

Unusual case of multilocular cystic renal cell carcinoma treated with nephron-sparing technique

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SUMMARY: Unusual case of multilocular cystic renal cell carcinoma treated with nephron-sparing technique

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Introduction. *The spectrum of cystic renal neoplasms includes both benign and malignant tumors and the order is as follows: benign multilocular cyst, multilocular cystic renal cell cancer and cystic renal cell cancer. Gross similarities among multicystic tumors of the kidney may cause conflict in the diagnosis and treatment of these lesions.*

Case report. *We report a 37-year-old male who presented with a mild persistent left flank pain and a painful left renal mass. After a series of examinations including abdominal ultrasound, intravenous pyelography and computed tomography, he underwent surgical exploration despite the benign appearance on radiological evaluation. A partial nephrectomy has been finally performed. The pathologic examination showed multilocular cysts lined by flattened to cuboidal epithelium, separated by cellular spindle cell stroma. Few scattered foci of lining cells showing the typical features of clear cell carcinoma of the kidney have been revealed also.*

Conclusion. *According to the current literature, prognosis of multilocular renal clear cell carcinoma is excellent in most of the cases. Indeed, metastases development is rare while local recurrence is related to inadequate local excision. Despite the relatively benign nature, urologist should be always aware of such complex renal masses since both the non specific clinical findings and poor contribution of imaging examinations make the preoperative distinction of benign from malignant cystic renal neoplasias difficult.*

RIASSUNTO: Caso raro di nefroma multiloculare cistico con foci di carcinoma a cellule chiare trattato con tecnica *nephron-sparing*.

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Il nefroma multiloculare cistico è una lesione benigna relativamente rara del rene da ascrivere al gruppo delle malattie cistiche non genetiche. Sia la presentazione clinica che l'imaging radiologica non sono caratteristici e la diagnosi esatta si fa solo con l'esame istologico definitivo del pezzo asportato.

Presentiamo un caso di nefroma cistico multiloculare (MLCN) con foci di carcinoma a cellule chiare. La diagnosi differenziale tra MLCN e altre malattie cistiche del rene è difficile perché la fenomenologia clinica non è specifica e l'imaging non consente una corretta diagnosi.

Anche se il MLCN è una malattia benigna, ci sono alcune rare pubblicazioni nella letteratura medica in cui si descrivono casi di carcinoma. Il nostro paziente è libero da malattia 12 anni dopo l'intervento chirurgico di exeresi.

KEY WORDS: Kidney - Cystic nephroma - Benign tumor - Nephron-sparing - Surgery.
Rene - Nefroma cistico - Lesione benigna - *Nephron-sparing* - Chirurgia.

Introduction

The kidney is one of the most common sites in the body for cysts. Although the lesions themselves in the

various cystic conditions are histologically similar (i.e., microscopic or macroscopic sacs lined with epithelium), their number, location, and clinical features are different. Most renal cystic conditions – congenital, sporadic, and acquired – arise from the nephrons and collecting ducts after they have formed, whether normally or abnormally. Multilocular cysts and other variants are an exception, rather considered a hamartomatous malformation or a neoplastic disease (1). The great majority of patients present before the age of 4 years or af-

ter 30 years. The patient is twice as likely to be male if younger than 4 years and eight times as likely to be female if older than 30 years of age (2).

The spectrum of renal multilocular cystic lesions in childhood includes both benign and malignant tumors and the order is as follows: cystic, partially differentiated nephroblastoma, multilocular cysts with nodules of Wilms tumor and Wilms tumors. In adults (as in this case) the order would be: a benign multilocular cyst, multilocular cystic renal cell carcinoma (MCRCC) and a cystic renal cell carcinoma. The non specific clinical findings and the poor contribution of imaging examinations make the preoperative distinction of benign from malignant cystic renal neoplasias difficult.

We report a case of a renal tumor composed by multilocular cysts lined by flattened to cuboidal epithelium with foci of clear cell carcinoma.

