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Case Report

Multilocular Cystic Renal Cell Carcinoma: Diagnostic Predicament

Dr. Brij Mohan Kumar Singh[1*], Dr. Pavithra P[2], Dr. Kanthilatha Pai[3]
[1]Associate Professor, Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Tiger Circle Road, Madhav Nagar, Manipal, Karnataka 576104, India
[2]Associate Professor, Department of Pathology, Melaka Manipal Medical College, Manipal campus, Manipal Academy of Higher Education, Tiger Circle Road, Madhav Nagar, Manipal, Karnataka 576104, India
[3]Professor & HOD, Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Tiger Circle Road, Madhav Nagar, Manipal, Karnataka 576104, India

***Corresponding author:** Dr. Brij Mohan Kumar Singh
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Abstract

Multilocular cystic renal cell carcinoma recently has been excluded from clear cell renal cell carcinoma (ccRCC) category and re-designated as multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) and represents an extremely rare renal entity comprising <2% of all renal carcinoma and bears a low malignant potential which benefits either with simple nephrectomy or nephron sparing surgery. The pathologists need to be more cautious in diagnosing this rare entity as it mimics other diseases having reasonable prognosis. We herein report a case of MCRNLMP in an elderly patients with non-specific symptoms of 6 months duration, having a renal mass in the lower pole of the left kidney seen on computerized tomography. The final diagnosis of MCRNLMP was rendered after thorough histological and immune-histochemical evaluation. The patient was discharged after uneventful post-op duration and put up on regular follow up.

Keywords: Multilocular cystic renal cell carcinoma of low malignant potential, Renal cell carcinoma, Immunohistochemistry.

CASE REPORT

A 68 year old male was admitted in the urology department of Kasturba Medical College, Manipal with complains of intermittent pain in the left loin and urinary irritant symptoms since 6 months. There was no history of fever, anorexia, weight loss or family history of neoplasms. The patient was a non-smoker of average built. A palpable mass was noticed on clinical examination and thus clinical diagnosis of renal cell carcinoma was made. His complete hemogram, blood glucose levels, serum electrolytes, liver and renal function tests were within normal limits.

Ultrasonography revealed a large mass in the lower pole of the left kidney. Computerized tomography showed a heterogeneously enhancing lobulated lesion with multiple septations measuring 7.4x7x6.1 cms in the lower pole with adjacent fat stranding with no other nodes elsewhere. The radiologists put forward the differential diagnosis of ccRCC with extensive cystic change. Left nephrectomy was performed and the specimen was sent for histopathologic examination.

On gross examination the mass was well encapsulated. The tumor was 9x5.5x4.5 cms and was located in the lower pole. Cut section through the kidney showed multiple variable sized cysts separated by thin septae, filled with hemorrhagic materials (Fig-1). Ureter and attached adrenal were unremarkable. Microscopic examination showed variably sized, multiple non- communicating cysts with intraluminal hemorrhage, lined by a single layer of tumor cells with abundant clear cytoplasm, small uniform nuclei with inconspicuous nucleoli and separated by fibrous septae with occasional clustering of tumor cells (Fig-2). No necrosis or sarcomatoid differentiation was seen. Ureteric resection margin and renal sinus was free from the tumour. Adjacent renal parenchyma did not showed any degenerative changes. International society of urological pathology (WHO/ISUP) grade of 1 was rendered. On immunohistochemistry, the tumor cells were positive for CK7 (Fig-3) and CD10 (Fig-4). The final diagnosis of MCRNLMP was rendered. The patient was discharged after good recovery on 3rd post-operative day and is on constant follow-up.

