Proteinaceous Renal Stones in a Kidney Transplant Candidate Presenting as Bilateral Filling Defects Suspicious for Upper Urinary Tract Transitional Cell Carcinoma

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CASE PRESENTATION

Our patient is a 60-year-old female with a past medical history significant for diabetes mellitus type 2, smoking, anal cancer status-post transrectal excision with no evidence of recurrence or metastasis, rheumatoid arthritis, systemic lupus erythematosus, and end-stage renal disease on hemodialysis (HD). She had progressive chronic kidney disease for approximately 25 years, ultimately starting HD 3 years prior to this evaluation. She presented to the urology department for evaluation prior to kidney transplantation. On initial presentation, she denies any urologic complaints. She makes approximately 3 cups of urine daily, normally 2 voids. She denies a history of gross hematuria, dysuria, or lower urinary tract symptoms. She has had no recent urinary tract infection. She denies fatigue and fever. On physical examination, she appears well, in no distress. Abdomen is soft without masses. Genitourinary examination is normal.

EVALUATION

The patient's laboratory studies are reviewed. She has serum creatinine of 6.8 and liver function tests are within normal limits. Urinalysis shows small leukocyte esterase, negative nitrite, no microhematuria, and significant proteinuria (>500 ug/mL). Evaluation of all available urinalyses shows the patient has had significant proteinuria since initiation of HD. The patient's imaging studies are evaluated for any signs of genitourinary malignancy. The patient had a computed tomography (CT) scan of the chest, abdomen, and pelvis with and without intravenous contrast, performed during the metastatic workup for anal cancer. This shows atrophic kidneys bilaterally, no hydronephrosis, multiple simple renal cysts, and a 13 mm mass within the right renal pelvis. There were also similar, smaller masses in the left renal collecting system. These were of soft-tissue density, measuring approximately 10-20 HU without enhancement on the contrast phase. (Fig. 1) Based on these findings, a urine cytology was sent, which showed atypical cells of unknown significance. She underwent flexible cystoscopy which was normal. Due to concerns for a primary renal collecting system neoplasm, the patient was offered bilateral ureteroscopy and biopsy of these lesions.

OPERATIVE DETAILS

The procedure began with cystoscopy and retrograde pyelogram on the right side. This confirmed the presence of a large filling defect in the right renal pelvis with otherwise normal ureteral and pelvicalyceal contour (Fig. 2). This filling defect did not seem to move with injecting the contrast dye toward the renal collecting system. A ureteral access sheath was inserted and flexible ureteroscopy and renoscopy were performed. The filling defect in the right renal pelvis proved to be a soft, nearly translucent, free-floating mass characteristic of a proteinaceous stone. The stone was too large to extract with the stone basket. Using the Holmium laser, the stone was broken into small fragments. The stone was noted to have many layers and fragmented easily into small soft shards (Figs. 3, 4). Basketing was attempted, however, given the fragments fragility and small size, no specimen could be retrieved. Our attention was turned to the left side, where we encountered similar, although smaller stones in the left renal pelvis. Holmium laser was used again to fragment these stones. Bilateral ureteral stents were placed with strings attached. The patient was awakened and transported to postanesthesia care in no distress. She was discharged home. She removed the stents without difficulty. On follow-up, she was cleared from urologic perspective for kidney transplant.

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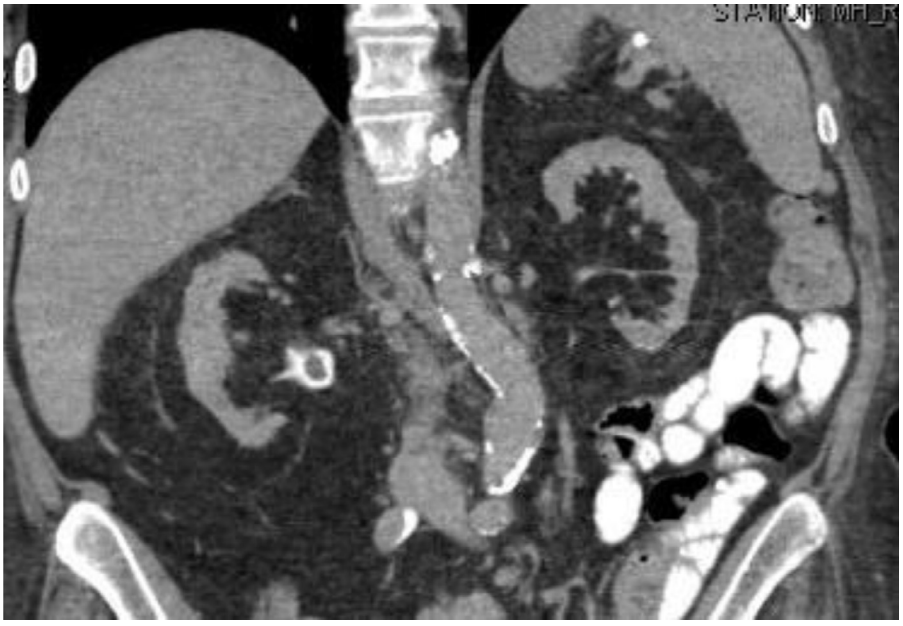

