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ORIGINAL PAPER

Flexible ureteroscopy and holmium laser lithotripsy for treatment of upper urinary tract calculi in patients with autosomal dominant polycystic kidney disease

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Abstract The objective of the study was to investigate the safety and efficacy of flexible ureteroscopy and holmium laser lithotripsy for the management of patients with autosomal dominant polycystic kidney disease (ADPKD) and associated nephrolithiasis. Between 2005 and 2010, flexible ureteroscopic stone treatment was attempted in 13 patients with ADPKD. Two patients had bilateral renal stones. Most of the stones were located in the renal pelvis and/or calices with a stone size 1.7 cm in the largest diameter. The success rate and morbidity and complications were recorded. A total of 45 intrarenal calculi with a mean stone size of 5.6 mm (range 3–17) were identified. The mean number of stones per patients was 3.2 (range 2–5). The mean number of primary procedures was 1.2 (range 1–2). The overall stone-free rates after one and two procedures were 84.5 and 92.3%, respectively. Complications occurred in three procedures and consisted of low-grade fever in one procedure, flank pain in another procedure and stent pain in another procedure. No patient died. Flexible ureteroscopy with holmium laser lithotripsy is a safe and effective method for the treatment of patients with ADPKD and associated nephrolithiasis.

Keywords Flexible ureteroscopy · Autosomal dominant polycystic kidney disease · Nephrolithiasis

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited systemic disorder and accounts for 8–10% of patients undergoing dialysis and renal transplantation [1, 2]. Frequently associated complications, including hypertension, infection and nephrolithiasis, can hasten renal failure, which was caused by ADPKD [3]. In 8–36% of patients with ADPKD nephrolithiasis may occur [4], and nearly half of them are symptomatic, of whom up to 20% ultimately require urological intervention [5].

Historically, the majority of patients with ADPKD and nephrolithiasis were treated with open surgery [4]. However, with medical and technological advancements, open surgery has been almost entirely replaced by minimally invasive techniques in the general population, including ESWL, retrograde ureteroscopy and PCNL [3, 6–8].

In recent years, flexible ureteroscopy and holmium laser lithotripsy was getting more attention in dealing with upper urinary stone [9–12], and herein, we present our initial experience in treatment of nephrolithiasis in patients with ADPKD using flexible ureteroscopy.

Materials and methods

From 2005 to 2010, 13 consecutive patients with ADPKD and stones were treated at our center using flexible ureteroscopy. The leading symptoms were recurrent flank pain (69.2%), hematuria (23.0%), recurrent urinary tract infection (15.4%) and fever (15.4%). Pretreatment evaluation included a detailed medical history, a thorough physical examination, routine blood studies, urine culture and renal function tests. A 24-h urine assay was performed in each patient to find metabolic disorders before treatment. All patients underwent ultrasonography, renal scan, excretory urography (based on normal renal function) and CT investigation before treatment. On CT scan, the size and number of cysts were determined. A proper antibiotic was given to the patients with infection including positive blood test and/or positive urine test with/without fever to control the infection (temperature below 37.3°C) before surgical intervention.

Two patients received 2-stage procedure because of damaged renal function (2.9 mg/dL and 3.3 mg/dL). Double-J ureteral stenting was performed under local anesthesia for complete drainage for the sake of renal function in the first stage. The second stage was postponed until the serum creatinine had decreased under 1.5 mg/dL. General anesthesia was used for all 13 patients because of large stone burden or conversion to open surgery. The patient was placed in the dorsal lithotomy or low lithotomy position and prepared and draped in sterile fashion. The bladder was entered with a 22-F cystoscope, allowing visualization of the ureteral orifice. This was cannulated with an open-ended 5-Fr catheter and a 0.038-in. guidewire. A second 0.038-in. guidewire was placed under fluoroscopic guidance with a Dual Lumen Flexi-Tip ureteral access catheter (Cook Medical, Bloomington, IN, USA). These tools enabled dilation of the ureteral orifice without necessitating balloon dilation of the ureteral orifice. A 7.2-F flexible ureteroscope (Storz FLEX-X, Tuttlingen, Germany) for stones located in the proximal ureter and intrarenal stones, a ureteral access sheath (9.5/11.5 F or 12/14 F) was placed to allow optimal visualization, maintain low intrarenal pressure and facilitate stone fragments extraction. Holmium YAG laser lithotripsy was performed through a 200-µm (Dornier Lightguide Super 200) core-sized fiber until only very small pieces (<1 mm) remained. Our preferred laser settings (Medilas H, Wave Light Laser Technology, Germany) was 0.8 J at 15 Hz for the 200-µm fiber. The entire collecting system was inspected at the end of calculi fragmentation. A double J stent was routinely placed at last. All patients were seriously performed with renal ultrasound (GE, LOGIQ, USA) to assess residual stone fragments at day 1 after operation, and patients with residual stone fragments larger than 1 mm were evaluated with a second look ureteroscopic procedure within 1 week. This was to allow time for spontaneous passage of stone fragments and visually inspect the kidney for a residual stone burden. Furthermore, all patients underwent renal ultrasound after 30 days after the second look procedure to ensure the absence of hydronephrosis and document the final stone burden.

