

Original Article

Detection of urinary cysts and renal carcinoma by biochemical analysis during laparoscopic decortication for renal cysts

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Received September 2, 2016; Accepted October 18, 2016; Epub January 15, 2017; Published January 30, 2017

Abstract: Simple renal cysts are the most common renal masses in Urology. In general, making a diagnosis of a simple renal cyst is not difficult. However, some patients with calyceal diverticulum or hydronephrosis are misdiagnosed with simple renal cysts. Our study aimed to differentiate the simple cysts from other abnormalities by biochemical analysis of the cystic fluid during the laparoscopic procedure. A retrospective multi-institutional review of 57 patients undergoing laparoscopic decortication for renal cysts between 2013 and 2015 was performed. The cystic fluid was analyzed biochemically during the operation for detecting whether the cysts communicate with renal pelvis. The biochemical results of cystic fluid and serum were compared and statistical significance between two groups was determined by Student's t-test. Biochemical analysis of cystic fluid showed 52 patients had simple cyst fluid, and pathological results confirmed as cyst wall. Four cases were considered as urinary fluid with high creatinine levels, among which, one was duplex kidney, two were calyceal diverticulum, and the other one was hydrocalycosis. Operation procedures were changed immediately for these 4 cases. The remaining one case had abnormal biochemical components with very low levels of potassium, sodium, calcium, and glucose and diagnosed as renal cell carcinoma by pathology. Thus, laparoscopic radical nephrectomy was applied afterwards. Therefore, biochemical analysis of cystic fluid during laparoscopic procedures can effectively differentiate simple cysts from urinary cysts and complications such as urinary leakage can be avoided. It can also provide a clue to detect cystic renal cell carcinoma.

Keywords: Renal cysts, cystic fluid, laparoscopy, renal cell carcinoma

Introduction

Simple renal cyst is a most common renal disease in Urology and 90-95% of simple renal cysts are found incidentally without any clinical symptoms. The prevalence of renal cysts increases with age. The incidence in people older than 40 is 20%, and 33% in people after age of 60 [1, 2]. Most of them are benign, asymptomatic, and usually treated conservatively. Symptoms, such as lumbago, hematuria, hypertension, infection, or renal hydronephrosis, may occur in some patients, hence surgical intervention is necessary. Managements for renal cysts consist of radiologic surveillance, ultrasound-or computed tomography (CT)-guided cyst aspiration with alcohol sclerotherapy, laparoscopic or open surgical exploration. Multiple

studies have shown that laparoscopic decortication is effective and safe for symptomatic simple renal cysts and offers better results than percutaneous aspiration with sclerotherapy, especially for cysts with large sizes [3-6].

Recent progress in radiology has expanded clinical approaches to asymptomatic renal masses, including benign cysts and other abnormalities, by ultrasound, computerized tomography or magnetic resonance imaging. In general, making a diagnosis of a simple renal cyst is not difficult. However, in clinical practice, although computed tomography urography (CTU) or retrograde pyelography is usually performed preoperatively, some patients with calyceal diverticulum or hydronephrosis are sometimes misdiagnosed with simple renal cysts, which results in

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Table 1. Comparisons of biochemical parameters in cyst fluid and blood in patients with simple renal cyst (n = 52)

Biochemical parameters	K ⁺ (mmol/L)	Na ⁺ (mmol/L)	Cl ⁻ (mmol/L)	Ca ²⁺ (mmol/L)	BUN (mmol/L)	Cr (μmol/L)	Glucose (mmol/L)	Osmotic pressure (osmo/kg)
Cyst fluid	3.92 ± 0.25	148.3 ± 4.33	1164 ± 5.2	1.78 ± 0.17	8.17 ± 2.38	64.98 ± 12.30	6.37 ± 1.09	310.67 ± 9.16
serum	4.04 ± 0.28	141.7 ± 2.70	106.3 ± 2.8	2.36 ± 0.14	4.78 ± 1.31	66.42 ± 16.00	5.41 ± 0.78	293.13 ± 5.40

K, potassium; Na, sodium; Cl, chlorine; Ca, calcium; BUN, blood urea nitrogen; Cr, creatinine.

unnecessary secondary operations due to serious postoperative complications such as urinary leakage or urinary cyst. In this study, we evaluated the biochemical components of cystic fluid during laparoscopic procedures, and based on the results of biochemical analysis, we aim to differentiate simple cysts from urinary cysts and other diseases immediately and help intraoperative decision-making with minimal costs. To our knowledge, it is the first time we reported the relationship between biochemical components of cystic fluid and different renal cystic diseases.