Case report

A 37-year old male patient was admitted with a history of a mild persistent left flank pain in July 1994. Physical examination did not reveal tenderness or palpable mass at the left costovertebral angle. Laboratory findings were normal. Urine cytology was negative for malignancy. Ultrasound scanning revealed a large complex mass (10x8,2 cm) having multiple septae within the mass and foci of dense echoes. Excretory urogram demonstrated normal excretion and diffused enlargement of the left kidney by a huge soft tissue mass. Computed tomography of the abdomen revealed a multilocular cystic mass (10x8,5 cm) at the upper pole of the left kidney

Although a Bosniac Classification of this multilocular cystic mass did not included in the radiology report, a minimal enhancement of a hairline thin wall, a mild thickening of the septa separating the cystic spaces and the presence of calcifications have been reported. No lymphadenopathy and metastatic disease were noted. Since such characteristics meet the criteria of a Category IIF renal mass a preoperative diagnosis of a benign renal mass was made. However, since there is a lack of evidence supporting the classification's ability to distinguish between these surgical and nonsurgical cases it has been decided for this cystic renal mass to be surgically explored. To our knowledge, as preoperative imaging and intraoperative frozen section analysis cannot distinguish cystic nephroma from malignant cystic RCC, pathologic examination of the completely resected tissue is the only effective method to differentiate cystic nephroma from a malignant lesion of the kidney. Despite the benign appearance on radiologic evaluation, a partial nephrectomy has been finally performed.

Results

On microscopy the lesion found to be a MLCN like tumor, consisting of multiple cysts from 0,3 to 2 cm in maximum diameter. The cystic walls were composed of fibrous and partly collagenous tissue with a few, scattered inflammatory cells

The lining cells were flat or cyboidal with no atypia or mitosis. Focally, the lining cells showed the typical

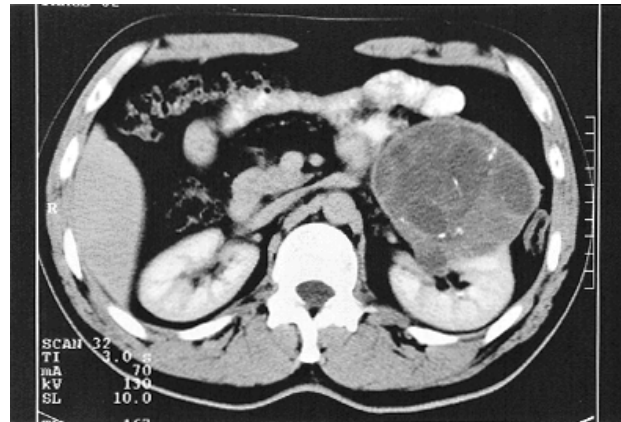


Fig. 1 - Computed tomography displayed a multilocular cystic mass (10x8,5 cm) at the upper pole of the left kidney with calcification on the septa, separating the cystic spaces.

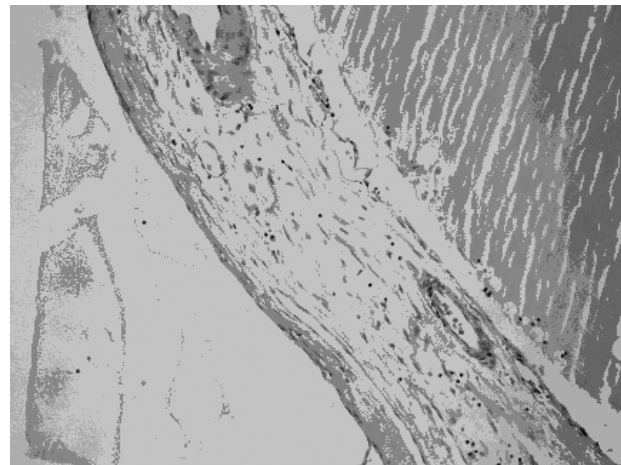


Fig. 2 - Multiple cysts lined by flattened epithelial cells with fibrous intervening stroma.

features of those of clear cell carcinoma of the kidney and few microscopic aggregates of the same cells were found in the stroma

The surgical margins were free of tumor. A diagnosis of multilocular cystic renal cell carcinoma (MCRCC) was made and systematic follow-up with ultrasonography and computed tomography is performed since.

