Urolithiasis in Renal Transplantation

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ABSTRACT

Urolithiasis in renal transplantation is uncommon. In the most of cases stones formation appear to form "de novo" after renal transplantation, although some studies suggest that the calculi are more often transplanted with the graft to the recipient. The etiology of stone formation in renal transplantation is multifactorial. Surgical factors, urinary tract infections and metabolic anomalies causing stone formation could be present in allograft rather than native kidneys. Urolithiasis is often asymptomatic and the clinicians are not able to diagnose urinary calculi in renal transplant at an earlier stage. Nevertheless, the prompt diagnosis and the subsequently stone removal is necessary for prevent adverse effects on a solitary kidney, where renal function is often borderline. Nowday, the development of endourological techniques, such us extracorporeal shock wave lithotripsy (SWL), ureteroscopy (URS) and percutaneous nephrolithotomy (PCN) 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. Furthemore, medical treatment should be required for the most cost-effective management.

INTRODUCTION

Renal transplantation remains the optimal treatment of patients with end-stage renal disease. Urinary stones represent a unusual urological complications in kidney transplantation, with reported prevalence rate between 0.2% and 6.3% [1-4]. Nevertheless, it is an important concern due to risk of significant morbidity from the risk of obstruction, sepsis and potential loss of allograft function.

Urolithiasis in renal transplantation can result from "de novo" stone formation or pre-existing stones in the transplanted kidney (donor gift) [5-7]. Although evidence suggests that the majority of cases of lithiasis occurs "de novo" after renal transplantation [1,8-12], the frequency with which renal allograft containing stones are transplanted may be underestimated [5]. Furthemore, metabolic anomalies promoting stone formation could be present on allograft rather in native kidneys [13]. Theremore, surgical factors such us stenosis of the uretero-vesical anastomosis, retention of suture materials or incrusted ureteral stent and immunosuppressive agents, causing chronic urinary infection, could change the urine chemistry in a lithogenic direction [14].

Urolithiasis is often asymptomatic. The clinical presentation of stones can occur 1.6-3.6 yeas after the kidney transplantation [15-17]. The absence of renal pain, haematuria, unexplained fever and decreased urine output could delay the diagnosis. Transplanted kidney and ureter are denervated and the risk of longstanding obstruction with acute renal failure will occur, without the patient's awareness of pain, or vague discomfort in the iliac region or a palpable mass due to renal dilation [1,2,5,18]. In some cases, concomitant increased of serum creatinine should be considered with caution to avoid a mistake episode of acute rejection or acute tubular necrosis [10]. Hydronephrosis could be present, as well anuria in the event of complete obstruction [2]. Furthemore, urinary infection, as a result of obstruction, could cause fever and mimics pyelonephritis [1]. In our study urolithiasis in renal transplantation was incidentally discovered on routine ultrasound (US) in 50 % of patients with calculi located in calices [19]. One patient with multiple pielocaliceal calculi presented with oliguria, 1 with calculus impacted in the uretero-vesical anastomosis with anuria and acute renal failure. In 2 patients urolithiasis was found at removal of the ureteral stent (Table 1). Nephrostomy tube was quickly placed in the following cases: calculi causing oliguria, anuria or hydronephrosis and in 2 patients discovered removing ureteral stent (Table 2).

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

Pts	Sex	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

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	uretero-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	

Prompt diagnosis of renal lithiasis in kidney transplantation is essential as patients in this are especially prone to significant morbidity due to the reliance of solitary kidney. The presence of uncomplicated and/or asymptomatic 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 [20].

Ultrasound is routinely used in the post transplantation period for the detection of potential complications. It also appears to be the most commonly used method for the detection of graft lithiasis, although any difficult in diagnosis due to bone and/or bowel interference or stone size could prompt the use of computed tomography (CT) [21].

Donor Gift Lithiasis

Asymptomatic stones could be present in kidney transplanted from cadaveric or living donors with approximately rate of 0.64% [22]. This is could be due to the lack of accurate donor organ screening. Consequently, early stone presentations likely due to donor gifted lithiasis, whereas late presentations may be either donor gifted or "de novo" stones. The presence of lithiasis in donors grafts could cause important implications for both the donor and recipient. In fact 50% of patients with renal stones are at risk of recurrence within 5 years [23]. In both cases the presence of stone, such us in solitary kidney, must be removed because it may pass in the ureter causing anuria with acute renal function. Furthemore, in the recipient it could bring complications such us infection risk for immunosuppressive agents.

Nowadays, there is an increasing number of living donor transplants and the presence of kidney stones has been a contraindication for living donation. According to American Society of Transplantation potential donors with a history of urolithiasis may proceed with donor evaluation if they have only passed one stone, or if they have had multiple stones, but have been asymptomatic for more than 10 years [24].

Furthermore, living donors can be proceed to donation if there is no current radiographic evidence for stones and have no metabolic abnormalities promoting stone formation. Metabolic evaluation includes laboratory data such us urine citrate, oxalate, calcium, uric acid and urinay pH. Renal tubular acidosis and hyperparathyrodism have been excluded and analysis of stone passed or removed performed when it is possible [25].

