Clinical Case Report

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Renal cell carcinoma originating in the free wall of simple renal cyst

Two unusual case reports with literature review

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Abstract

Rationale: Simple renal cyst (SRC) is a benign disease. However, rarely renal cell carcinoma (RCC) may be raised at the wall of a preexisting SRC. We herein describe 2 unusual cases of RCC arising from the outer surface of the free wall of the renal cyst.

Patient concerns: A 75-year-old female and a male were admitted to our department because of an asymptomatic renal cystic mass. Although the case history, preoperative imaging, and intraoperative examination of the cyst were carefully evaluated, no concerns were raised with respect to the underlying malignancy.

Diagnosis: RCC of the clear cell type was diagnosed based on the histology and pathological examination.

Interventions: With an initial diagnosis of SRC, the retroperitoneal laparoscopic de-roofing of the SRC was performed in both of the patients. When the diagnoses were confirmed 7 days postoperative, both of them were readmitted to our department for a radical nephroureterectomy.

Outcomes: The postoperative course was uneventful and the two patients did not undergo further chemotherapy. They are currently well and have no clinical or radiological signs of recurrence.

Lessons: Such cases remind us that seemingly benign renal cysts may harbor underlying neoplasia. Further evaluation and periodical follow-up are also recommended on the management of those seemingly benign renal cysts.

Abbreviations: CT = computed tomography, H&E = hematoxylin and eosin, IVP = intravenous pyelography, SCC = renal cell carcinoma, SRC = simple renal cyst.

Keywords: literature review, radiologic examination, renal cell carcinoma, simple renal cyst

1. Introduction

Simple renal cyst (SRC) is one of the most common nonneoplastic diseases of the renal parenchyma. The current management relies heavily on radiological appearances aided by Bosniak's classification.[1,2] Category I and II cysts are known to be radiographically benign, requiring no further evaluation, or follow-up. Although widely used, this criteria has not always been accurate. When pathology was related to the Bosniak classification, the risk of malignancy in a simple cystic lesion was 1.7%.[3] Rarely, renal cell carcinoma (RCC) may present as a cystic tumor. Herein, two cases of RCC arising from the free wall of the radiographically simple cyst are described along with review of the literature with the aim of warning clinicians that those seemingly benign renal cysts may harbor underlying malignancy. For the present study, a formal approval from the ethics committee was obtained (2017-85-1), and the principles of the Declaration of Helsinki were followed. Written informed consent was obtained from the patients for using their data for research purposes.

2. Case presentation

2.1. Case 1

A 75-year-old female was referred to our hospital with microscopic hematuria and ultrasonic abnormality of the right kidney during a medical checkup on August 11, 2014. On admission, no abnormality was found on physical examination except for a previous postoperative scar due to abdominal hysterectomy for benign gynecological disease 22 years ago. Ultrasonography examination revealed a 50 × 40-mm cyst in the middle pole of the right kidney. The cyst was sonographically benign and did not show any signs of solid components. Further

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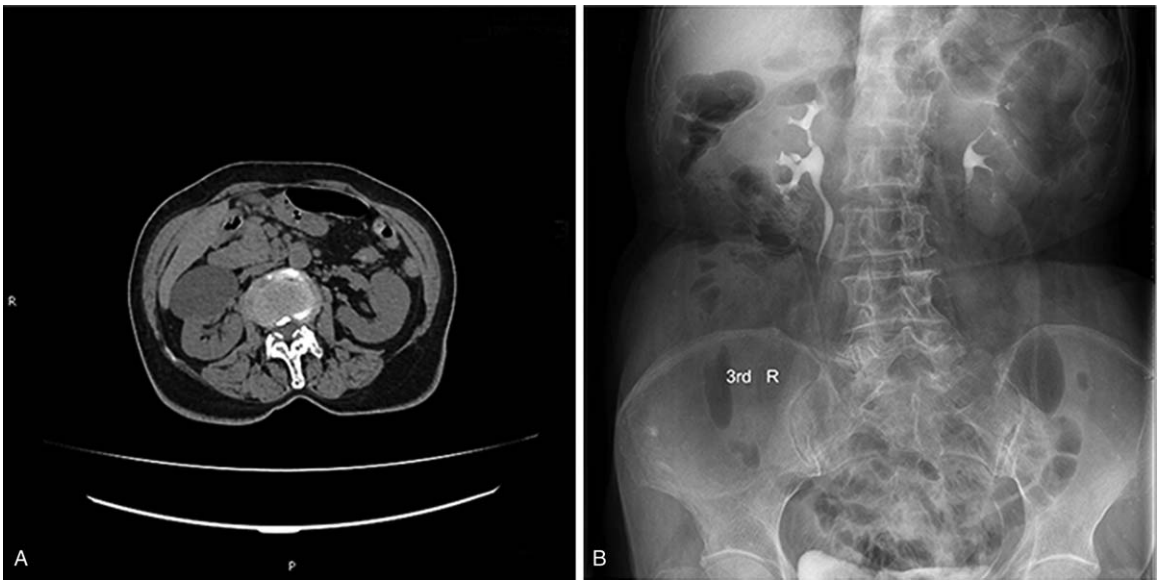