Material and methods

Subjects

Between April 2013 and April 2015, 57 patients with renal cysts were enrolled at Sir Run Run Shaw Hospital. Inclusion criteria were as follows: (1) Simple renal cyst diagnosed using preoperative ultrasound and contrast enhanced CT scan. Only patients with simple renal cysts (Bosniak Class 1 category and Class 2) were included in the study. Patients with Bosniak Class >2 renal cysts were excluded from the study; (2) Presence of one or more symptoms, such as lumbago, hematuria, hypertension, obstruction of the renal pelvis and calyces, etc.; (3) Presence of renal cyst adjacent to the collecting system as indicated by the preoperative CT scan, or urinary cysts or other diseases suspected. Patients were informed about laparoscopic surgery and their written informed consent was acquired.

All patients underwent laparoscopic procedures under general anesthesia and endotracheal intubation. Patients were placed in a 70-90° lateral decubitus position. Pneumoperitoneum of 15 mmHg was conducted used a Veress needle introduced in the umbilical region. The first 10-mm trocar (camera trocar) was inserted through the access tract created with a Veress needle. Then, two more 5-mm

trocars were inserted under direct vision in the flank lateral to the rectus. Then, the peritoneum and adipose capsule were opened to expose the renal cysts. 10 mL cystic fluid was aspirated and sent for biochemical analysis while the remaining was completely aspirated using the suction irrigation device. Then, the cyst was opened, and excised, and extracted using laparoscopic scissors connected to a cautery about 0.5 cm away from the normal renal parenchyma. Presence of excrescence at the bottom of the cyst or conduct of the collecting system was inspected. Specimen of the cyst wall was sent for histopathological assessments. Based on the results of biochemical analysis of cystic fluid, surgical approaches were changed for patients with urinary cyst fluid.

Statistical analysis

Results are expressed as mean ± standard deviation, unless otherwise indicated. Biochemical results of patients' cystic fluid and serum were compared by Paired-Samples t Test. SPSS 16.0 package program was used (SPSS Inc, Chicago, Illinois, USA) and P<0.05 was considered statistically significant.

Results

Among the 57 patients, 29 were male and 28 were female and mean age was 56.1 ± 9.4 years (range 31-74 years). Cysts with a mean size of 7.67 ± 1.24 cm (range 5-12 cm) were located in the left (26 cases), and right (31 cases); upper (29 cases), middle (9 cases), lower (14 cases), multiple sites (2 cases), and near the renal pelvis (3cases). Based on the Bosniak classification, 56 cysts were classified as category I and 1 as category II. Two patients had a prior surgical history of the upper urinary tract. Among all patients, 54 had lumbago, and 7 hypertension, 3 hematuria, 4 lumbar masses, and 5 hydronephrosis or hydrocalycosis as well.

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Table 2. Comparison of biochemical parameters between patients' urinary cyst fluid and serum (n =4)

Biochemical parameters	K ⁺ (mmol/L)	Na ⁺ (mmol/L)	Cl ⁻ (mmol/L)	Ca ²⁺ (mmol/L)	BUN (mmol/L)	Cr (μmol/L)	Glucose (mmol/L)	Osmotic pressure (osmo/kg)
Patient 1	>10	<100	65	1.01	22.06	2950	<0.28	/
Patient 2	14.54	4	59	0.63	39.26	1500	5.35	297
Patient 3	>10	<100	<50	<1.0	15.72	2705	<0.28	/
Patient 4	>10	<100	<50	<1.0	21.11	1578	3.10	/
Mean value					24.54 ± 10.20	2183.25 ± 751.28		
Serum	3.90 ± 0.27	142.0 ± 2.16	104.8 ± 3.59	2.39 ± 0.21	3.96 ± 0.67	64.25 ± 18.46	4.91 ± 0.44	292.25 ± 5.25
P-value					0.028	0.011		

K, potassium; Na, sodium; Cl, chlorine; Ca, calcium; BUN, blood urea nitrogen; Cr, creatinine.

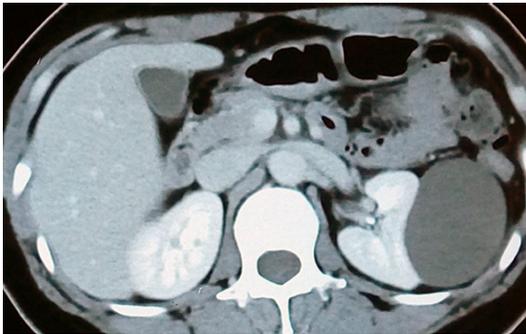


Figure 1. Abdominal CT scan with contrast was performed preoperatively for the patient diagnosed with renal cell carcinoma.

Biochemical analysis of renal cystic fluid were evaluated including potassium, sodium, chlorine, calcium, blood urea nitrogen (BUN), creatinine (Cr), glucose, and osmotic pressure. The composition of cyst fluid from 52 patients diagnosed with simple renal cysts preoperatively tended to parallel that of serum (**Table 1**). Laparoscopic decortication was successfully performed and pathological results were confirmed as cyst walls postoperatively. No urinary leakage, bleeding, infections, or other complications were observed.

