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Complex, Crusty Calculi: A Case Study Report of Renal Transplant Lithiasis and Encrustation

Shriram Swaminathan, BMed,[1] In-Ah Park, MBBS,[1] and Bobby Chacko, FRACP[1,2]

Abstract. Ureteric encrustation and lithiasis after renal transplantation are rare but not without risk of obstruction and graft loss. Patients are usually asymptomatic, and a majority present with graft dysfunction with imaging demonstrating hydronephrosis and rarely with acute graft pyelonephritis. We compare a case of transplant lithiasis with encrusted pyelitis and highlight key differences in their presentation and workup. A key focus for transplant physicians is to recognize when dealing with transplant hydronephrosis that the presence of a high urine pH and pyuria should be a key indicator to suspect ureteric encrustation to look for a urease-producing organism, recognizing that such organisms require prolonged incubation with urine culturing for up to 72 h.

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Lithiasis after renal transplantation is a rare phenomenon, with an incidence of 0.2% and 4.4%.[1] This presents several possible complications, including obstruction, complex sepsis, and risk of graft loss, with additional morbidity and mortality risk.

Ureteric encrustation, defined as mineral crystal deposition onto the urothelial surface of the ureter, is an even rarer complication first described in renal transplant patients, with limited evidence to guide management. Factors that predispose patients to encrusted pyelitis include immunocompromise and urogenital tract trauma,[2] both of which are common in our renal transplant population. Additional risk factors include the presence of urease-splitting bacteria such as *Corynebacterium*, the confirmation of which contributes to the diagnosis, causing alkaline urine, allowing for the precipitation of solutes causing stone formation.[2]

Patients are usually asymptomatic, and up to 96.9% of cases present with an increase in serum creatinine (Cr) and ultrasound of the renal tract showing hydronephrosis[3] and rarely with acute pyelonephritis in the transplant graft. In this report, we present a case of acute renal transplant lithiasis and a case of transplant ureteric encrustation. We aim to raise awareness of this issue and highlight key concepts for transplant physicians to recognize when they may be potentially dealing with these issues. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

CASE DESCRIPTION 1

A 62-y-old woman underwent deceased donor transplantation for native renal hypoplasia and nephrectomy of a nonfunctioning right kidney. There was no donor history of renal stones or urinary tract infections (UTIs).

At the 3-mo protocol scans, there was a 7-mm nonobstructing calculus in the lower pole of the transplanted kidney without hydronephrosis. This calculus was not present during the postoperative transplant investigations, and normal bladder emptying was observed. Abnormal blood results at 5 mo showed Cr 774 μmol/L and estimated glomerular filtration rate 4 mL/min/1.73 m^2 from a baseline of approximately Cr 140 μmol/L. CT scan of the abdomen and pelvis confirmed an 18 × 12-mm vesicoureteric junction calculus in the anastomosis site of the transplant kidney, causing hydroureteronephrosis (Figure 1). Urine cultures were found to be negative by polymerase chain reaction testing for urease-splitting organisms or any other growth.

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[1] Nephrology and Transplantation Unit, John Hunter Hospital, Newcastle, NSW, Australia.

[2] School of Medicine and Public Health, University of Newcastle, Callaghan, NSW, Australia.

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Correspondence: Bobby Chacko, FRACP, Renal Services, Nephrology and Transplantation Unit, John Hunter Hospital, Newcastle, NSW 2310, Australia; School of Medicine and Public Health, University of Newcastle, Callaghan, NSW, Australia. (bobby.chacko@health.nsw.gov.au).

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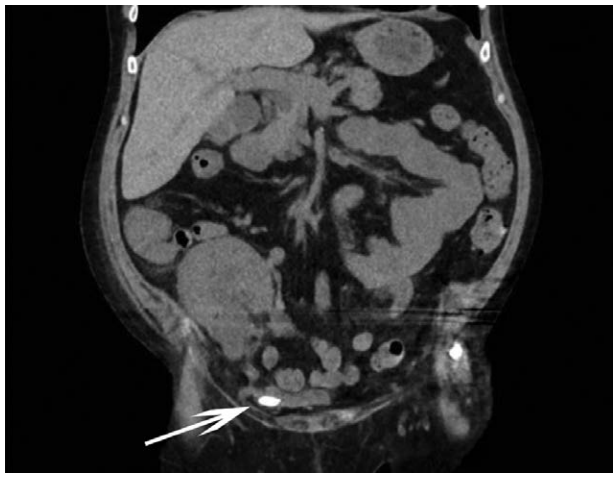

FIGURE 1. Computerized tomography imaging of a 62-y-old patient confirming vesicoureteric junction calculus with transplant hydronephrosis.