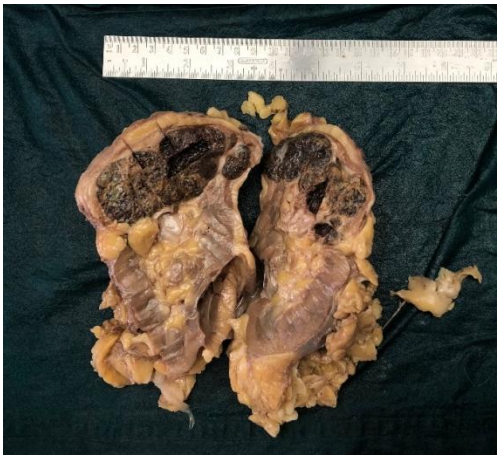

Fig-1: Gross image of tumour

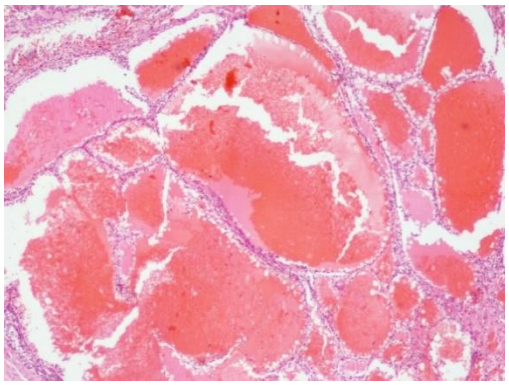

Fig-2: H&E, Multiple cysts with hemorrhage X10

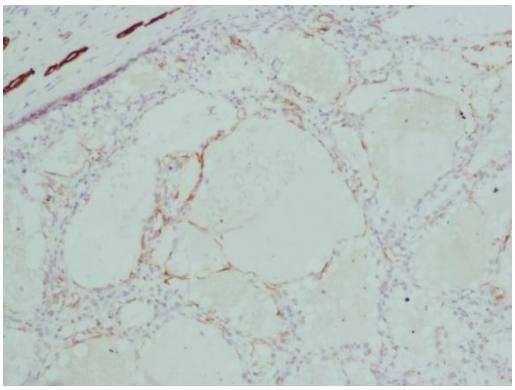

Fig-3: Cytokeratin 7 positive tumour cells, X10

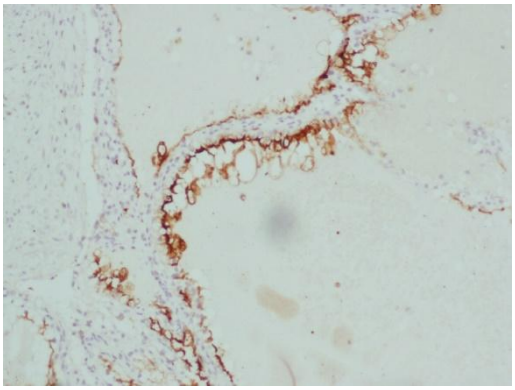

Fig-4: Cytokeratin 10, Positive tumour cells, X20

DISCUSSION

Perlmann reported first case of multilocular cystic renal cell carcinoma (MCRCC) in 1928 and named it lymphangio hemangioma [1]. Since then various investigators have presented cases of this rare entity. Largest series came in 1999 by Corica *et al*., [2] were 24 cases of MCRNLMP was presented and has demystified this lesion in the kidney as of low malignant potential and stressed that none of the lesions have ever recurred or metastasized. MCRNLMP was considered as a distinct subtype of clear cell RCC derived from the proximal tubular epithelium, according to 2004 WHO classification, based on the observations and suggestions by Eble and Bonsib [3]. MCRNLMP presents as non-specific symptoms, it is a tumor of low grade and low malignant potential which benefits with surgical resection; either simple nephrectomy or nephron-sparing surgery [4].

According to 2004 WHO classification, MCRNLMP is considered as a distinct subtype of clear cell RCC on the basis of the characteristic gross features with no expansive nodules or necrosis [3, 5, 6]. At the 2012 International Society of Urological Pathology (ISUP) consensus meeting on adult renal neoplasia, the new term of "Multilocular cystic clear cell renal cell neoplasm of low malignant potential" was designated based on the nonaggressive behavior and better prognosis of this tumour [7]. In the 2016 WHO Classification of Tumors of the Urinary System and Male Genital Organs, this new term has been included and is defined as tumors composed entirely of numerous cysts, lined by a single layer of tumor cells with abundant cytoplasm with low-grade tumor cells [8].

MCRCC usually presents at the age of between 30-80 years. In a series reported by Corica *et al*., [2] 12.5% of the cases were in T3 stage and 92% of patients had no evidence of disease at a mean follow up period of 77.6 month. This large number of cases in stage T3 may be due to inclusion solid component of this tumour in their study, which in 2004 WHO classification of tumours of kidney did not get any place for reporting MCRNLMP. It was previously reported that the incidence in men is higher as compared with that in women, with a ratio of 3:1 [9]. In the present scenario, the patient was a 68 year old male patient with sentinel nodes and is doing well as observed on follow up.

Pathologists should sample the tumour extensively to rule out the mimics which may not be of low malignant potential. According to recommendation by ISUP, in MCRNLMP cysts should be separated by fibrous septae which may have groups of low grade clear cells. These groups must not be expansile nodules and must not show infiltrative growth. No papillary growth should be seen [10]. The present case fulfills all the above criteria. The presence of any solid component of clear cells in the septae indicate a malignant lesion, therefore, those lesions should be sampled carefuly and thus labeled as clear cell carcinoma with cystic change [4]. The mimics or close differentials of MCRNLMP consists of other cystic lesions of kidney viz. primarily cystic nephroma, extensively cystic clear cell RCC, clear cell papillary RCC, and tubulocystic carcinoma. In cystic nephroma, the clear cells in the septa are distributed focally and should not be present as a cluster. Clear cell papillary RCC is usually cystic with the walls lined by clear cells and with papillary fronds in the cysts which is characteristically lacking in MCRNLMP [11]. In tubulocystic carcinoma, the cystic spaces are lined by flat cuboidal to hobnail-type cells with eosinophilic cytoplasm and variable nuclear atypia, typically with nucleolar prominence in the range of ISUP grade 2 or 3, a feature incompatible with MCRCC. Also, the septal structures of tubulocystic carcinoma do not harbor clusters of clear cells [12].

