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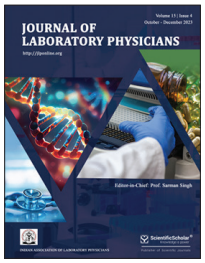

Case report

Multilocular cystic renal neoplasm of low malignant potential in a patient with chronic pyelonephritis and end-stage renal disease: A rare case report

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ABSTRACT

Multilocular cystic renal neoplasm of low malignant potential (MCNLMP) is a rare subtype of clear cell carcinoma having an excellent prognosis. These tumors exhibit distinct morphology and consist of multiple cysts separated by thin septa lined by clear cells with no expansile growth. These cysts, though rare in a setting of chronic pyelonephritis and end-stage renal disease, are usually diagnosed on radiography using the Bosniak classification. But in certain situations where cysts are not visible radiologically, a final diagnosis is made with the help of histopathology and immuno- histochemistry only. We, hereby, report such a rare incidental case of MCNLMP diagnosed on histopathology in a nephrectomy specimen of an elderly male with chronic pyelonephritis and end-stage renal disease.

Keywords: Bosniak, cystic disease, end-stage renal disease, pyelonephritis

INTRODUCTION

Multilocular cystic renal neoplasm of low malignant potential (MCNLMP) is a multiloculated benign cystic lesion separated by a thin septum.[1] Incidence of MCNLMP ranges from 0.5 to 2.5% of all renal tumors and approximately 10% of all cystic tumors. This tumor was previously referred as multilocular cystic renal cell carcinoma (RCC) as it shares a similar genetic profile and histopathological features to that of clear cell renal cell carcinoma (ccRCC), but differs entirely in its prognostic features. Till date no data of its metastasis has been reported in English literature. Historically grouped under multilocular/ multicystic RCC (World Health Organization [WHO] 2004 classification), these lesions are now subclassified as a distinct entity (WHO 2016 classification) due to their low malignant potential, no incidence of metastasis, and having a favorable outcome.[2] Renal cysts are formed due to abnormal microtubules formation and primary cilia destruction, owing to von Hippel-Lindau (VHL) germline mutations. These are known to play a pivotal role in MCNLMP pathogenesis via cyst dependent pathway. The WHO defines these cysts to be lined by a single layer of tumor cells with abundant clear cytoplasm and small nucleoli (WHO/ ISUP grade 1 or 2) with absence of expansile growth.[1]

Chronic kidney disease and end-stage renal disease (ESRD) are frequently associated with renal cystic diseases, including a wide spectrum of tumors with cystic changes.

However, only few resemble those in sporadic cases (ccRCC, chromophobe RCC), others being unique to ESRD (acute cystic disease associated renal cell carcinoma [ACD-RCC], clear cell papillary RCC [ccPRCC]).[3] Differentiation between tumors with cystic change and acquired cystic lesions are difficult preoperatively by imaging. An enhanced computed tomography (CT) and magnetic resonance imaging is helpful in evaluating the possibility of malignancy in cystic renal masses on radiograph as per Bosniak classification.[4] We present a case of MCNLMP detected incidentally on histopathology in a background of chronic pyelonephritis and ESRD. Even though the literature search showed occurrence of acquired cystic disease of the kidney and RCC with ESRD[3,5] however, there have been only two previous case reports[6,7] documenting MCNLMP co-existing in a setting of chronic pyelonephritis and ESRD in the literature. We, thus, like to add a third case report with these distinctive features.

CASE REPORT

A 74-year-old male patient presented to the urology outpatient department with complaints of right-side loin pain radiating to the back, with no association with nausea and vomiting. There was no history of fever, hematuria, pyuria, or lithuria. No other significant medical history was identified.

Hematological (hemoglobin: 12.6 g/dL, total leucocyte count: 4.55 × 1000/cumm, prothrombin time: 9.8 seconds, international normalized ratio: 0.91) and biochemical parameters (total bilirubin: 1.13 mg/dL, direct bilirubin: 0.21 mg/dL, serum glutamic-pyruvic transaminase: 22 U/L, serum glutamic-oxaloacetic transaminase: 17 U/L, alkaline phosphatase: 102 U/L, creatinine: 1.37 mg/dL) were almost within the normal range. Urine routine examination revealed calcium oxalate crystals with trace proteins. Urine culture grew *Enterococcus faecalis*. Viral markers were nonreactive. Non contrast computed tomography (NCCT) of the kidney, ureter, bladder region showed right ureteric (7mm × 4.5mm) and renal calculi (2.7cm × 1.5cm) with gross hydroureteronephrosis. No mass lesion was detected. Diethylenetriamine pentaacetate (DTPA) scan of the right kidney showed 7% split function and 4.1 mL/min glomerular filtration rate (GFR) suggesting impaired renal function; however, DTPA scan of the left kidney was normal. A clinical working diagnosis of poorly functioning kidney due to nephrolithiasis was made following which right open simple nephrectomy was done under general-epidural anesthesia and the specimen was sent for histopathological examination.