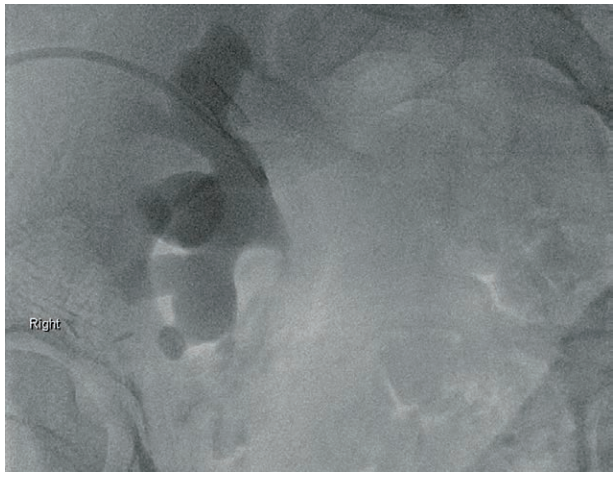

FIGURE 2. Angiographic imaging of the 29-y-old patient demonstrating tight stenosis of the proximal ureter of the transplanted kidney, which was proven to be encrustation on cystoscopy.

This patient underwent multiple procedures for the next several months, including nephrostomy and antegrade and retrograde procedures, to break up the stone before ultimately placing a metallic self-expanding stent. Stone analysis revealed the composition of calcium oxalate and calcium carbonate. The patient was noted to be hypercalcemic intermittently in the posttransplant course with corrected calcium levels ranging as high as 2.7 to 2.8 mmol/L and a parathyroid hormone level of 60.2 pmol/L just before her obstructive complication, which is now medically managed. No other metabolic abnormalities were observed in the patient.

CASE DESCRIPTION 2

A 29-y-old woman with a living unrelated ABO incompatible HLA 3/6 mismatch kidney transplant in the setting of native immunoglobulin A nephropathy initially presented with nonspecific urinary symptoms <6 mo after transplantation. The donor was an otherwise healthy man of a similar age from the Paired Kidney Exchange program with no known history of donor-specific antibodies, and there was no donor history of renal stones or UTIs.

Her initial posttransplantation course was uneventful, although her ureteric stent removal was delayed by 2 to 4 wk because of nonadherence to attending urology appointments. There was a known persistent moderate hydronephrosis after stent removal with a resultant hematoma that had developed 4 mo posttransplantation; however, a subsequent MAG3 scan showed no evidence of obstruction. She had no known history of urinary retention and a previous postvoid bladder residual of only 10 mL. At the time of presentation, urine cultures were positive by polymerase chain reaction for *Ureaplasma ureolyticum*, for which she was treated with a 2-wk course of sensitive oral antibiotics.

Follow-up imaging after treatment showed a new proximal ureteric obstruction of the transplanted kidney secondary to a stone requiring insertion of a nephrostomy (Figure 2). Follow-up planned cystoscopy and ureteroscopy were complicated by further UTIs in the setting of instrumentation but ultimately progressed to laser lithotripsy and stent exchange. Stone analysis revealed a chemical makeup consisting of calcium, carbonate, ammonium, phosphate, and magnesium. No other metabolic abnormalities suggested stone-forming tendencies.

Follow-up cystoscopy revealed extensive mucosal-associated encrustations in the transplanted ureter with heavy calcification around the pelviureteric junction. Definitive management of this complication requires corrective surgery involving anastomosis of the transplant renal pelvis directly to the bladder as a means of reducing scarring and allowing adequate drainage.

DISCUSSION

There are 2 ways nephrolithiasis occurs: "donor-gifted," when the stone is present in the donor kidney, or formed "de novo" in the transplant kidney. Previous systematic reviews suggest that if there are no metabolic stone-forming abnormalities, potential donors with a limited history of kidney stones may still be considered with a preference to inspect the donated kidney and remove large stones using flexible ureteroscopy.[4] De novo allograft stones are rare, with risk factors typically related to metabolic changes in the serum and urine, favoring the development in the transplanted kidney. Hyperparathyroidism, as seen in our first patient, and low citraturia, high oxaluria, alkaline urine, and cyclosporine-induced hyperuricosuria contribute primarily to calcium oxalate and calcium phosphate stones, as well as uric acid stones.[5] Our first case appears to be consistent with a hyperparathyroid-induced calcium oxalate stone. Alongside metabolic risk factors are urological risk factors, such as voiding dysfunction, retained double-J stents, and ureteral obstruction.[5]

Ureteral encrustation is essentially the deposition of mineral crystals, such as struvite on the urothelial surface of the ureter.[6] Encrusted uropathy has become recognized with increasing instrumental urological procedures and the use of immunosuppressive therapies, predisposing patients to long-term hospitalization in renal transplantation.[6] It is a chronic inflammatory disorder caused by urease-producing organisms,[6] mainly *Corynebacterium urealyticum,* which can create struvite stones.