Williamson S R *et al*., [13], assessed the immunohistochemical profile of MCRCC in comparison with clear cell renal cell carcinoma and found that the promising results with CD10 (63% versus 96%), CK7 (92% versus 38%), α-methylacyl-CoA-racemase (21% versus 67%), vimentin (58% versus 33%), estrogen receptor (8% versus 8%), CAM 5.2 (100% versus 96%), EMA, CA-IX, PAX-2 (100%), and progesterone receptor (0%). In the present case, tumor cells were positive for CD10 and CK7.

With unknown pathogenesis of MCRCC, it is suggested that deletion in chromosome 3p and mutation in the cancer suppression gene, Von Hippel-Lindau gene play a significant role in development and progression of the disease [14, 15].

CONCLUSION

MCRNLMP is a rare cystic tumor of the kidney with an excellent disease free survival period. The benign clinical course of these lesions suggests that patients may benefit from nephron-sparing surgery. Since patients with MCRNLMP have an excellent prognosis, the follow-up interval after surgery can be longer to minimize unnecessary hospital visits.

REFERENCES

1. Cheng, L., & Huang, W. (2014). Multilocular cystic clear cell neoplasm of low malignant potential: evolving concept, classification and unifying terminology. *Chinese Journal of Pathology*, *43*(11), 721-722.
2. Corica, F. A., Iczkowski, K. A., Cheng, L., Zincke, H., Blute, M. L., Wendel, A., ... & Bostwick, D. G. (1999). Cystic renal cell carcinoma is cured by resection: a study of 24 cases with long-term followup. *The Journal of urology*, *161*(2), 408-411.
3. Eble, J. N., Sauter, G., & Epstein, J. (2004). Pathology and Genetics of Tumours of the Urinary

System and Male Genital Organs. Lyon, France: IARC. *World Health Organization Classification of Tumours*.

4. Wahal, S. P., & Mardi, K. (2014). Multilocular cystic renal cell carcinoma: a rare entity with review of literature. *Journal of laboratory physicians*, *6*(1), 50-52.
5. Castillo, O. A., Boyle Jr, E. T., & Kramer, S. A. (1991). Multilocular cysts of kidney: a study of 29 patients and review of literature. *Urology*, *37*(2), 156-162.
6. Takeuchi, T., Tanaka, T., Tokuyama, H., Kuriyama, M., & Nishiura, T. (1984). Multilocular cystic renal adenocarcinoma: a case report and review of the literature. *Journal of surgical oncology*, *25*(2), 136-140.
7. Srigley, J. R., Delahunt, B., Eble, J. N., Egevad, L., Epstein, J. I., Grignon, D., ... & Zhou, M. (2013). The International Society of Urological Pathology (ISUP) vancouver classification of renal neoplasia. *The American journal of surgical pathology*, *37*(10), 1469-1489.
8. Moch, H., Cubilla, A. L., Humphrey, P. A., Reuter, V. E., & Ulbright, T. M. (2016). The 2016 WHO classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. *European urology*, *70*(1), 93-105.
9. Chowdhury, A. R., Chakraborty, D., Bhattacharya, P., & Dey, R. K. (2013). Multilocular cystic renal cell carcinoma a diagnostic dilemma: A case report in a 30-year-old woman. *Urology annals*, *5*(2), 119-121.
10. Eble, J. N., & Bonsib, S. M. (1998). Extensively cystic renal neoplasms: cystic nephroma, cystic partially differentiated nephroblastoma, multilocular cystic renal cell carcinoma, and cystic hamartoma of renal pelvis. In *Seminars in diagnostic pathology*, 15(1), 2-20.
11. Gobbo, S., Eble, J. N., Grignon, D. J., Martignoni, G., MacLennan, G. T., Shah, R. B., ... & Cheng, L. (2008). Clear cell papillary renal cell carcinoma: a distinct histopathologic and molecular genetic entity. *The American journal of surgical pathology*, *32*(8), 1239-1245.
12. Amin, M. B., MacLennan, G. T., Gupta, R., Grignon, D., Paraf, F., Vieillefond, A., ... & Cheville, J. C. (2009). Tubulocystic carcinoma of the kidney: clinicopathologic analysis of 31 cases of a distinctive rare subtype of renal cell carcinoma. *The American journal of surgical pathology*, *33*(3), 384-392.
13. Williamson, S. R., Halat, S., Eble, J. N., Grignon, D. J., Lopez-Beltran, A., Montironi, R., ... & Baldridge, L. A. (2012). Multilocular cystic renal cell carcinoma: similarities and differences in immunoprofile compared with clear cell renal cell carcinoma. *The American journal of surgical pathology*, *36*(10), 1425-1433.
14. Yamaguchi, S., Yoshihiro, S., Matsuyama, H., Nagao, K., Fukunaga, K., Matsumoto, H., ... & Naito, K. (2003). The allelic loss of chromosome 3p25 with c-myc gain is related to the development of clear-cell renal cell carcinoma. *Clinical genetics*, *63*(3), 184-191.
15. Halat, S. K., & MacLennan, G. T. (2007) Multilocular cystic renal cell carcinoma. *Journal of Urology*, 177:343.