Right nephrectomy specimen measuring 9 × 6 × 4.5cm with attached ureter was received in the department of pathology. The outer surface of lower pole of the kidney showed multiple tiny surface cysts of varying sizes ranging from 0.5 to 1.0 cm in diameter. Serial sections through the specimen revealed markedly dilated pelvicalyceal system with loss of corticomedullary differentiation and dilated pelviureteric junction (Figure 1A). A cortical cyst was identified at the upper pole measuring 1 × 0.7 × 0.7 cm having a multiloculated cut surface separated by thin fibrous septa containing gelatinous material (Figure 1B). The attached ureter measured 7 cm in length and showed no gross abnormality.

Histopathological examination from the upper pole cystic lesion revealed a multilocular cyst lined by a single layer of clear cells with grade I nuclei and absent nucleoli. Focal aggregates of clear cells were also seen within the fibrous septae (Figure 2). Cyst lumen showed eosinophilic secretions. No necrosis, vascular invasion or sarcomatoid change was noted. Sections from the dilated pelvicalyceal system exhibited focal squamous metaplasia of lining epithelium. The compressed renal parenchyma showed global sclerosis of more than 50% of the glomeruli along with periglomerular fibrosis. Majority of the tubules were atrophied and exhibited thyroidization and tubulitis. The interstitium showed marked fibrosis with infiltration by intense chronic lymphoplasmacytic infiltrate along with foci of dystrophic calcification. Few medium sized vessels showed vascular wall thickening. Sections from the lower

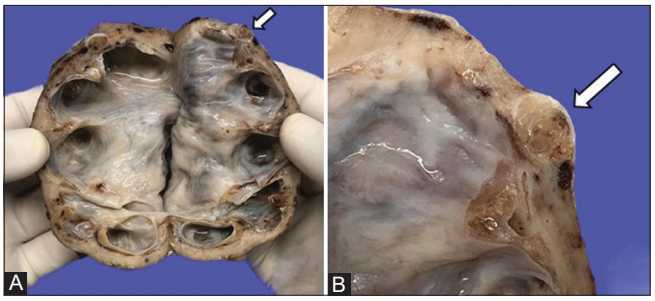

Figure 1: Gross photograph showing (A) multiple dilated calyces with loss of corticomedullary differentiation and multilocular cyst (arrow) seen in the cortex at the upper pole; (B) The cyst is separated by thin septae, measuring 1 × 0.7 × 0.7 cm and contain gelatinous material (arrow).

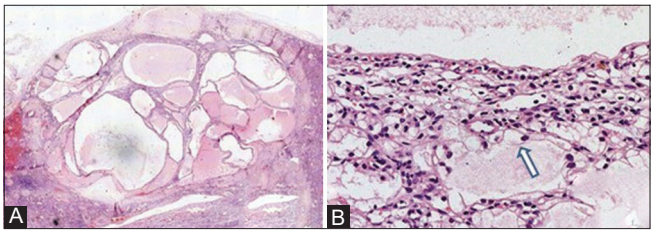

Figure 2: Photomicrograph showing (A) multilocular cyst separated by fibrous septae (hematoxylin and eosin [H&E], 40x) and (B) cyst lined by a single layer of tumor cells with abundant clear cytoplasm and small nuclei (arrow) (H&E, 400x).

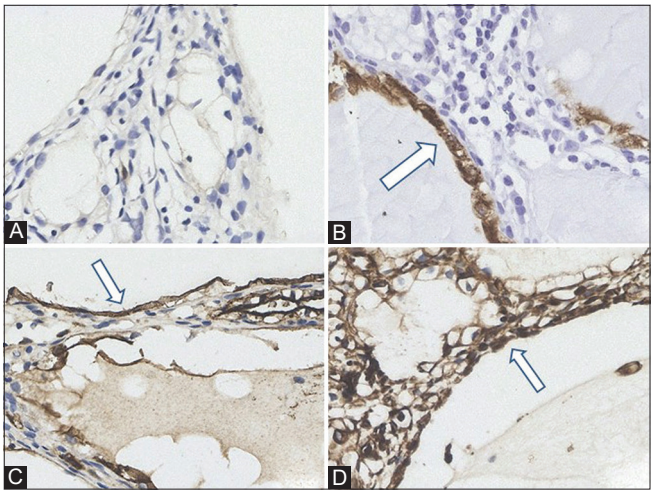

Figure 3: Photomicrograph showing (A) diffusely negative CD-10, (B) CK-7 positivity (arrow), (C) diffuse membranous epithelial membrane antigen positivity (arrow), and (D) diffuse vimentin positivity (arrow) (immunohistochemistry, 400x).

pole cysts were seen lined by flattened epithelium without any atypia.

Immunohistochemistry was done with tumor cells showing immunoreactivity with vimentin, epithelial membrane antigen (EMA), CK-7, and negative staining for CD-10 (Figure 3). The histopathological features along with immunohistochemistry confirmed the diagnosis of MCNLMP existing in a background of chronic pyelonephritis and ESRD. The patient has been on a close follow-up over the last 7 months and has not shown any recurrence.

