between MCRNLMP, RCC variants and other cystic lesions with clear cells is important as prognosis, treatment differ markedly. Radiological Bosnaik classification of complex cysts in category IIF and III is challenging and requires microscopic examination for correct diagnosis. Histopathology shows cysts separated and fibrous septae having groups of clear cells with low grade nuclei. Immunohistochemistry with Carbonic Anhydrase-IX (CA-IX), Epithelial Membrane Antigen (EMA), Cytokeratin (CK7) and CD10 is confirmatory. Diagnosis requires detailed imaging studies, meticulous grossing of nephrectomy specimens, extensive sampling of cystic tissue to find clear cells and immunohistochemistry (IHC).

Keywords: Bosniak classification, Complex renal cystic lesions, Immunohistochemistry

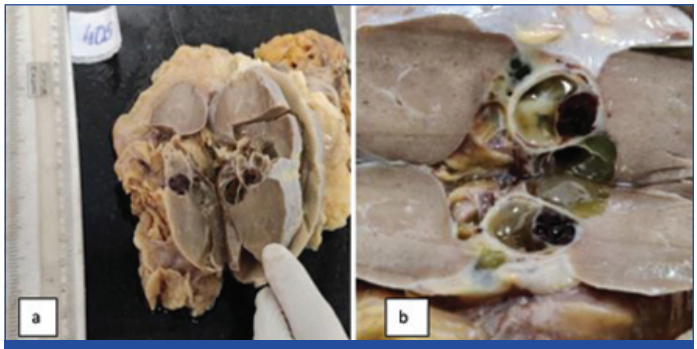
CASE REPORT

A 67-year-old male presented in surgical Outpatient Department (OPD) with pain in abdomen for two weeks. He had a history of recurrent urinary tract infection and hernia. There was no other significant medical history. He had soft reducible inguinal swelling on left side. Inguinal hernia reduction surgery was planned. As a part of preoperative work up abdominal ultrasonography was done. Left kidney showed cystic lesion near the hilum. Hence, Contrast Enhanced Computed Tomography (CECT) was advised. It showed a multilobulated septated cystic lesion and heterogeneously enhancing cystic nodule involving posteromedial cortex of middle 1/3rd of left kidney, suggestive of neoplasm [Table/Fig-1]. Provisional diagnosis was renal cell carcinoma in underlying chronic pyelonephritis. The patient underwent left radical nephrectomy.



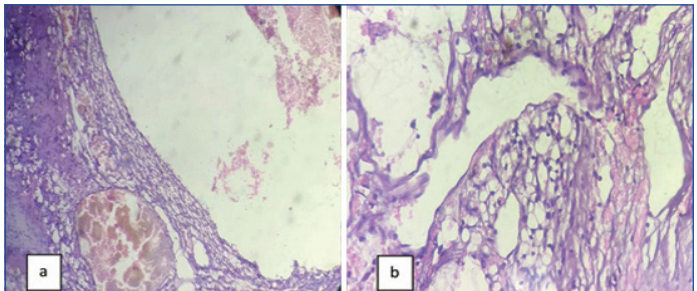
[Table/Fig-1]: Contrast Enhanced Computed Tomography (CECT) showed multilobulated septated cystic lesion involving posteromedial cortex of middle one third of the left kidney.

Pathology laboratory received the specimen. Grossly, the left kidney along with perinephric fat measured 9.5×5.5×4.5 cm and ureter 1.0 cm in length. Left side adrenal and lymph nodes not identified. Cut surface of the kidney showed a well circumscribed multiloculated cystic lesion measuring 3×2.5×1 cm, situated near the hilum of the kidney. Thin septae were seen in between the cysts [Table/Fig-2a,b].