Figure 1. Abdominal plain CT scans of the first patient showing a 50 × 40-mm cyst in the middle pole of the right kidney, the density of the cyst contents was similar to that of water (A); IVP showing a mass arising from the middle pole of the right kidney, which does not distort the pelvis or calyces (B). CT = computer tomography, IVP = Intravenous pyelography.

imaging with computed tomography (CT) scan demonstrated that the normal right renal parenchyma was compressed in the lateral aspect of the cyst (Fig. 1A). The density of the cyst contents was comparable to that of water and there was no enhancement (Bosniak type 1). Intravenous pyelography also showed a mass arising from the middle pole of the right kidney. However, it did not distort the pelvis or calyces (Fig. 1B). Based on these findings, an initial diagnosis of SRC was made. Since the patient refused open surgery and percutaneous aspiration therapy, which may be required repeatedly, an uncomplicated retroperitoneal laparoscopic de-roofing of the SRC was performed. The histopathological examination of the resected cyst wall showed a clear cell carcinoma one week later. Hematoxylin and eosin (H&E) staining showed numerous clear cells with small nuclei forming alveolar or small nest structures in the wall of the renal cyst (Fig. 2A), and immunohistochemical staining showed that these cells were positive for cytokeratin (Fig. 2B). As this was malignant, the patient was readmitted for an open right radical nephroureterectomy on September 10, 2014. The pathological examination showed no clear tumor cells in the residual cyst wall of the nephrectomy specimen and there was no evidence of vascular invasion (Fig. 2C). The postoperative course was uneventful and the patient did not undergo further chemotherapy. The patient is currently well and has no clinical or radiological signs of recurrence after 44 months of follow-up by phone and regular outpatient examination.

2.2. Case 2

A 75-year-old male was admitted to our hospital on June 24, 2016, because of an asymptomatic mass on the right flank. A 78 × 51 × 41-mm cystic mass on the right kidney superior pole was detected incidentally by CT when he was hospitalized in the department of respiration due to emphysema. He also had a medical history of hypertension and gout, which were well-controlled by long-term management with antihypertensive medications and allopurinol. Three weeks after the remission of the respiratory symptoms, the patient was referred for further