DISCUSSION

MCNLMP is a rare subtype of RCC having a low malignant potential and a relatively favorable outcome with majority of them being asymptomatic. These are discovered incidentally on imaging as multiloculated cystic lesion with septations. Radiological findings for these tumors are variable making their preoperative diagnosis a challenge. Bosniak classification helps to predict malignancies in these complex cystic lesions. MCNLMP mostly qualifies as Bosniak category IIF to IV.[4] However, the final diagnosis can be made only after histopathological examination.

In the present case, no cystic lesion was reported on NCCT imaging. However, a multilocular renal cortical cyst measuring 3 cm was identified on gross examination and the diagnosis confirmed on histopathology. Grossly, these neoplasms have been reported to be ranging from 6 to 150 mm, unilateral, containing clear, serous or gelatinous fluid with hemorrhagic debris, and are composed of multiple cysts of variable sizes separated by thin septa. Microscopically, the cysts are lined by a single layer of tumor cells with abundant clear cytoplasm and small nucleoli (WHO/ ISUP grade 1 or 2). The septae may contain tumor cells comprising of abundant clear cytoplasm in nests and scattered singly. However, they do not show any expansile mass or exceed 20x (1mm) microscopic field of view.[1,2]

A large number of cystic lesions enter the differential diagnosis of MCNLMP that include benign renal cortical cyst (absence of clear cells with in the wall of cyst), ccRCC with cystic and/or regressive changes (cysts filled with hemorrhage, necrosis and hemosiderin deposits; keyboard like arrangement of nuclei), cystic nephroma (cysts lined by bland non clear cells with presence of ovarian stroma), cystic clear cell papillary RCC (contains clear cells with low-grade nuclei, but differentiating feature is the presence of papillary architecture), MiT family of tumors (high grade tumors with focal solid areas), and tubulocystic carcinoma (cells have eosinophilic cytoplasm with high-grade nuclei instead of clear cells).[8] MCNLMP is genetically related to ccRCC demonstrating 3p loss by fluorescence in situ hybridization and VHL mutations. However, next-generation sequencing identified six genes namely SETD2 (SET domain-containing 2), GIGYF2 (GRB10 interacting GYF protein 2), FGFR3 (Fibroblast Growth factor Receptor 3), BCR (Breakpoint Cluster Region), KMT2C (lysine methyltransferase 2C) and TSC2 (Tuberous Sclerosis complex 2) for differentiating MCNLMP from ccRCC with cystic change.[9]

The present case presented in a background of chronic pyelonephritis and ESRD. Cystic diseases and tumors are common in a setting of ESRD. Oxidative stress has been thought to be one of the important etiologies that promote carcinogenesis in patients with ESRD.[5] The morphological diagnosis of MCNLMP in a background of ESRD is difficult, when neoplastic cystic conditions like ccRCC, ACD-RCC, ccPRCC, and other acquired cystic diseases of kidney need to excluded. Immunohistochemistry can play a crucial role in the differential diagnosis. The tumor cells in MCNLMP show reactivity for PAX 8, PAX 2, CA-IX, CK7, EMA, CAM5.[2], and focal positivity in CD10, whereas they are negative for AMACR, CK 34βE12, HMB45, A-103, and synaptophysin.[2,8] The immunohistochemical profile of our case was found to be in concordance with that reported in the literature.

Most MCNLMP can be cured by surgical resection, as evident from literature search,[10–14] advocating a prognostically favorable outcome of these neoplasms. The good prognosis can also be advocated by the fact that only two case reports of recurrence have been reported.[15,16] Majority of the cases of MCNLMP have been reported as low-stage tumors (ranging from T1, 90%; T2, 8–10% and T3, 1–3%) with only two previous case reports[17,18] demonstrating renal sinus fat involvement (T3). Therefore, current tumor staging system

is not applied to these tumors.[1] MCNLMP has shown to have an excellent prognosis, irrespective of tumor stage, with negligible risk of recurrence or metastasis. Nephron sparing surgery can be offered to patients if MCNLMP is suspected preoperatively and gets confirmed intraoperatively.[9] Radiology plays an important role in the workup of cystic renal neoplasms; however, tumors with size less than 3 cm have been misinterpreted as solid lesions,[19] turning out to be MCNLMP advocating the importance of histopathology, concurring with features studied in our case.

CONCLUSIONS

Pathologists should be aware of this rare entity, which is usually diagnosed incidentally. This case highlights the importance of adequate grossing technique, as a small lesion can easily be missed out as renal cysts and not get sampled. In literature, only two MCNLMPs have been described in a setting of ESRD; herein we describe one more such case. These tumors bear an excellent prognosis and therefore need to be separated from other tumors with a cystic component and the tumors commonly encountered in a setting of ESRD.

Authors' contributions

R.K., V.S.N., and V.D. conceptualized the study. A.K., V.D., S. S., and A.J. helped in data curation. R.K., V.S.N, and V.D. helped in critical and intellectual evaluation. R.K., V.S. N., V.D., and A.K. drafted the manuscript. All authors have approved the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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