Previously, imaging modalities such us ultrasound (US) and intravenous pyelography (IVP), used to screen renal disorders in potential kidney donors may have missed small asymptomatic small stones. Nowday, a greater number of incidental small stones could be found due to computed tomography (CT), which is more regarded more sensitive than magnetic resonance (MRI) and intravenous pyelography(IVP) for calculi detection [26,27].

Recently, an increased patient population requiring renal transplantation has modified the donor selection criteria. In 2011, the British Transplantation Society guidelines state that in absence of significant metabolic abnormalities potential donors with a history of previous small stones or small renal stones on imaging should be considered [28]. However, various guidelines suggest that kidney stones secondary to underlying (or uncorrectable) metabolic anomalies are a contraindication to renal graft donation.

Metabolic abnormalities are present in more than 50% of patients with renal calculi [29,30]. Nevertheless, the donation of kidney could be performed only is there isolated and correctable metabolic anomalies. The presence of struvite and cistine stones and systemic illness such us sarcoidosis are contraindications to graft donation [31].

Removing stones from the donor kidney prior of transplantation is desirable. There are four possible options in dealing with donors with stones: stones can be removed pre-transplantation, at the time of donation, donation of the stone bearing kidney can take place without stone removal or the non stone bearing kidney can be used for transplantation [32]. Extracorporeal shock wave lithotripsy, pyelolithotomy and ureterolithomy have been performed prior of the donation [33,34]. "Ex vivo" ureteroscopy (ex-URS), a technique whereby stone removal attempted once the kidney was removed and transferred to a prepared back table and immersed in ice-slush. Intraoperative ultrasound could be performed in parallel with transplantation so that ischaemia time is not influenced [5].

Abnormalities Leading to Stone Formation

Previous reports have reported that calculi occurring in transplantation kidney are composed of calcium oxalate and calcium phosphate [5,13]. 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 and chronic urinary tract infections (UTIs), urinary stasis, incrusted double J stent and nidus such as nonabsorbable suture [13]. Hyperparathyroidism has been reported the most important factor in calculus formation in kidney transplantation [16,17]. Medical treatments, such as cinecalcet hydrochloride, have been shown to be efficacious in treating hyperparathyroidism by soppression the action of parathyroid hormone. However, if the hyperparathiroidism persist after 1 or 2 years, a parathyroidectomy must be carried out [2].

Furthermore, 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 hyperuricemia [35]. However, this has not necessarily transplanted into an increase in uric acid calculi risk [16,36]. Ciclosporin has been superseded by tacrolimus, another calcineurin inhibitor which has not been shown to affect uric acid levels [37]. Stapenhorst et al. [38] 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. 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 and a complete metabolic did not carried out in all patients [19]. However, it has been reported that low urinary excretion of citrate could also due to the degradation of urinary citrate by bacterial enzymes from chronic urinary infections [39], such as in patients with renal transplantation (incrusted ureteric stents, retention of suture materials, immunosopressive 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 to prevent stone recurrence and and or regrowth, as previously it has been reported [40,41].

Management

Previous studies have shown that SWL is the treatment of choice for unobstructive calculi with diameter less than 1.5 cm [42]. 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 [15]. An additional disadvantage of SWL is the need for multiple session. Challacombe et al have reported stone free rate in 13 patients with kidney transplantation and urolithiasis undergone SWL, but in 8 of them multiple procedures were required. In our study two patients with asymptomatic calculi were primarily treated by SWL and 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 [19].

Actually URS is the treatment of choice emerging as for small renal and ureteral calculi within kidneys transplantation [43]. 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 transplantation 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 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 ureteroscope. This method and disintegration of calculi with holmium laser is effective method for the treatment of urolithiasis in kidney transplantation and the neo-ureteric orifice and the pelvis may be accessed achieved by introducing the ureteroscope over a guide wire. Instruments with "active" secondary deflection are particularly useful in reaching calculi in transplantation kidney. In our experience three patients were treated with URS and in one of them two treatments were carried out. In one patient with calculus impacted in uretero-vesical anastomosis, ureterolithotomy with re-do ureterocistoneostomy was performed after failure of URS [19]. According to Hymas et al. [43] we could suggest that URS is a viable treatment modalitity 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 justified by maximal stone clearance and carried out in special Centers because the greater important of solitary kidney [44].

In fact, due to the proximity of the bowels to the renal graft, the risk of perforation is high. Furthemore, there have been reported 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 [45]. In our study percutaneous nephrolithotomy was only carried out in two patients, in one with staghorn calculus located in the lower calyx and in the other with multiple pielocaliceal calculi [19].

Open surgery could be required in selected cases after the failure of endourological procedures or for large staghorn calculi [17]. In fact, there are increased risks related to the proximity of the transplant iliac vessels to the renal pelvis and immunosoppressive agents could increase the risk for bleeding, graft loss, sepsis and poor wound healing.

CONCLUSIONS

The incidence of urolithiasis in renal transplantation is uncommon. The diagnosis requires a high degree of suspicion and vigilance as delay in diagnosis can lead renal graft loss. "De novo" stone formation in renal transplantation is caused by urinary infection and or metabolic anomalies. Consequently these patients should undergone further metabolic evaluation to identify and prevent risk of stone formation or regrowth. An accurate organ screening has to be performed for detecting of calculi in living donors. URS for its safe 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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