Figure 1. Representative cut of the patient's CT scan showing bilateral soft tissue density masses in the renal collecting system. In this image, the 1 mm density mass is seen in the right renal pelvis.

DISCUSSION BY DR. SHAHEEN ALANEE

All eligible kidney transplant recipients are recommended to have a urologic evaluation.[1] Therefore, the urologic pretransplant visit is a common reason for consultation in an otherwise asymptomatic patient. The clinical assessment of a kidney transplant candidate begins with a detailed history and physical examination. The primary cause and duration of the renal disease, requirement and type of dialysis and history of urologic or vascular operations should be evaluated. Volume of urine production and lower urinary tract symptoms should be assessed. Minimum investigations include urinalysis, urine culture, and renal ultrasound.[2] Urodynamics and cystoscopy should be obtained on an individualized basis depending on the severity of lower urinary tract symptoms and the cause of the renal disease. For instance, in patients with a primarily obstructive cause of renal disease, history of pyelonephritis, neurogenic bladder, or abnormal voiding

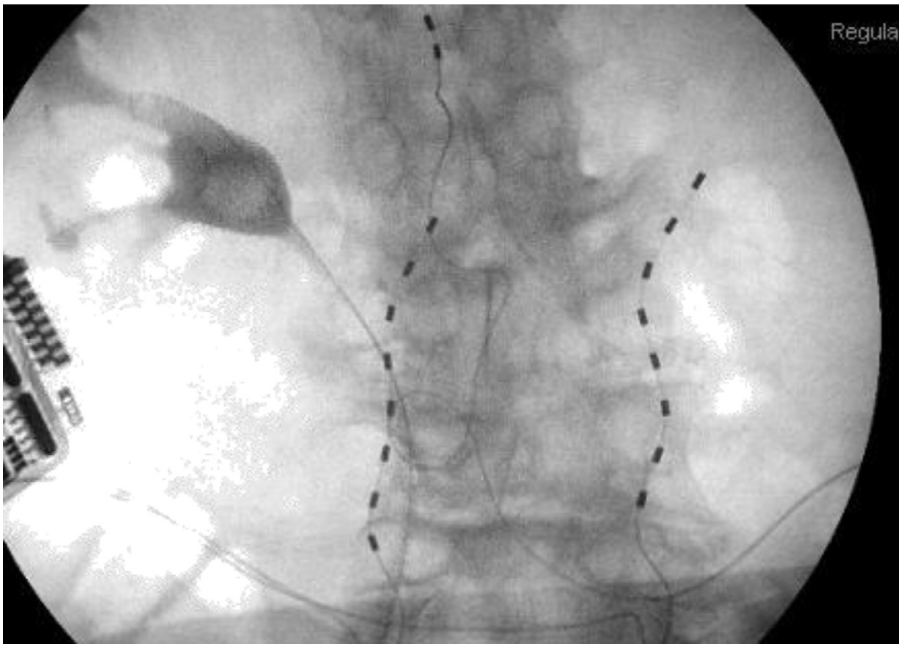

Figure 2. Intraoperative fluoroscopic image of the retrograde pyelogram showing a large filling defect in the right renal pelvis. Of note, patient has bilateral spinal cord stimulators.