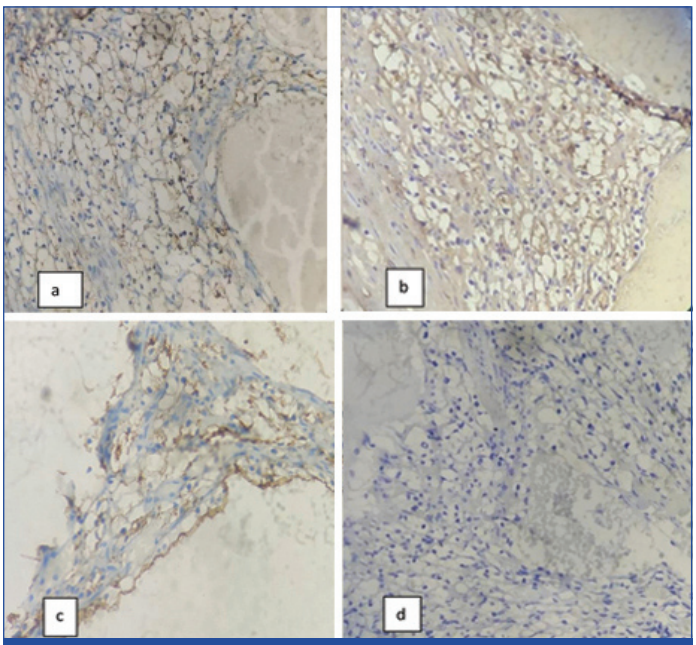
[Table/Fig-2a-b]: a): Left radical nephrectomy specimen showing cystic growth near the hilum of the kidney. b) Encapsulated multiloculated cystic growth filled with secretions.

Microscopy showed variably sized, non communicating cysts lined by flattened to cuboidal epithelium with clear cytoplasm. The septae showed clear cells. They had well defined cell borders with abundant clear cytoplasm and uniform round to oval hyperchromatic nuclei and inconspicuous nucleoli (Fuhrman Nuclear Grade 1). Cyst lumen was filled with eosinophilic secretions [Table/Fig-3a,b]. Lymphovascular invasion was not seen. Surrounding renal parenchyma showed glomerular sclerosis, thyroidisation of renal tubules. Interstitium showed vascular wall thickening, fibrosis and lymphoplasmacytic infiltrate.



[Table/Fig-3a-b]: a): Cyst filled with haemorrhagic material (H&E, 10x). b): cyst wall lined by clear cells, uniform round to oval hyperchromatic nuclei and inconspicuous nucleoli, clear cytoplasm and well defined cell borders (H&E, 40X).

Microscopically, differential diagnosis of clear cell rich cystic lesions of the kidney was cystic nephroma, clear cell papillary RCC, tubulocystic carcinoma, clear cell rich RCC with cystic degeneration and Multilocular Cystic Renal Neoplasm of Low Malignant Potential (MCRNLMP). The IHC with CD68 was done to rule out macrophages in xanthogranulomatous pyelonephritis as the patient had recurrent urinary tract infection. Tumour cells showed immunoreactivity with Carbonic Anhydrase-IX (CA-IX) [Table/Fig-4a], cytokeratin (CK7). [Table/Fig-4b], Epithelial Membrane Antigen (EMA) [Table/Fig-4c], and negative staining of CD10. [Table/Fig-4d] and CD68. Renal cut margin including renal vein, renal artery and ureter, as well as Gerota's fascia were free of tumour. The histopathological features along with IHC confirmed the diagnosis of MCRNLMP co-existing in chronic pyelonephritis. The patient is stable and in good condition and without any recurrence till now.



[Table/Fig-4a-d]: Immunohistochemistry showed positivity for Carbonic Anhydrase-IX (CA-IX) a), cytokeratin 7 (CK 7) b), Epithelial Membrane Antigen (EMA) c), and negative for CD10 d), (IHC 200x).

DISCUSSION

In clinical practice renal cysts are commonly encountered incidental findings. Cystic lesions comprise a wide spectrum of hereditary, acquired, developmental, and neoplastic conditions. Differential diagnosis are polycystic kidney disease, unilateral renal cystic disease, renal simple cysts, multicystic dysplastic kidney, pluricystic kidney of the multiple malformation syndromes, juvenile nephronophthisis and medullary cystic disease, medullary sponge kidney, glomerulocystic kidney disease, cystic kidney in tuberous sclerosis, and in von Hippel-Lindau syndrome, cystic nephroma, cystic variant of congenital mesoblastic nephroma, mixed epithelial stromal tumour of the kidney, renal lymphangioma, pyelocalyceal cyst, peripelvic cyst and perinephric pseudocyst, acquired renal cystic disease of long term dialysis, and cystic renal cell carcinoma and sarcoma [1]. Most of the cysts are benign simple cysts. Renal cystic lesions are common cause of end stage renal disease in adults.

