MULTILOCULAR CYSTIC RENAL CLEAR CELL CARCINOMA
- CASE REPORT

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MULTILOCULAR CYSTIC RENAL CLEAR CELL CARCINOMA - CASE REPORT (Abstract): MCR CCC is a rare subtype of renal clear cell carcinoma with specific morphologic and immunohistochemical features. No progression of multilocular cystic renal cell carcinoma is known. We present the case of a 56-year-old male, with an accidentally discovered renal tumor due to its unusual gross appearance and a rare clinical entity. He subsequently underwent a radical right nephrectomy and further histological examination revealed the tumor to be a multilocular cystic renal clear cell carcinoma, Fuhrman grade 2. Keywords: CLEAR CELL, KIDNEY, MULTILOCULAR CYSTIC RENAL CELL CARCINOMA.

Multilocular cystic renal clear cell carcinoma (MCR CCC) is a rare cystic renal tumor composed entirely of numerous cysts, the septa of which contain small groups of clear cells resembling grade I clear cell carcinoma (1). Grossly, MCR CCC consists of a well-circumscribed mass of small and large cysts filled with serous fluid and separated from the kidney by a fibrous capsule (2). The tumor has an excellent outcome and a good prognosis, having no known recurrence or metastasis (3). Histologically, the cysts are lined by a single layer of epithelial cells, usually composed of polygonal or cuboidal clear cells. Occasionally, the lining epithelium consists of several layers of cells or few small papillary structures. The nuclei are almost always small, spherical, and have dense chromatin (4). The septa consist of fibrous tissue, sometimes containing a population of epithelial cells with clear cytoplasm, resembling those lining the cysts. The tumoral stroma is also highly vascularized. MCR CCC is usually positive for CD10, vimentin, and epithelial membrane antigen (EMA) (5). We present a case of MRC CCC diagnosed incidentally, during pre-operatory CT investigation, in a 56-year-old male patient, admitted to our Hospital for aortic aneurysm management.

CASE PRESENTATION
We present the case of a 56-year-old male who was admitted to our hospital for abdominal aortic aneurysm management. The patient had a history of abdominal and lumbar pain. A pre-operatory CT scan revealed an abdominal aortic aneurysm, and a
well-defined multiseptated cystic mass in the lower pole of the left kidney. There was no evidence of left renal vein involvement nor was lymphadenopathy seen (fig. 1).

Fig. 1. Post contrast CT scan showed a multiseptated cyst in the lower pole of the left kidney

There was no family history of von Hippel Lindau syndrome or renal tumors of any kind. The biochemical assessment of the renal function was normal. Complete blood count and other preoperative investigations revealed high inflammatory markers (ESR=30mm/hr., fibrinogen= 627mg%, and CRP=17.2 mg %). Since cystic renal cell carcinoma (RCC) could not be excluded, a left-side nephrectomy was performed. The gross examination of the kidney revealed a cystic tumor in the renal lower pole measuring 48 × 40 × 30 mm. The tumor cut surface showed a multiloculated cyst with proteinaceous content, well defined margins, bulging under the renal capsule, without its involvement. No necrotic area and hemorrhagic infiltration was found in the yellowish tumor mass (fig. 2).

On histological examination, the dissected tumor specimen proved to be a multiloculated cyst consisting of cystic cavities separated by septal walls (a). The cyst wall was lined by single or multiple layers of clear cells with well-defined borders, clear cytoplasm and small hyperchromatic nuclei (Furhman nuclear grade 2) (b). No mitotic figures were seen. Focally, few cysts showed small papillary structures (c). The septa between the cysts also contain cords and clusters of similar tumor cells. Few stromal foci exhibited increased vascularity.
and hemosiderin laden macrophages. No necrosis or vascular invasion was seen. The tumor did not invade the renal capsule and hilar structures (d) (fig. 3).

**Fig. 2.** Gross examination of the kidney revealed a multiloculated cyst in the renal lower pole

**Fig. 3.** Histological examination revealed cyst walls lined by one (a: EVG, x10) or multiple layers of clear cells with well-defined cytoplasmic borders and small nuclei (b: HE, x40); few cysts showed small papillary structures (c: EVG, x20); no capsule invasion was seen (d: HE, x10).
The histomorphology was compatible with MCR CCC. TNM staging and Fuhrman nuclear grading were stage T1a and grade 2, respectively.

**DISCUSSION**

According to the 2004 World Health Organization (WHO) classification of kidney tumors (2), MCR CCC is a rare subtype of renal clear cell carcinoma (1). 90% are discovered incidentally, on radiology for other purposes (6). MCR CCC is also known as multicystic renal clear cell carcinoma (7). The 2016 WHO classification of renal tumors (8) contains significant changes of the 2004 WHO renal tumor classification. The revision of the previous classification was performed under consideration of new knowledge on pathology (and not only), including changes of the existing renal tumor types, new renal tumors and grading system for renal tumors.