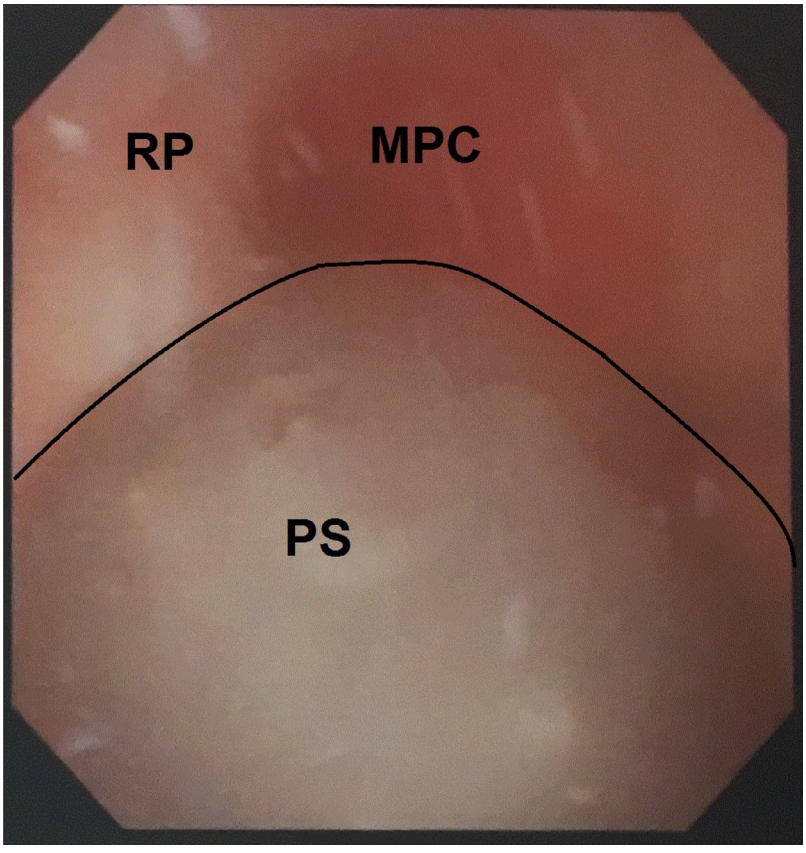

Figure 3. Ureteroscopic view of the right renal pelvic proteinaceous stone. The PS is outlined with black line for clarity. The soft gelatinous texture of the PS is noted in this view. RP, renal pelvis, MPC, middle pole calyx, PS, protein stone. (Color version available online.)

patterns, the determination of bladder capacity and voiding pressures will be important for management of renal function following transplant.[1]

Our patient presented for transplant evaluation with an unremarkable urologic history and normal physical examination. However, given the recent abdominal imaging findings, specifically, bilateral, soft-tissue like densities in the renal collecting systems, additional investigations were mandatory.

The primary diagnostic suspicion in our patient was upper urinary tract urothelial carcinoma (UTUC). These tumors are relatively rare, only accounting for 5%-10% of urothelial cancer. Typically, patients with UTUC present with hematuria or flank pain from an obstructing lesion, however, this cancer can also be incidentally detected on imaging.[3]

Urine cytology results showed atypical cells, with no overt evidence of malignancy. Cystoscopy was performed to rule out an undiagnosed bladder mass and ureteroscopy was performed for visualization, biopsy, and possible endoscopic management of the lesions seen on CT. Although endoscopic management of UTUC is becoming more common,[3] our patient with end-stage renal disease would not benefit significantly from this approach.

Our operative findings were unexpected. We discovered that the filling defects in the renal collecting system suspicious for soft tissue density masses seen on CT were soft, freely mobile stones most likely composed of protein considering the patient's significant proteinuria.