We defined the stone-free rate as the absence of any stones in the kidney or stone fragments less than 1 mm, which can pass spontaneously at last. The outcomes regarding the success rate and postoperative complications were examined.

Results

We identified 13 patients with ADPKD in whom ureter and intrarenal stones were treated with flexible ureteroscopy in a total of 15 renal units. Table 1 showed patients demographics and presenting symptoms. Of the 13 patients, 9 were men and 4 were women. The mean age was 34.5 years (range 19–45). The main symptom was flank pain (69.2%, 9/13). The serum creatinine level in the two patients with damaged renal function decreased from 2.9 to 1.4 mg/dL and 3.3 to 1.3 mg/dL after stage-1 procedure. Table 2 showed the serum and urinary parameters and the metabolic disturbances and stone composition. The most common stone composition was uric acid (60%, 9/15); metabolic evaluation and 24-h urinalysis revealed hyperphosphaturia in four patients, hyperuricosuria in two patients, hypocitraturia in one patient and hyperoxaluria in one patient. Table 3 showed the number of cysts and the largest renal cyst size in ADPKD patients. Table 4 showed stone demographics and outcome of procedure. The total stone number was 45, the mean stone size was 5.6 mm (range 3–17), and the mean number of stones per patient was 3.2 (range 2–5). Stone site in the collecting system was highly variable, most of which located in renal pelvis and caliceal (95.6%, 43/45). 84.6% (11/13) of patients required only one procedure for complete fragmentation of intrarenal calculi, and 15.4% (2/13) required two procedures for the large stone burden (>1.5 cm), not including the final ureteroscopic inspection at the time of stent removal. A double-J ureteral stent was placed at the end of each therapeutic procedure and was removed at the final diagnostic ureteroscopy at our outpatient department. The mean operative time was 45.5 min (range 36–60) for a total of 15 treatments. The operative time was calculated from the time of cystoscope insertion to the completion of stent placement. The overall stone-free rate was 92.3%. The stone-free rates after one and two procedures were 84.6 and

Table 1 Patient demographics and presenting symptoms

Feature	No. of patients (%)
Gender	
M	9 (69.2)
F	4 (30.8)
Presenting symptoms	
Flank pain	9 (69.2)
Hematuria	3 (23.0)
Fever	2 (15.4)
Frequency and urgency	2 (15.4)
Stone burden	
Unilat	11 (84.6)
Bilat	2 (15.4)

Table 2 Serum, urinary and stone parameters

Parameter	Results (n = 13) Median (range)
Serum	
Creatinine (mg/dL)	1.2 (0.8–3.3)
Sodium (mEq/L)	141 (135–145)
Potassium (mEq/L)	4.3 (3.4–6.1)
Calcium (mg/L)	9.0 (8.3–9.8)
Uric acid (mg/dL)	5.3 (2.5–9.6)
Chloride (mmol/L)	106 (103–114)
Urine	
Calcium (mg/day)	113 (41–276)
Uric acid (mg/day)	460 (130–989)
Citrate (mg/day)	290 (91–925)
Oxalate (mg/day)	31 (20–69)
Sodium (mEq/day)	170 (75–389)
Potassium (mEq/day)	52 (19–95)
Magnesium (mg/day)	78 (40–162)
Phosphate (mg/day)	780 (369–1596)
Creatinine (mg/day)	120 (698–2301)
Primary stone composition	
Uric acid	9 (60%)
Calcium oxalate monohydrate	3 (20%)
Calcium phosphate	2 (13.3%)
Struvite	1 (6.7%)
Hyperphosphaturia	4
Hyperuricosuria	2
Hyperoxaluria	1
Hypocitraturia	1