In four patients, the cysts were considered as urinary cysts, due to higher levels of Cr and BUN compared with the simple cyst fluid. Values of the other parameters were beyond the range of detection (**Table 2**).

Among the four patients, one was found with urinary cyst fluid in the upper segment 'cyst' of the left kidney (Patient 1 of **Table 2**). The cystoscopy examination showed two left ureter orifices. The diagnosis of duplex kidney was confirmed and laparoscopic heminephroureterectomy for the upper renal unit was performed. This patient had successful restoration of the

inner cyst wall tissue, and the pathological results revealed as transitional epithelium. The patient was followed up for 22 months without obvious complications. Two patients were diagnosed with calyceal diverticula (Patients 2 and 3 in **Table 2**), as intraoperative injection of methylene blue through the ureteral stent indicated that the diverticula were connected with the collecting systems. Therefore, surgical approach was changed to open diverticular unroofing. Continuous suturing was adopted for the incisional margins with absorbable sutures. Diverticular neck was closed and diverticular wall was cauterized followed by a drainage tube placed properly. The pathological result indicated that the inner wall was originated from the transitional epithelium. No recurrence was detected for a follow up of 8 months postoperatively.

One subject was diagnosed with hydronephrosis because no obvious leakage was observed after the injection of methylene blue through the ureteral stent (Patient 4 in **Table 2**). Subsequently, laparoscopic partial nephrectomy was performed and no urinary leakage or infection occurred postoperatively. The pathological result indicated that the inner cyst wall was originated from the transitional epithelium. Ultrasound examination at 1 year follow up indicated no recurrence.

In addition, a 39-year-old female patient was diagnosed with simple renal cyst preoperatively based on enhanced abdominal CT scan (Bosniak category 1) (**Figure 1**). The diameter of the cyst was 6.3 cm and the intraoperative biochemical analysis of the cyst fluid showed abnormal results with extremely low levels of potassium, sodium, calcium, and glucose (**Table 3**). Histological examination of the cyst floor indicated malignancy. Laparoscopic nephrectomy was performed 20 days after decor-

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Table 3. Biochemical results of the patient with renal cell carcinoma

Biochemical parameters	K ⁺ (mmol/L)	Na ⁺ (mmol/L)	Cl ⁻ (mmol/L)	Ca ²⁺ (mmol/L)	BUN (mmol/L)	Cr (μmol/L)	Glucose (mmol/L)	Osmotic pressure (osmo/kg)
Cyst fluid	<1.0	<100	<50	0.87	2.40	22	1.94	/

K, potassium; Na, sodium; Cl, chlorine; Ca, calcium; BUN, blood urea nitrogen; Cr, creatinine.

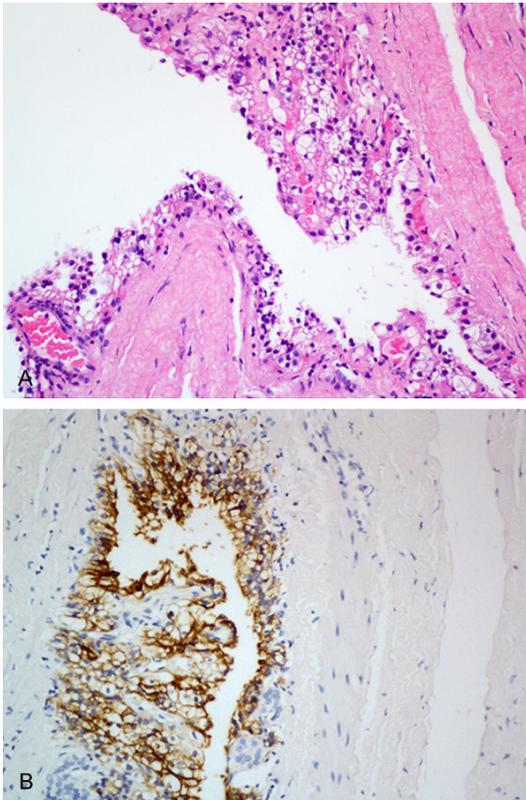


Figure 2. Histologic findings of the tumor. A: Hematoxylineosin staining of the tumor showing alveolar structure of clear cells with relative small nuclei; B: Immunohistochemical staining for RCC (Magnification, ×200).

Table 4. Sensitivity and specificity of biochemical parameters for differentiating the nature of cyst

	Number of patients				Sensitivity	Specificity
	TP	TN	FP	FN		
Single cyst	52	5	0	0	1.00	1.00
Urinary cyst	4	53	0	0	1.00	1.00

FN, false negative; FP, false positive; TN, true negative; TP, true positive.

tication. The postoperative course was uneventful and the pathologic examination was verified as RCC, clear cell type. By immunohis-

tochemistry, the tumor cells were stained positive for RCC, CD10 and vimentin, and negative for CK7 (**Figure 2**). During the 2 years' follow-up, no tumor recurrence or metastasis was detected by CT scan, ultrasonography and x-ray test.