Proteinaceous stones have been described in the literature. Although decidedly rare, the true incidence of protein stones in patients on long-term HD is not known.[4] Bommer et al describes 7 patients with renal calculi consisting of microfibrillar protein in patients on HD. In these patients, glomerulonephritis was present with or without proteinuria. These stones exhibited a distinctive laminated structure, similar to what we saw in our patient. With transmission electron microscopy, they found these calculi to consist of microfibrils. The proteinaceous material differed from fibrin or Tamm-Horsfall protein, as indicated by ultrastructure, carbohydrate analysis, and amino-acid analysis. On X-ray diffraction and scanning electron microscopy, they noted the presence of small amounts of Whewellite (calcium oxalate monohydrate) and/or uric acid in some specimens. Histological examination of these calculi showed laminar concentric rings of organized matrix with an orderly, layered deposition of minerals.[4]

Although, because of our treatment method of flexible ureteroscopic laser lithotripsy, we were unable to obtain a tissue sample, the history of lupus nephritis, end-stage renal disease on HD and the visual appearance of these stones on ureteroscopy argue for this diagnosis, as

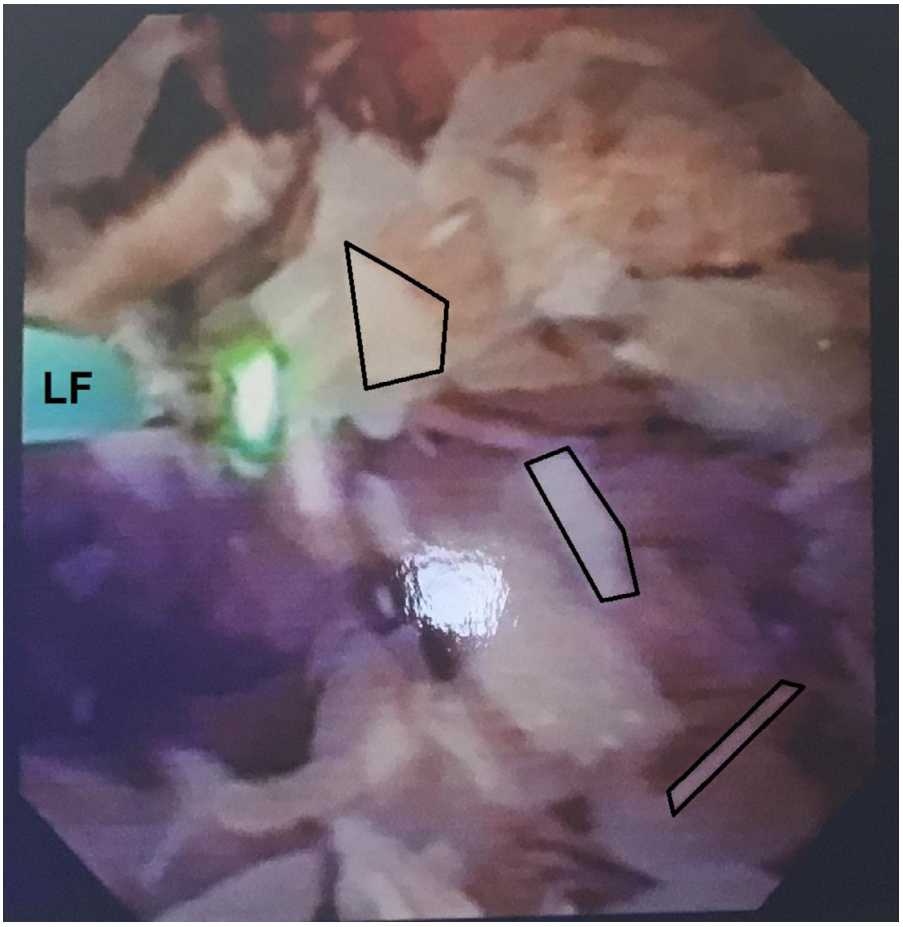

Figure 4. Ureteroscopic image as the proteinaceous stone is fragmented with Holmium LF. The soft, fragmented shards are noted in this view and outlined with black polygons. LF, laser fiber. (Color version available online.)

opposed to urinary matrix stones. Urinary matrix stones are also predominantly protein, but are associated with recurrent urinary tract infections from *Proteus mirabilis* or *Escherichia coli*.[5]

This case illustrates the need for diagnostic ureteroscopy with direct visualization and consideration of biopsy in all patients with suspicious upper urinary tract imaging findings in the absence of positive cytology, hematuria, and significant risk factors for urothelial cell carcinoma before proceeding with radical nephroureterectomy. Proteinaceous stones in patients with proteinuria on HD are exceedingly rare and poorly described in the literature. Further research efforts and perhaps institutional collaboration are needed to better understand this rare disease process and may raise awareness of their incidence in patients on HD among urology and nephrology providers.

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