Discussion

MLCN (also known as benign multilocular cyst, multilocular renal cyst, and cystic nephroma) is a relatively rare benign lesion of the kidney of unknown origin grouped along the non genetic cystic diseases. Edmunds reported the first case of MLCN in 1892 as cystic adenoma of the kidney (3). 187 published cases were reviewed by Castillo et al. in 1991(4), but the numbers

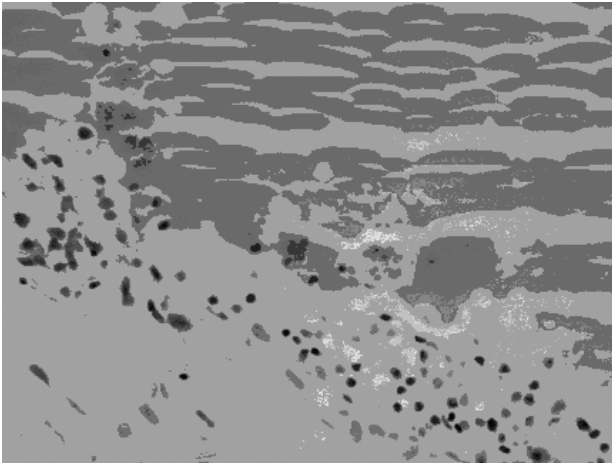


Fig. 3 - Clear epithelial cells lining a cyst.

should be regarded with caution because of the variety of terms used to describe this entity (cystic renal hamartoma, cystadenoma, polycystic nephroma etc). The etiology of this entity has been controversial since the first described case while the precise nosology of the adult cystic nephroma is still unresolved. According to some investigators this entity is classified among the mixed epithelial stromal tumors, while others consider it as a separate entity (5). Eight diagnostic criteria for the diagnosis of MLCN has been established by Powell et al. in 1951 (6): unilateral involvement, solitary lesion, multilocular lesion, no communication of cysts with each other, locules lined by epithelium, intralocular septa devoid of renal parenchyma, no communication with the renal pelvis, and normal residual tissue if present. These criteria were partially revised by Joshi and Beckwith in 1989 (6).

On the other hand, MCRCC (also known as multilocular clear cell renal cell carcinoma and multicystic clear cell carcinoma) is also a rare cystic tumour of the kidney with an excellent outcome (7). A notable difference between MCRCC and conventional RCC is the absence of nodal or metastatic spread at diagnosis in MCRCC (8). Diagnostic criteria for MCRCC were defined by the 2004 World Health Organization (WHO) classification of kidney tumors based on previous reports and the suggestions of Eble and Bonsib (3). The main pathologic features of m MCRCC according to the 2004 World Health Organization Classification of Kidney Tumors are as follows (9): Multilocular cystic appearance, yellowish solid component limited to small areas, no expansive nodules, absence of tumor necrosis, cysts lined by cuboidal clear cells or flattened epithelium, septa containing aggregates of epithelial cells with clear cytoplasm and low Fuhrman grade. An important issue is the differential diagnosis of MCRCC, which in adults in-

cludes multicystic kidney, segmental cystic disease, MLCN and other cRCCs, including cystic necrosis in RCC (pseudocystic necrotic carcinoma). Several authors have reported on the difficulty of differentiating between MLCN and MLCC, while Omar AM et al, reported an unusual case of cystic renal cell carcinoma arising from multilocular cystic nephroma (10).

The non specific clinical findings and the poor contribution of imaging examinations make the preoperative distinction between benign and malignant, non-surgical and surgical masses difficult. The common symptoms and signs include abdominal mass with or without abdominal pain, hematuria, and hypertension. Plain radiographs may show a mass, rarely with calcification in both cases. The excretory urogram usually demonstrates a well-defined, intrarenal mass in a normal functioning kidney in both cases also. Delayed excretion with hydro calycosis or no visualization occurs in cases with obstruction by pelvic herniation of the tumor. Bosniak described the US features of a benign lesion; good 'through transmission', no echoes within the mass, and sharply marginated smooth walls. He also described the CT findings suspicious for malignancy; septa, calcification, irregular margins, solid vascular elements, and high-density cyst fluid (11). The diagnostic performance of the Bosniak system is broadly sound, but it can be difficult to accurately classify category II and III cysts. There is a lack of evidence supporting the classification's ability to distinguish between these surgical and nonsurgical cases (12). Unfortunately, both lesions appear as category II or III cysts in sonography and CT scan. Color Doppler flow imaging is suggested as a useful tool for the differential diagnosis of malignant versus benign lesions. On angiographic examination MLCN is usually hypo vascular and less commonly avascular. MRI angiography is an alternative in preoperative evaluation for possible partial nephrectomy. Similar to the preoperative imaging, intraoperative frozen section analysis cannot distinguish cystic nephroma from malignant cystic RCC, therefore, pathologic examination of the completely resected tissue is the only effective method to differentiate cystic nephroma from a malignant lesion of the kidney (13). For the aforementioned reason, nephrectomy is the most preferable treatment. Partial nephrectomy and local excision of the lesion are also performed if a benign lesion is the preoperative diagnosis or in bilateral involvement. Given the excellent outcome of MCRCC's described cases patients with MCRCC might benefit from nephron-sparing surgery (8, 14). To our knowledge, small cystic renal cell carcinomas up to 4 cm in diameter have usually favourable pathology and prognosis, which offers the minimally invasive nephron-sparing treatment options such as excision, ablation or partial nephrectomy (15). No specific guidelines for the follow up of

