DOI: 10.4081/aiua.2014.4.257

ORIGINAL PAPER

Urolithiasis in renal transplantation: Diagnosis and management

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Summary ***Objectives: To report our experience of diagnosis and multimodal management of urolithiasis in renal transplantation.***
Patients and Methods: From January 1995 to December 2012, 953 patients underwent renal transplantation in the Kidney Transplant Unit of Treviso General Hospital. Ten (10%) of them developed urinary calculi and were referred at our institution. Their mode of presentation, investigation and treatment were recorded.
Results: Seven had renal and 3 ureteral calculi. Urolithiasis was incidentally discovered on routine ultrasound in 6 patients, 1 presented with oliguria, 1 with anuria and acute renal failure and in 2 urolithiasis was found at removal of the ureteral stent. Nephrostomy tube was placed in 5 patients. Hypercalcemia with hyperparathyroidism (HPT) was present in 5 patients and hyperuricemia in 3. Two patients were primary treated by shock wave lithotripsy (SWL) and one of them was stone-free after two sessions. Two patients, one with multiple pielocaliceal calculi and the other with staghorn calculus in the lower calyx, were treated with percutaneous nephrolitothotomy (PCNL). Three patients were treated by ureteroscopy (URS) and in one of them two treatments were carried out. One patient had calculus impacted in the uretero-vesical anastomosis and surgical ureterolithotomy with re-do ureterocystoneostomy was performed after failure of URS. Two patients with calculi discovered at removal of the ureteral stent were treated by URS. Conclusions: The incidence of urolithiasis in renal transplantation is uncommon. In the most of patients the condition occurs without pain. Metabolic anomalies and medical treatment after renal transplantation may cause stone formation. Advancements in endourology and interventional radiology have influenced the management of urolithiasis that can be actually treated with a minimal incidence of risk for the renal allograft.

KEY WORDS: *Urolithiasis management, Renal transplantation.*

Submitted 15 March 2014; Accepted 30 June 2014

INTRODUCTION

Urolithiasis in renal transplantation is uncommon, with reported prevalence rates between 0.2% and 6.3% (1-4). In the most of cases stone formation appears to form "*de novo*" after renal transplantation, although some studies suggest that the calculi are more often transplanted with the graft to the recipient (1, 5, 6). Theremore, metabolic anomalies causing stone formation could be present in allograft rather than native kidneys (7). Urolithiasis is often asymptomatic and the clinicians are not able to diagnose urinary calculi in renal transplant at an earlier stage. Neverthless, the prompt diagnosis and the subsequently stone removal is necessary to prevent adverse effects on a solitary kidney whose renal function is often borderline. Today the development of endourological tecniques for calculi management and interventional radiology for the emergency management of acute obstruction have minimized the potential risk for renal graft. However, such minimally invasive procedures could be performed only in centers that are well equipped and have expertise to offer the appropriate treatment.
We evaluated our experience of renal transplant patients with urolithiasis, regarding the risk factors associated with the condition and the management by endourological and open procedures.

PATIENTS AND METHODS

From January 1995 to December 2012, 953 patiens underwent renal transplantation in the *Kidney Transplant Unit of Treviso General Hospital*. The transplant were performed in the right or left iliac fossa with vascular anastomosis to the iliac artery and vein. Ureteral implantation (ureterocistoneostomy) was performed using the extravesical tecnique of Lich-Gregoir, with routine use of ureteral catheter that was removed 4-6 weeks later by flexible cystoscopy. Immunosoppression varied with the transplantation era.
Ten (10%) of them developed urinary calculi and referred to our institution. For the diagnosis of urolithiasis one or more of the following investigations were required: *ultrasonography* (US), plain abdominal X-ray, *intravenous urography* (IVP), nephrostography and *computed tomography* (CT). Chemistry profile including serum analysis for urea, creatinine, calcium, phosphate, urate, sodium, potassium, phosphate, alkaline phosphatase and parathyroid hormon and urine analysis (routine and culture) were performed. Management of

No conflict of interest declared.

these calculi involved *shock wave lithotripsy* (SWL), *ureteroscopy* (URS), *percutaneous nephrolithotomy* (PCNL) and ureterolithotomy with re-do ureterocistoneostomy.