92.3%, respectively. All stone-free rates were confirmed by renal ultrasound at day 1 after operation and a follow-up renal ultrasound in 30 days. One patient still had a 5-mm lower pole fragment after the second procedure, as evidenced by follow-up ultrasound test, with no symptoms and with no further intervention. There were no major intraoperative or postoperative complications in any of the cases. Three patients had minor complications postoperatively, including one case of low-grade fever (37.9°C) at day 1 but had returned to normal at day 2 with strong anti-infection and one case of flank pain postoperatively at day 1 but disappeared at day 2 with proper pain medications. One patient had moderate stent pain but relieved after removal of stent 30 days after operation in outpatient department.

Table 3 Size of largest cyst and number of cysts

Parameter	Results (n = 15, including 11 unilateral and 2 bilateral)
Largest renal cyst size (cm)	3.6 (1.4–8.5)
Median (range)	
No. of cysts (%)	
0–6	3 (20)
7–14	1 (6)
≥15	11 (74)

Table 4 Stone characteristics and outcome of procedure

Total stone number	45
Mean stone size (mm)	5.6 (3–17)
Mean number of stones per patient	3.2 (2–5)
Mean number of treatments per patient	1.2 (1–2)
Overall SFR (%)	92.3
SFR after first treatment (%)	84.6
SFR after second treatment (%)	92.3
Mean OR time per patient (min)	45.5
Stone location	
Multiple sites (renal pelvis and caliceal) (%)	43 (95.6)
UPJ (%)	1 (2.2)
Lumber ureter (%)	1 (2.2)

SFR stone-free rate, *OR* operating room

Mean follow-up was 3.4 years (range 0.2–4). One patient was lost to follow-up. No recurrent nephrolithiasis occurs by means of renal ultrasound at a median of 34 months after the last retrograde endoscopic procedure, except one case with 5 mm stone in the lower pole but with no symptoms and no intervention (Fig. 1).

Discussion

Nephrolithiasis is a frequent cause of morbidity with ADPKD, which affects 8–36% [4]. The etiology has not been completely elucidated but is clearly multivariate. Reports [13] showed a combination of anatomical and metabolic abnormalities, including low urinary PH, hypocitraturia and low ammonia excretion, caused by ADPKD seems to be the reasons. Studies [3, 7, 13] confirmed that stones in ADPKD are mainly constituted by uric acid (55–71%), which are similar to our study. In our series, 60% had uric acid calculi, and all patients were treated with 10 mEq Urocit®-K (Mission pharmacal Co., Ltd, USA) three times daily before and/or after operation, which was reported to be effective for uric acid lithiasis and hypocitraturic calcium oxalate nephrolithiasis [14].

Flexible endoscopy and laser lithotripsy for intrarenal stones and ipsilateral ureteral stones is promising therapeutic method in recent years [9–12], but there are few reports about using this method for the treatment of nephrolithiasis in ADPKD patients. The shortcomings of this method are that the optical fiber is thin in diameter, and the effect of fragmentation and passage of stones is not