Multilocular Cystic Renal Neoplasm of Low Malignant Potential (MCRNLMP) is a rare variant of clear cell (conventional) renal carcinoma. It accounts for less than 1% of all renal tumours. Most of the cases were discovered incidentally as overt symptoms of renal mass were usually absent [2]. The term Renal Cell Carcinoma (RCC) is obsolete now and MCRNLMP is the preferred term in the latest WHO classification of tumours of the urinary system and male genital organs (2016) [2]. According to World Health Organisation (WHO) 2016 classification, diagnostic criteria of MCRNLMP are as follows:

a) Tumour containing multiple cysts with low grade tumour cells (ISUP-International Society of Urological Pathology/WHO grade 1/2).

b) Cysts are lined by a single layer of tumour cells of low grade with abundant clear cytoplasm.

c) Septae contains few clusters of clear cells with non expansile growth.

Several studies report no recurrence or metastasis in patients after surgical treatment. Surgical resection is curative [2-4]. Cystic nephroma, clear cell papillary renal cell carcinoma with predominant cystic configuration, tubulocystic carcinoma of the kidney, benign multilocular renal cortical cyst have to be differentiated from MCRNLMP [2]. The MCRNLMP is differentiated from cystic nephroma according to location and arrangement of clear cells lining the septa. Focal presence of the lining clear cells and characteristic ovarian-like stroma seen in cystic nephroma. Cystic clear cell papillary RCC has clear cells in papillary architecture in most areas and linear arrangement of nuclei away from basement membrane; a feature not found in MCRNLMP [5]. The CA-IX immunostaining pattern also differs. Diffuse membranous box-like positivity seen in MCRNLMP while diffuse membranous cup shaped (sparing luminal border of tumour cells) positivity seen in other [6]. Tubulocystic carcinoma shows small to medium sized tubules lined by tumour cells with high grade nuclei. Oncocytic change with hobnailing can also be seen. The intervening septa are fibrotic. These cells express CD10, Alpha-Methylacyl-CoA Racemase (AMACR) and sometimes CK7 and High Molecular Weight Cytokeratin (HMWCK) with less than half expressing CA-IX [4]. Regressing Clear Cell (RCC) with cystic degeneration has more than 75% cystic areas with expansile growth of clear cells [7]. Clear cells have to be distinguished from macrophages. Nuclear features, cell arrangement and IHC with CD68 help in differentiation.

The differentiation between simple benign and complicated cystic renal lesions remains a major challenge in modern imaging. The incidental detection of cystic renal lesions has increased due to the more widespread use of cross-sectional imaging techniques [8]. The Bosniak classification categorises renal cysts into Category I, II, IIF, III, or IV discovered via computed tomography [9]. When a cystic lesion has more than three or four septa, it should be considered a multilocular cyst. The cyst wall and septa are grossly thickened (≥2 mm), nodules, thick or irregular calcifications can be present [10]. Nodular and septal enhancements in cystic tumours are highly sensitive for differentiation between RCC and MCRNLMP. Renal cortex extension can be found in cystic RCC [11]. Sometimes clear cut differentiations between Categories IIF and III are not as obvious as those between other categories. Contrast Enhanced Ultrasound (CEUS) is superior to unenhanced ultrasound and Computed Tomography (CT) scan in diagnosing malignancy in complex cystic renal masses using features such as the presence of septa, thickenings in walls and/or septa, and solid components. The CEUS has lower costs, fast availability, and an excellent safety profile [8,12,13].

Imaging guided percutaneous core needle biopsies of indeterminate complex cystic renal lesions (Category III) are not reliable. The target tumour cells in the cyst wall may not be sampled and leading to false negative results. Biopsies can be used in selective cases having poor general condition to avoid surgery and based on when imaging studies are complete [14].

CONCLUSION(S)

Multilocular cystic renal neoplasm of low malignant potential is a rare entity. Correct diagnosis of complex cystic renal lesions is challenging. Histopathological examination is diagnostic. Differentiation between MCRNLMP and other cystic lesions with clear cells is important as the prognosis and treatment of lesions varies tremendously. It requires a high degree of suspicion of malignancy, detailed imaging studies, meticulous grossing of nephrectomy specimens, extensive sampling of cystic tissue to find clear cells and IHC.

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