Results

Six patients were females and 4 males. Ages ranged from 31 to 59 years (mean 43 years). Seven had renal and 3 ureteral calculi. The overall diameter range was 0.7-3 cm (mean 1.2 cm). Urolithiasis was incidentally discovered on routine ultrasound in 6 patients with calculi located in the calices. One patient with multiple pielocaliceal calculi presented with oliguria and 1 with calculus impacted in the vesico-ureteral anastomosis with anuria and acute renal failure. In 2 patients urolithiasis was found at removal of the ureteral stent. Nephrostomy tube was quickly placed in the following cases: calculi causing oliguria, anuria or hydronephrosis and in 2 patients with calculi discovered removing ureteral stent.
Hypercalcemia with hyperparathiroidism was present in 5 patients and hyperuricemia in 3. Four patients had urinary tract infections (UTIs), in 3 infecting organism was E. Coli and in 1 Proteus mirabilis (Table 1).

Table 1.
Characteristic of patients with renal transplantation and urolithiasis.

Pts	Ex	Age	Clinics	Metabolic anomalies	UTIs
1	F	31	oliguria	HPT	no
2	F	41	anuria	HPT	yes
3	M	45	renal US	hyperuricemia	yes
4	M	47	renal US	no	no
5	F	48	hydronephrosis	hyperuricemia	no
6	M	51	renal US	no	no
7	F	59	renal US	HPT	no
8	F	34	failure to remove DJ	HPT	yes
9	F	42	failure to remove DJ	HPT	yes
10	M	35	renal US	hyperuricemia	no

Two patients were primary treated by SWL (Lithostar plus Siemens) in prone position and one of them with calculus in the upper calyx was stone free after two sessions, while in the other with calculus in the lower calyx URS was performed after failure of SWL. Two patients, one with multiple calculi and the other with staghorn in the lower calyx, were treated with PCNL. Three patients were treated with ureteroscopy and in one of them two treatments were carried out. One patient had calculus impacted in the uretero-vesical anastomosis and ureterolithotomy with re-do ureterocistoneostomy was performed after the failure of URS (Table 2).

Discussion

Urolithiasis in patients with kidney transplantation is often asymptomatic. A possible explanation for this observation is denervation of the transplanted graft (1, 2, 5, 8). In some cases, concomitant increase of serum creatinine should be considered with caution to avoid a misdiagnosis of episode of acute rejection (9). In our experience urolithiasis was incidentally discovered on routine ultrasound in one-half of them. The presence of uncomplicated calculus is not a contraindication to urological procedures. In fact, as it has previously been reported, calculus in the kidney transplantation, such as in patients with solitary kidney, must be removed in every case because it may cause urinary infection or pass in the ureter causing anuria with acute renal failure (10). Previous studies have shown that SWL is the treatment of choice for unobstructive calculi with diameter less than 1.5 cm (11). However, there are potential difficulties in locating transplant calculi because of the overlying bony pelvis which may limit visualization of stones on fluoroscopy as well mitigate the propagation of shock waves energy. Prone position with ultrasound targeting may counter these disadvantages (12). An additional disadvantage of SWL is the need for multiple sessions. *Challacombe et al.* have reported stone free rate in 13 patients with kidney transplantation and urolithiasis who underwent SWL, but in 8 of them multiple procedures were required. In our study two patients with asymptomatic calculi were primarily treated by SWL and

Table 2.
Characteristic of calculi and urologic treatments.

	Diameter (cm)	Location	Nephrostomy	SWL	URS	PCN	Ureterolithotomy with re-do ureterocystoneostomy
1	3	pielocaliceal	yes			yes	
2	1.3	ureteral-vesical anastomosis	yes		failure		yes
3	0.8	lower calix	no	failure	yes		
4	0.7	upper calix	no	yes			
5	1.2	UPJ	yes		yes		
6	1.1	upper calix	no		yes		
7	1.0	middle calix	no		yes		
8	1.4	distal ureter	yes		yes		
9	1.5	distal ureter	yes		yes		
10	1.2	lower calix	no			yes	