The first cases of encrusted pyelitis were reported among renal transplant recipients who presented with a higher risk for this condition in the setting of immunosuppression, frequent

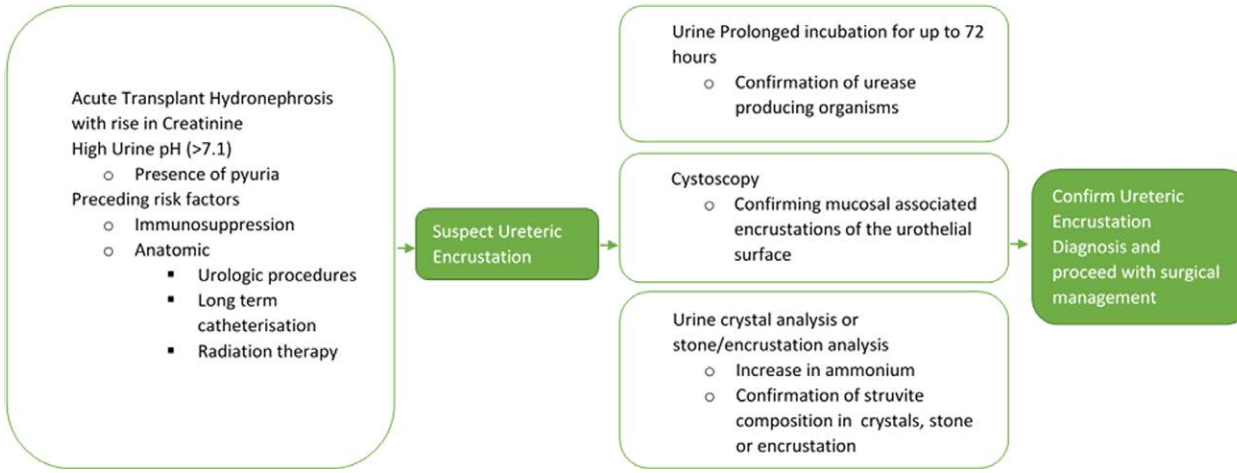

FIGURE 3. Diagnostic approach to suspected ureteric encrustation.

and prolonged hospital admissions, frequent antibiotic treatment, bladder and ureteral catheterization, and a history of urological procedures.[2] Immunosuppression raises concerns about the increased risk of infection with urease-producing organisms, with studies showing immunosuppressed status in 27% to 41% of patients with *Corynebacterium urealyticum* bacteriuria.[6] An area for further study is the predisposing risk of specific immunosuppressive therapies to urease-producing bacteriuria.

Preceding urologic procedures causing urogenital tract trauma are among the major recognized risk factors[7] and are certainly a component of renal transplant surgery. Other risk factors for urogenital tract trauma include long-term vesical and ureteral catheterization, radical cystoprostatectomy, and radiation therapy.[8] Therefore, a concern raised by the above cases, particularly the second case, is whether urologic stent placement and duration in situ contribute to urogenital tract trauma and predispose to encrustation. The time frame for stent removal in renal transplant patients is not well defined, but an increased association with UTIs with stents in situ for >30 d has been found,[9] raising concerns for an increased risk of infection with urease-producing organisms. In the same randomized trial, cases of ureteric encrustations were not described, although this was a single population study of 200 patients,[9] and we acknowledge that this is an area that requires further study to determine whether longer duration stents, as seen in our second patient, contribute to encrustation through an increased risk of infections and urogenital trauma or whether this is a protective factor through improved ureter patency.

Ureteropyeloscopy, laser lithotripsy, and antegrade stenting were performed. One case confirmed the presence of urease-producing bacteria with encrustations, and the other confirmed a large obstructing stone in the grafts. A high urine pH with negative cultures, particularly in the presence of pyuria, is grounds to suspect ureteric encrustation, and the urine should undergo prolonged incubation. This has been demonstrated by an increase in ammonium and the formation of struvite crystals after 24 h, as well as infection with *Corynebacterium urealyticum*.[10] *Corynebacterium urealyticum* is an aerobic gram-positive rod that is multiresistant and splits urea, causing urease production. Other urease-producing organisms include *Ureaplasma urealyticum* (as seen in our second case) and some *Streptococcus* and *Staphylococcus* species.[6] Adequate culturing often requires up to 72 h of incubation because of the slow-growing nature of these organisms.[7] See Figure 3 for the diagnostic approach to ureteric encrustation. Antibiotic treatment is guided by sensitivity, but *Corynebacterium urealyticum* is uniformly sensitive to glycopeptides, such as vancomycin and teicoplanin; an optimal duration is not well established and depends on the case severity, but treatment for several weeks to months is often necessary.[6]

Urological interventions with chemolysis are recommended for ureteric encrustation management. Prognosis depends on the timely removal of encrustation with antibiotics and urinary acidification. In de novo transplant nephrolithiasis, ureteroscopy appears to be a safe management option with stone-free rates between 80% and 100%.[4] Stone removal and drug therapy for the prevention of further stone formation after surgical intervention are suggested on the basis of the stone composition.[6]

This condition needs to be recognized with the likelihood of underdiagnosis, considering the atypical presentation of denervated transplant patients. Graft outcome data are limited, and more cases must be collected to analyze the predisposing risks of renal transplant lithiasis and encrustation. Further advice on the adjustments to standard immunosuppression used in renal transplantation could also be a potential area for research.

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