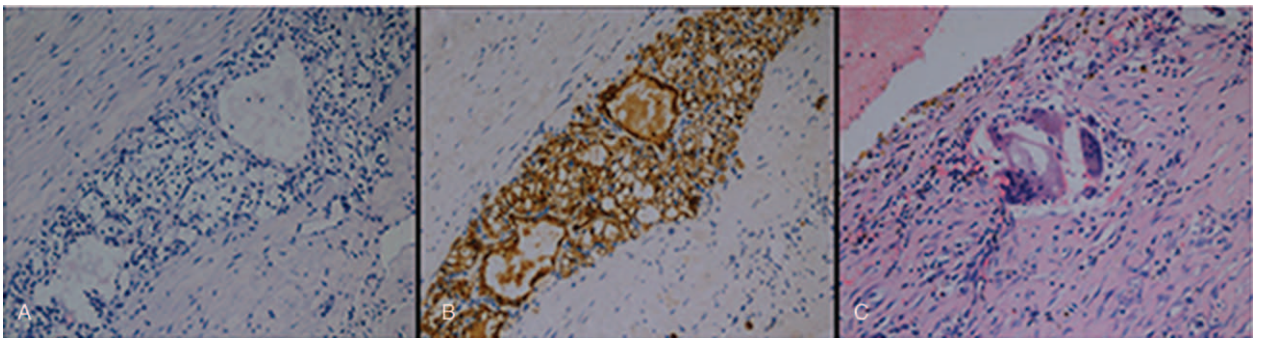

Figure 2. Pathology of the first patient. (A) In biopsy specimen of the cyst wall, H&E staining shows clear cells with small nuclei forming alveolar or small nest structures; (B) imunohistochemical staining shows these cells are positive for cytokeratin; (C) H&E staining shows there are some giant cells but no clear tumor cells in the residual renal cyst all of nephrectomy specimen (all magnifications, ×200). H&E = hematoxylin and eosin.

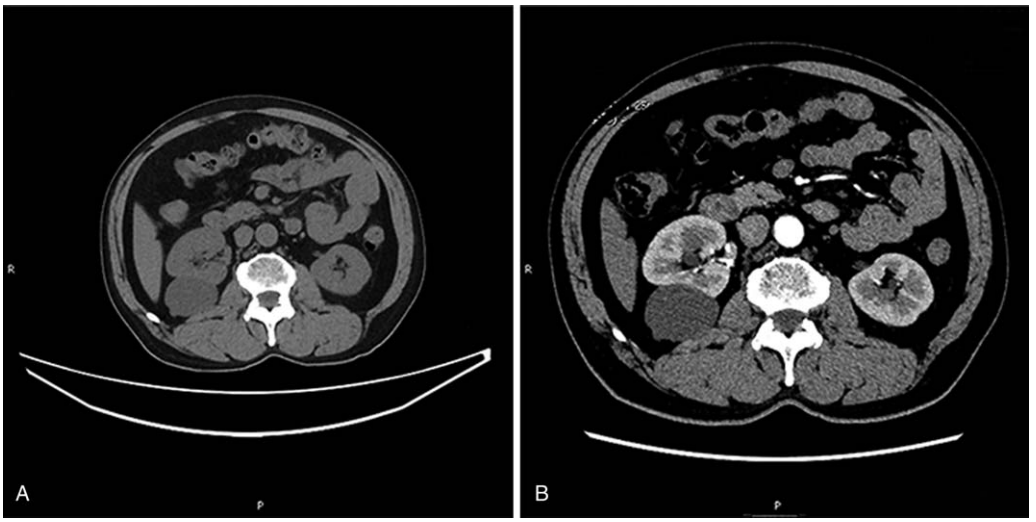

Figure 3. Abdominal plain CT scans of the second patient showing a 78 × 51-mm cyst in the superior pole of the right kidney. An 8-mm mural nodule projecting from the outer surface of its free wall was then detected (A). Enhanced CT scans showing a renal cyst without septa, wall thickening or any enhanced solid component (B). CT = computer tomography.

evaluation of the renal cystic mass. On physical examination, a smooth-surfaced mass was felt in the right flank region. Though the CT scan showed a large fluid-filled structure with low attenuating (12 HU) homogeneous content that was consistent with the SRC, there was a 0.8 cm mural nodule projecting from the outer surface of its free wall (Fig. 3A). Therefore, the patient received an abdominal contrast-enhanced CT examination (Fig. 3B), which revealed a SRC without any radiological evidence of malignancy (no septa, solid component, wall thickening, or hypervascularity). After consultation with the referring physician, a retroperitoneoscopic de-roofing was performed under general anesthesia. Approximately 120 mL of clear yellow fluid was released and a large portion of the cyst wall was excised and sent for histological examination. The histopathological examination of the resected cyst wall also showed a RCC of the clear cell type one week later. The H&E staining revealed a cyst wall lined by some clear cells with small nuclei (Fig. 4A), and immunohistochemical staining showed that these cells were positive for cytokeratin (Fig. 4B). As this was malignant, the patient underwent open right radical nephroureterectomy on October 26, 2016. The pathological examination confirmed the diagnosis of RCC and there were many clear tumor cells forming alveolar structures in the residual renal cyst wall of the nephrectomy specimen (Fig. 4C). Since there was no evidence of vascular or other invasion, the patient did not undergo any chemotherapy. There has been no evidence of local recurrence or metastatic disease to date.