only one of them was stone-free. In both cases not more than 2 treatments were performed and URS was carried out in 1 patient after failure of SWL.
Actually URS is the treatment of choice emerging as for small renal and ureteral calculi within kidneys transplantation (13). Access to these kidneys may be difficult because of their position in the pelvis and the location of the neo-ureteric orifice. Using both retrograde and anterograde approaches, stone-free rate of the calculi in kidney transplantion could be obtained with minor complications. We used both approaches in those patients with nephrostomy tube placed because urinary tract obstruction and after failure to remove ureteral stent, while in the other cases only a retrograde approach was performed. However, as endoscopes have become increasingly miniaturized and deflectable, ureteral dilation has become unnecessary and all urinary collecting system can be accessed in a straightforward manner. In our experience semirigid retrograde URS was performed over a decade ago and the access to the ureter was facilitated with angled catheters and hydrophilic wires and ureteral orifice was balloon dilated with a high-pressure balloon dilator. Nowday, URS has carried out by flexible ureteroscopy. This method and disintegration of calculi with holmium laser is an effective method for the treatment of urolithiasis in kidney transplantion and the access to the neo-ureteric orifice and to the pelvis may be achieved by introducing the ureteroscope over a guide wire. Instruments with "*active*" secondary deflection are particularly useful in reaching calculi in transplanted kidney. In our experience, according to *Hymas et al.*, we could suggest that URS is a viable treatment modality as well.
For renal calculi with diameter greater then 1.5 cm, PCNL has been effective to remove all stone fragments in one procedure. The superficial position of transplanted kidney makes straightforward percutaneous procedure so that may be justified by maximal stone clearance and carried out in special centers because of the greater risk in patients with solitary kidney (14).
In fact, due to the proximity of the bowels to the renal graft, the risk of perforation is high. Furthemore, there have been reports of allograft renal artery injury and arteriovenous fistulae after trans abdominal access.
Theremore, tract dilatation can become difficult to perform because of the presence of a fibrous sheath and limited mobility of the kidney during rigid nephroscopy (15). In our experience percutaneous nephrolithotomy was only carried out in two patients, one with staghorn calculus located in the lower calyx and the other with multiple pielocaliceal calculi.
Previous reports have reported that calculi occurring in transplanted kidney are composed of calcium oxalate and calcium phosphate (5, 7). Infected stone consisting of struvite or mixed form of struvite and calcium phosphate are also relatively common (4, 16). Lithogenic factors include hyperparathyroidsm, hypercalciuria, hypocitraturia, hyperuricosuria, chronic urinary tract infection (UTIs), urinary stasis, incrusted double J stent and nidus such as nonabsorbable suture (7). Hyperparathyroidism has been reported the most important factor in calculus formation in kidney transplantion (16, 17). Medical treatments, such as cinecalcet hydrochloride, have been shown to be efficacious in treating hyperparathyroidism by soppression of the action of parathyroid hormone. However, if the hyperparathiroidism persist after 1 or 2 years, a parathyroidectomy must be carried out (2).
Furthemore, immunosoppressive agents may have a contributory role in the cause of calculi in transplant. Ciclosporin, a calcineurin inhibitor used more commonly in the past, is associated with hypeuricemia (18). However, this has not been necessarily associated to an an increase in uric acid calculi risk (16, 19). Ciclosporin has been superseded by tacrolimus, another calcineurin inhibitor which has not been shown to affect uric acid levels (20). *Stapenhorst et al*. have reported that calcineurin inhibitor, treatment can lead to hypocitraturia, whereas hyperoxaluria can be primarily the result of a removal of significant body oxalate stores deposited during the dialysis (21).
These authors have suggested to treat these patients with alkaline citrate to increase their urinary citrate excretion and urinary solubility index decreasing the risk for calculi formation. In our experience hyperparathiroidism was present in 5 patients and hyperuricemia in 3, but complete metabolic assessment was not carried out in all patients. However, it has been reported that low urinary excretion of citrate could also due to chronic urinary infections (22), that can be present in patients with renal transplantation (incrusted ureteric stents, retention of suture materials, immunosopression agents).
Consequently, if urinary infection is present, antibiotic prophilaxis could be associated to specific therapies for underlying metabolic anomalies present in patients with renal transplantation and urolithiasis.

Conclusions

The incidence of urolithiasis in renal transplantation is low. In our experience hyperparathyroidism is the most frequent cause of stone formation. URS for its safety and effectiveness could be the treatment of choice of urolithiasis in renal transplantation. Open surgery could be carried out after failure of endourological procedures in selected cases.

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