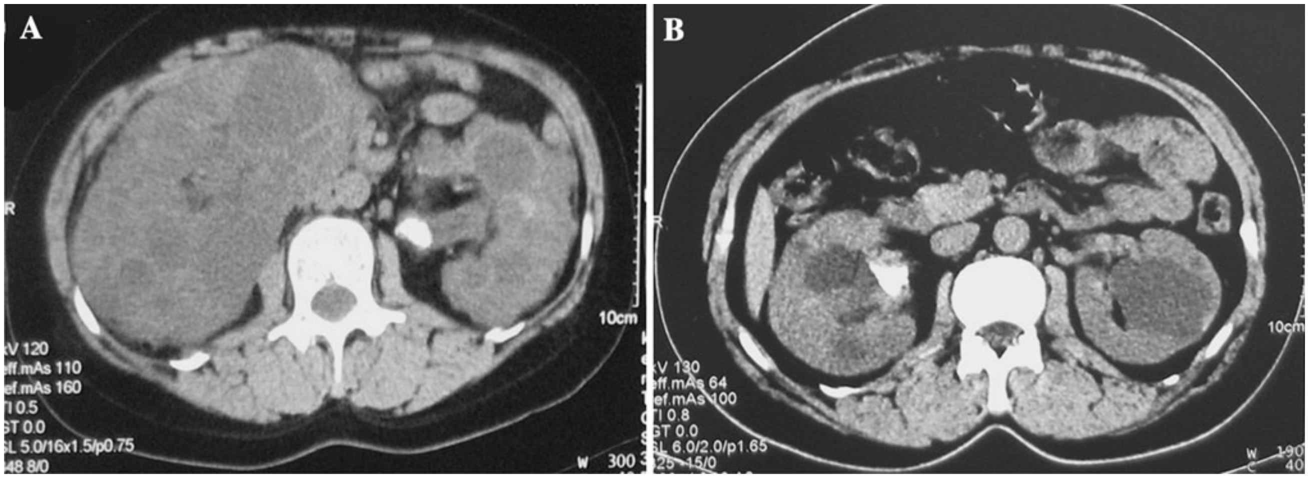

Fig. 1 Representative sections of renal calculi on abdominal CT: **a** 34-year-old male presenting with left flank pain had 15 mm obstructing UPJ calculus; **b** 45-year-old male presenting right flank pain had mid calices calculus

satisfactory. Thus, the relatively small stones were chosen for our study. In our series, the mean stone size is 5.6 mm. Moreover, considering the compressive effect of parenchymal cysts, the caliceal spaces are often narrow and elongated, which might impede passage of stone fragments; we made the stone fragments less than 1 mm as much as possible during our surgical procedure, which could pass spontaneously at last. Meanwhile, as we found the residue stone larger than 1 mm after the first procedure, a second therapeutic flexible endoscopy was arranged. These two steps ensured the high stone-free rate. The results were encouraging. After the first procedure, the stone-free rate was 84.6%, but with the second procedure, the results increased up to 92.3%.

With normal anatomy, Breda et al. [10] demonstrated that the overall stone-free rate was 93.3% using flexible ureteroscopy and laser lithotripsy for single intrarenal stones. Cocuzza et al. [9] demonstrated that only 76% of the patients with multiple renal stones became stone-free after retrograde flexible ureteroscopic lithotripsy. In Breda [10, 12] study, patients underwent an average of 1.4 procedures to become stone-free and a mean of 2.3 when including the final diagnostic ureteroscopy and stent removal. Their mean operative time was 83 min (range 45–140). However, Mariani [15] reported a mean operative time of 64 min (range 30–240). In our series, patients underwent an average of 1.2 procedures to become stone-free, and the mean operative time was 45.5 min (range 35–60), which is shorter than that of Alberto and Mariani. We guess the reason was that the stones in our series were smaller than theirs, which needed shorter operation time.

ESWL and PCNL are other two methods treating urolithiasis in ADPKD patients. Because of obstructive effect of the cysts and the resultant urinary stasis, which impedes passage of the stone fragments [5], the stone-free rate at 3 months in several studies on ESWL was not satisfactory, with only 25–46% [16].

There are a few reports about the application of PCNL to nephrolithiasis with ADPKD [7, 8]. However, owing to the compressive effect of multiple parenchymal cysts, the caliceal spaces are often narrow and elongated, which could make the accurate caliceal puncture hard. Moreover, persistent radiation is great harmful to patients. Meanwhile, as to compression of renal parenchymal, chronic renal impairment is more or less wide among patients with ADPKD, which is commonly associated with a coagulation defect; thus, the risk of bleeding during or after the procedure could be increased. In Al-Kandari report, there was one patient showing bleeding but with good results. As for the complications, both PCNL reported and our series, no major complication occurred. Compared with PCNL, flexible endoscopy and laser lithotripsy use the natural lumen, avoiding bleeding as much as possible, which is better for patients with coagulation defect.

Our study also had limitations. The use of ultrasound for detecting the residue stones might increase false negative rate. The small sample size due to relative rarity of a large stone burden was another drawback in our series. However, more successful reports about flexible endoscopic lithotripsy make the application to nephrolithiasis with ADPKD promising. Accurate indication and knowledge of capability and limitations of flexible endoscopes are crucial for a high success rate.

Conclusion

Flexible ureteroscopy and holmium laser lithotripsy is a safe and effective option for the treatment of nephrolithiasis with ADPKD, with comparable stone-free rate but lower complication rate.

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