3. Discussion

SRC is one of the most common benign diseases that does not cause any discomfort to the patient. Clinically, the cystic renal mass evaluation primarily depends on the Bosniak classification system.[1,2] According to the guidelines,[4] Bosniak category I and II renal cysts are deemed as radiographically benign, requiring no further evaluation or follow-up. In categories III and IV, a certain extent of malignant cystic disease is included and adequate treatment may be required.

Regarding the malignancy rates of the Bosniak classification for the cystic renal lesions, a recent meta-analysis also revealed that the likelihood of cancer in histopathological analysis of a cystic renal mass of category 2F or below is low.[5]

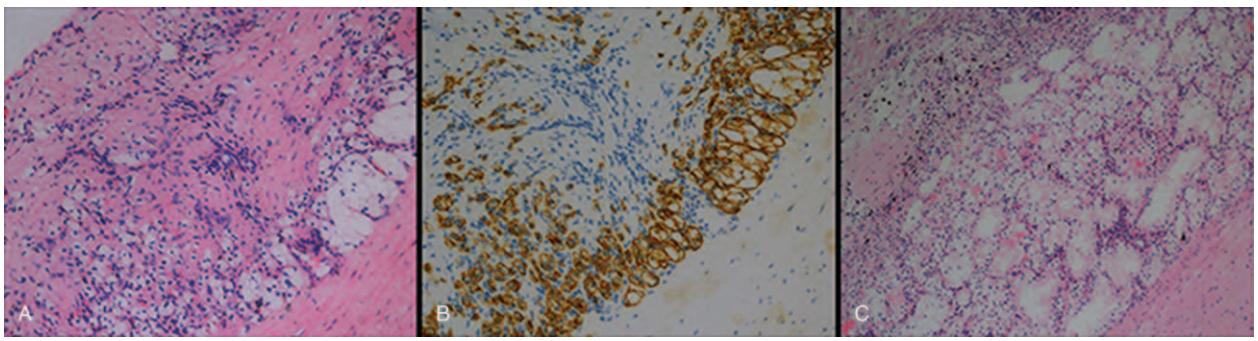

Figure 4. Pathology of the second patient. (A) In biopsy specimen, H&E staining shows clear cells with small nuclei in the wall of the renal cyst; (B) imunohistochemical staining shows these cells are positive for cytokeratin; (C) H&E staining shows many clear tumor cells forming alveolar structures in the residual renal cyst all of nephrectomy specimen (all magnifications, ×200). H&E = hematoxylin and eosin.

Table 1

Summary of the previously published literatures concerning RCC arising from the SRC.

Author, years	Case number	Age, sex	Kidney side	Bosniak category	Location		Size (cm)		Histology of RCC	Follow-up
					Cyst	Tumor	Cyst	Tumor		
Srimannarayana et al[10]	1	49 years, M	Left	I	Lower pole	In cyst wall	6	NM	Clear cell	NM
Bruun and Nielsen[8]	2	60 years, M	Left	I–II	Lower pole	In cyst wall	NM	NM	Clear cell	Progressing disease
		48 years, M	Right	I–II	Middle part	In cyst wall	5	NM	Clear cell	Fine, 2 years
Ljungberg et al[9]	1	71 years, M	Right	II	Lower pole	In cyst wall	NM	0.7	Clear cell	Fine, 1.5 years
Waguespack and Kearse[1]	1	69 years, M	Left	II	Lower pole	In cyst wall	5	1	Papillary	NM
Bowers et al[6]	1	25 years, F	Right	I	Middle part	In cyst wall	5	NM	Clear cell	NM
Sakai et al[7]	1	43 years, M	Left	I	Upper pole	NM	NM	6	Clear cell	NM
Bastian et al[14]	1	47 years, M	Left	I	Upper, middle	In cyst wall	8	NM	Papillary	Fine, 2.7 years
Ritchie et al[16]	1	45 years, M	Right	II	Upper, middle	In cyst wall	17	NM	Papillary	Fine, 1 year
Lin et al[13]	1	48 years, M	Right	I	Upper, middle	In cyst wall	16	NM	Papillary	NM
Kadekawa et al[15]	1	12 years, F	Left	I	Lower pole	In cyst wall	4	0.7, 0.4	Clear cell	Fine, 5 years
Yu et al[12]	1	39 years, F	Left	I	Upper pole	In cyst wall	7	NM	Clear cell	Fine, 1 year