The nature of the cyst fluid was speculated based on the biochemical analysis, and the speculations were proved to be reliable with both high sensitivity and specificity using surgical exploration, postoperative pathological results, and clinical results (**Table 4**). Biochemical parameters are of high value to determine the nature of renal cysts laparoscopically. However, further studies with larger sample sizes are still required to confirm the findings of the present study.

Discussion

As an effective, safe and minimally invasive technique, laparoscopic decortication has become one of the most popular therapeutic approaches for symptomatic renal cyst. However, postoperative complications, such as bleeding, urinary leakage, and infection, may still bother some patients with complex renal cysts. Once urinary leakage occurs in these patients, they are susceptible to peritonitis and other secondary infections; moreover, ureter stent and urethral catheterization may be required as well. Sometimes, open repair or ureteroscopic injection of fibrous gel should be performed when the complications are serious. The most common causes for urinary leakage include intraoperative injuries to the renal calyces, and calyceal diverticulum or hydrocalycosis misdiagnosed with simple renal cyst preoperatively. The incidence of intraoperative injuries has been decreasing with the maturity of the surgical technique, as well as the surgeons' skill and knowledge. Therefore, misdiagnosis has been the major cause for urinary leakage after the renal cyst surgery.

Calyceal diverticula are eventrations of the upper collecting system lying within the renal

parenchyma [7]. These outpouchings are lined by transitional cell epithelium without urine secretory function, and communicate with the main collecting system via a narrow channel, filling with urine. The incidence of calyceal diverticula is as low as 0.21% to 0.6% of intravenous urograms [8]. However, its actual incidence should be higher since some calyceal diverticula can only be detected in retrograde urography [9-11]. Patients with calyceal diverticula usually experience lumbago, infection, renal dysfunction, and other symptoms; and 35-50% of them also have complications such as urolithiasis. Patients with calyceal diverticulum are often misdiagnosed to have simple renal cyst during the ultrasound or CTU examinations [12]. Moreover, calyceal diverticula may not be detected using the preoperative retrograde urography if the narrow passageways between the calyceal diverticulum and collecting systems are obstructed due to inflammation or other causes [13].

To differentiate the simple renal cyst from calyceal diverticulum or hydronephrosis, the passageways at the bottom of the cyst can be detected with careful examination during the operation, or by injecting methylene blue solution via a pre-indwelling ureteral stent. However, all these methods are not always ideal, as misdiagnoses are occasionally unavoidable, which can result in urinary leakage or unnecessary over-treatment in some instances.

In the early 1990s, researchers analyzed the biochemical components in simple renal cysts and compared them with those from serum and urine samples. They found that the composition of cyst fluid was similar to that of serum but different from the urine [14, 15]. In our study, we found that the results of simple cysts were consistent with previous studies and the simple renal cyst might originate from glomerular proximal convoluted tubule of the renal unit; while, biochemical components of urinary cysts including duplex kidney, calyceal diverticulum or focal hydronephrosis were significantly different from those of the blood, with greatly increased levels of potassium, BUN, and Cr. The differential results were verified through the intraoperative exploration and postoperative pathological examination, and we found that biochemical analysis was highly reliable with both sensitivity and specificity approximating 100%, although the sample size was

small. Intraoperative aspiration does not result in extra injuries to the patients and is easy to conduct. The results can be obtained within 15-20 min, which could guide the surgeon to change the procedure immediately during the operation.

Additionally, we found one patient whose diagnosis was simple renal cyst based on preoperative CT scan (Bosniak category I) had significantly different component of cyst fluid = from those of other patients. Postoperative pathological examination revealed that the cyst wall was actually renal cell carcinoma, clear cell type. The Bosniak classification system has been the most commonly accepted radiological rating system to evaluate the risks of cancer due to renal cystic lesion [16]. There are currently five categories (categories I, II, IIF, III, and IV) [17]. Meta-analysis showed that the rates of malignancy of Bosniak categories I, II, IIF, III, and IV were 0%, 15.6%, 0%, 65.3%, and 91.7%, respectively [18]. The incidence of renal cyst of Bosniak category I becoming malignant is extremely rare. This case also demonstrates that biochemical analysis of cystic fluid facilitates the diagnoses of rare diseases.

Conclusions

In this study, we determined the feasibility of utilizing biochemical analysis of cystic fluid during laparoscopic procedures to help differentiate simple from urinary cysts and other unusual disorders. However, large populations are still warranted to further confirm our findings.

Disclosure of conflict of interest

None.

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