The new 2016 WHO classification refers to tumor subtypes named on the basis of predominant cytoplasmic features (e.g. clear cell RCC), architectural features (e.g. cystic RCC), anatomical tumor location (e.g. cortical RCC) and correlation with previous renal disease (e.g. acquired cystic disease-associated RCC) (8, 9).

MCR CCC is used to describe a cystic RCC composed entirely of numerous cysts, the septa of which contain a small mass (less than 25%) with no infiltrative growth (8). Microscopically, per Williamson SR et al (10), MCR CCC is a tumor consisting entirely of cysts with small groups of non-expansive clear cells in the septa. Cysts are lined by polygonal clear cells, with clear cytoplasm and low nuclear grade. Suzigan S et al (3) noted that tumoral cells are also arranged in cords, alveolar structures with small cysts and large cysts covered by a single cell layer; few tumor cells forming small papillary structures are accepted (11). In our case, the tumor histomorphology was suggestive of multicystic clear RCC with no expansive growth. Multiple publications report no recurrence or metastases in patients with MCR CCC (3, 5, 12).

As concerns renal tumors grading, the Fuhrman system was the most frequently used grading system applied to cystic RCC (13). For grade 1 to 3 tumors, the system defines tumor grade based on nuclear prominence. In our case, the tumor was composed of clear cells with low grade nuclei (Fuhrman nuclear grade 2.)

Acquired cystic RCC is a new tumor entity included in the 2016 WHO classification (8). Per Moch H et al (13), acquired cystic disease-associated RCC occurs in patients with acquired cystic renal disease, which was an unknown condition in our case.

Given the presence of cystic and papillary structures covered by clear cells, the differential diagnosis of MCR CCC consists of other cystic lesions of kidney tumors, such as renal cell carcinoma with cystic changes and clear cell papillary RCC.

While cysts are common in clear cell RCC, only rarely is the tumor entirely composed of cysts. Unlike regressing clear cell renal cell carcinoma with cystic degeneration, these cysts are filled with hemorrhage and necrosis. There are areas of expansive growth of neoplastic cells in the septa between the cysts indicating a fully malignant, clear cell carcinoma with cystic changes (12). Clear cell papillary
RCC is usually cystic and the cyst walls are lined by clear cells. However, much of the tumor exhibits papillary architecture, a feature not found in MCR CCC (14).

CONCLUSIONS

We reported this case because of its rarity and for avoiding a misdiagnosis as conventional clear cell RCC.

The limits of the paper are represented by the lack of other exams: no IMH and genetic investigations were made. The criteria for MCR CCC, defined by the 2004-2016 WHO classification of kidney tumors, were enough for diagnosis setting. The elucidation of different mutations on the onset and progression of MRC CCC will be an important future area of research. The identification of new therapeutic agents that are effective on CC RCC will be an important ongoing research topic, as well.

REFERENCES


Regional lymph node (LN) metastasis is a strong negative prognostic factor in colorectal carcinoma. The 5-year disease-free survival of patients with LN metastasis is reduced by up to 48%, depending on the T stage and the number of positive LNs, as compared to patients with nodenegative cancer. Moreover, nodal status is also a predictive factor for the efficacy of adjuvant chemotherapy that confers a definite survival benefit in stage III but not stage II carcinoma. The 5-year disease-free survival in stage II colon cancer ranges from 64% to 79% depending on the T stage. Potential causes for relapse in stage II colon cancer include peritoneal involvement, lymphovascular or perineural invasion and understaging of nodal disease status that leads to a patient being inappropriately denied adjuvant chemotherapy. The critical importance of accurate LN staging has led previous studies to address the question of minimum number of LNs that need to be examined for optimal evaluation of nodal status. The recommended minimum number of LNs to be examined varies significantly across publications and ranges anywhere from 6 to 20. Others have suggested that there is no minimum threshold that can accurately stage cancer for all patients and all LNs must be examined to ensure optimal nodal staging of colon cancer resections. There are large population-based studies that do not show an association between increasing numbers of evaluated LNs and the proportion of LN-positive cancers. The current American Joint Committee on Cancer (AJCC) guidelines suggest evaluation of 10 to 14 LNs in colorectal cancer resections as a minimum standard but encourage recovery of more LNs. The Association of Directors of Anatomic and Surgical Pathology recommends that the mean number of LNs in a series of dissections should be approximately 12 to 15 and the current College of American Pathologists colorectal cancer protocol recommends that specimens be reexamined if fewer than 12 LNs are identified. Unfortunately, none of the current guidelines emphasize the importance of the location from where most LNs should be examined and the numerical threshold continues to be the only quality indicator used in current practice. The aim of the study was to evaluate distribution of positive LNs in colon cancer resections in the immediate vicinity and distant from the tumor site and to determine the proportion of cases that could be upstaged by instituting a “second look” protocol in all cases that were negative after the first search (Lisovsky M, Schutz SN, Drage MG, et al. Number of Lymph Nodes in Primary Nodal Basin and a “Second Look” Protocol as Quality Indicators for Optimal Nodal Staging of Colon Cancer. Arch Pathol Lab Med 2017; 141: 125-130).