F = female, M = male, NM = not mentioned, RCC = renal cell carcinoma, SRC = simple renal cyst.

Nevertheless, it is not always accurate. In our current cases for example, the radiological benign renal cystic lesions (Bosniak category I) were finally demonstrated to be RCC. Therefore, it is difficult to preoperatively determine whether a cyst is malignant solely based on imaging examinations.

After reviewing the literature of the past several decades, we found 11 cases[6–16] of the transformation of a SRC into RCC (Table 1). The basic mechanisms by which RCC presents as a renal cyst can be classified into the following types:[17]

(1) intrinsic cystic growth as a multiloculated fluid-filled mass;
(2) intrinsic cystic growth as a unilocular fluid-filled mass (cyst adenocarcinoma);
(3) cystic necrosis (pseudocyst); and
(4) origin from the epithelium of a preexisting simple cyst.

With respect to the disease prognosis, RCC with predominantly cystic components are considered less aggressive than solid RCC.[18,19] Moreover, the updated World Health Organization classification of renal tumor classified the multilocular cystic RCC as a cystic renal neoplasm of low malignant potential.[20] Spaliviero et al also revealed that the surgical outcomes of laparoscopic partial nephrectomy (LPN) for suspicious cystic masses were similar to those of LPN for solid tumors.[21] Therefore, nephron sparing surgery could serve as the optimized treatment.

Despite the fact that these lesions are usually of low grade malignancy with slow proliferation, establishing an accurate preoperative diagnosis appears to be extremely important. To the best of our knowledge, once the potential malignancy of a simple cyst was not taken into consideration or misdirected, a disastrous outcome may happen. For instance, Ritchie et al[16] reported an incidental finding of malignancy within a marsupialized SRC that clearly conferred a significant risk of seeding the abdominal cavity with neoplastic cells. Meng et al[22] also described a case of disseminated RCC shortly after laparoscopic decortication of an apparently SRC, which was categorized as Bosniak type 1 by CT when it was first diagnosed. That is why all the 14 patients (including our current two cases) underwent a salvage radical surgery immediately. Nevertheless, if the clinicians could have conducted an earlier evaluation and achieved a clearer understanding of the underlying malignancy, these patients could be diagnosed at a stage when the tumor was more amenable to resection.

Although presented as a single case, they are well described and documented, and are acceptable as valid evidence.

This highlights the importance of making an early, accurate diagnosis. Clinically, apart from radiological surveillance, additional management options for renal cysts include ultrasound or CT-guided cyst aspiration or biopsy, which was performed as standard diagnostic tests during the 1970s. However, current studies[23,24] showed that cytological analysis of cystic fluid had a low sensitivity and difficulty in differentiating malignant from benign. Therefore, only histopathological examination led to confirmed diagnosis.

In summary, conducting a rapid intraoperative frozen section study of the cyst wall is necessary. If the malignancy is pathologically confirmed, an immediate partial or radical nephrectomy could be performed under the same anesthetic, which would be able to reduce the risk of peritoneal seeding and recurrent disease. In addition, we also recommend regular follow-up even for the management of a SRC. Bowers et al[6] and Sakai et al[7] indicated that a SRC also had the potential to transform to a RCC after six years of follow-up. Therefore, more emphasis should be given to the management of those seemingly benign renal cysts. They are really not so "simple".

Author contributions

Conceptualization: Xiuhong Wang, Xin Xu, Guan Zhang.
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Supervision: Guan Zhang.
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Writing – original draft: Shicong Lai, Binbin Jiao.
Writing – review & editing: Shicong Lai, Binbin Jiao.

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