patients with MCRCC exists, however a follow up every 6 months with ultrasonography or computed tomography initially for the first three years and then annually is reasonable. According to the current literature prognosis of both MLCN and MCRCC is excellent in most of the cases. Indeed, metastases development is rare while local recurrence is related to inadequate local excision. Most MLCN and MCRCC patients are likely to achieve long-term survival after surgery. Despite the benign nature, urologist should be always aware of su-

ch complex renal masses since malignant changes can occur.

Consent

The authors state that written informed patient consent was obtained for publication of the report and the accompanying images.

List of abbreviations

Multilocular cystic nephroma (MLCN)

Multilocular cystic renal cell carcinoma (MCRCC)

References

1. Arey JB. Cystic lesions of the kidney in infants and children. *J Pediatr* 1959;54:429.
2. Eble JN, Bonsib SM. Extensively cystic renal neoplasms: Cystic nephroma, cystic partially differentiated nephroblastoma, multilocular cystic renal cell carcinoma and cystic hamartoma of the renal pelvis. *Semin Diagn Pathol* 1998;15:2-20.
3. Edmunds W. Cystic adenoma of the kidney. *Trans Pathol Soc Lond* 1892;43:89-90
4. Castillo OA, Boyle ET, and Kramer SA. Multilocular cysts of the kidney. *Urology* 1991;37:156-162.
5. Bonsib SM. Cystic nephroma. Mixed epithelial and stromal tumor. In: Eble JN, Epstein JI, eds. *Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. World Health Organization Classification of Tumors. Lyon: IARC Press; 2004;. pp 76-79.
6. Joshi VV, Beckwith JB. Multilocular cyst of the kidney (cystic nephroma) and cystic, partially differentiated nephroblastoma. *Cancer* 1989;64:466-479.
7. Grignon DJ, Bismar TA, Bianco F. VHL gene mutations in multilocular cystic renal cell carcinoma: evidence in support of its classification as a type of clear cell renal cell carcinoma [abstract]. *Mod Pathol*. 2004;17:154A.
8. Suzigan S, López-Beltrán A, Montironi R, Drut R, Romero A, Hayashi T, Gentili AL, Fonseca PS, deTorres I, Billis A, Japp LC, Bollito E, Algaba F, Requena-Tapias MJ. Multilocular cystic renal cell carcinoma : a report of 45 cases of a kidney tumor of low malignant potential. *Am J Clin Pathol* 2006;125:217-22.
9. Eble JN. Multilocular cystic renal cell carcinoma. In: Eble JN, Sauter G, Epstein JI, et al, eds. *Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. Lyon, France: IARC Press; 2004:98.
10. Omar AM, Khattak AQ, Lee JA. Cystic renal cell carcinoma arising from multilocular cystic nephroma of the same kidney. *Int Braz J Urol* 2006;32:187-9.
11. Bosniak MA. The current radiological approach to renal cysts. *Radiology* 1986;158:1-10.
12. Warren K, McFarlane J. The Bosniak classification of renal cystic masses *BJU Int* 2005;95:939-942.
13. Hsiao HL, Wu WJ, Chang MY, Ke HL, Huang CH. Unusual case of multilocular cystic nephroma treated with nephron sparing technique: a case report. *Kaohsiung J Med Sci* 2006;22:515-8.
14. Gong K, Zhang N, He Z, Zhou L, Lin G, Na Y. Multilocular cystic renal cell carcinoma: an experience of clinical management for 31 cases. *J Cancer Res Clin Oncol* 2007;1; [Epub ahead of print]
15. Weibl P, Lutter I, Breza J, Pechan J, Blazko M, Gajdosova T, Pindak D. Cystic renal cell carcinoma – rare clinical finding. Radiographic variations of tumor/cyst appearance and further diagnostic work-up. *Bratisl Lek Listy* 2006;107:96-100.