Fungal Pyelonephritis and Fungemia Due to Obstructive Uropathy

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ABSTRACT

Introduction: Funguria is often a benign and common occurrence in the hospital. However, invasive fungal pyelonephritis due to obstructive uropathy is uncommon and can be difficult to treat. Typically, there are 2 mechanisms by which *Candida albicans* infects the upper urinary tract: by ascending from the lower urinary tract or via hematogenous spread to the kidneys.

Case Presentation: We present a case of fungal pyelonephritis, likely due to obstructive uropathy, leading to fungemia in a 70-year-old man who had a recent history of colovesicular fistula and indwelling foley catheter.

Discussion: The patient had many identified risk factors contributing to the development of fungal pyelonephritis, including diabetes mellitus and structural urinary tract aberrancies, which were further complicated by his recent colovesicular fistula and repair.

Conclusion: Although fungal pyelonephritis with fungemia is relatively rare, it should not be excluded from differential diagnostics. Despite a unique host of risk factors, a direct approach led to successful treatment.

INTRODUCTION

Fungal pyelonephritis is an invasive fungal infection of the kidney pelvis, which is uncommon and notoriously difficult to treat. Although *Candida* found in measurable quantities in the urine (candiduria) occurs in less than 1% of healthy individuals, it common in hospitalized patients.[1,2] One study found *Candida* as the third most common organism found in the urine of hospitalized individuals.[3] Additionally, candidemia or disseminated *Candida* infection remains associated with crude mortality rates between 40% and 81%, increased costs of care, and longer hospitalization durations.[4-6]

The vast majority of fungal infections of the urinary tract are caused by *Candida albicans*, either ascending from the lower urinary tract or via hematogenous spread to the kidneys. Risk factors for urinary tract fungal infections include prior antibiotic therapy, bladder catheterizations, and diabetes.[1,7] Additionally, ascending infection causing fungal pyelonephritis is presumed to develop in the setting of urinary tract abnormalities—notably urinary tract obstruction or following a urinary tract procedure.[8,9] Based on our literature search, primary fungal pyelonephritis is relatively uncommon, with a handful of cases.[10] Of these cases, approximately 37 reported primary fungal pyelonephritis presumedly and specifically resulting from obstructive uropathy.[11] One report illustrates the variability of this pathology and clinical course as it describes 3 separate cases: an elderly man with *Candida* pyelonephritis complicated by fungemia, a 64-year-old woman with type 2 diabetes mellitus who developed emphysematous pyelonephritis and cystitis due to *Candida albicans*, and an immunocompetent 2-year-old boy with primary renal aspergillosis and xanthogranulomatous pyelonephritis.[12] In this case, we present a 70-year-old White man with fungal pyelonephritis due to obstructive uropathy and precipitated by a recent history of colovesicular fistula, indwelling catheter, and diabetes leading to fungemia.

CASE PRESENTATION

A 70-year-old White man came into the emergency department with complaints of sharp, stabbing left lower quadrant abdomi-

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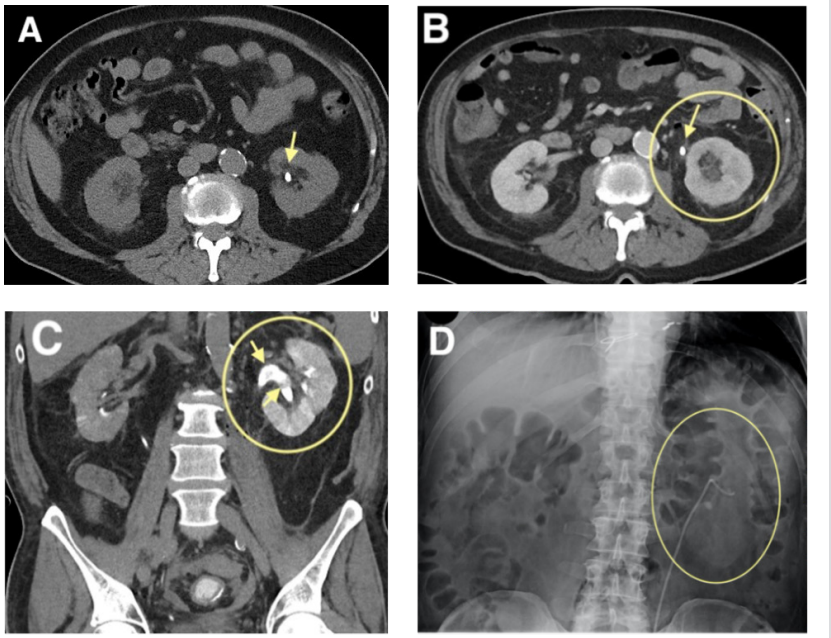
Published online June 23, 2022.

nal pain, nausea, and maximum fever of 100.8 ˚F (38.2 ˚C) earlier in the day. Eight days prior he had a laparoscopic sigmoid colectomy for colovesicular fistula. He had undergone laparoscopic sigmoid colectomy under general anesthesia with epidural catheter and foley catheter. He was discharged after a 5-day stay. Over the 2 days following discharge, he developed a decreased appetite, nausea, and abdominal pain.

His past medical history included hypertension, diabetes mellitus type 2, and nephrolithiasis. Previous surgeries included a herniorrhaphy, coronary artery bypass grafting, lithotripsy, tonsillectomy and adenoidectomy, sigmoidoscopy, and colonoscopy with biopsy, in addition to the most recent laparoscopic sigmoid colectomy for diverticular colovesical fistula.

Physical exam revealed an acutely ill male with temperature 99.1 ˚F (37.3 ˚C), pulse 123, blood pressure (BP) 119/73, and respiratory rate of 20. His physical exam revealed left flank pain and ecchymosis of the posterior aspect of the left lateral abdomen. His abdomen was soft with mild tenderness in the left lower quadrant without guarding. His surgical sites were well-appearing, clean, dry, and intact. There was mild tenderness of the bladder, but no bladder distension was appreciated. His urine was cloudy.

Figure. Imaging Showing Progression of Obstructive Uropathy to Fungal Pyelonephritis and Treatment With Ureteral Stent



A. Axial plane abdominal computed tomography (CT) without contrast obtained before colovesicular fistula repair (20 days prior to presentation with pyelonephritis) demonstrating a calculus (yellow arrow) within an infundibulum or lower pelvis on the left kidney.

B. Axial plane abdominal CT with contrast obtained upon admission for pyelonephritis demonstrating obstructive calculus at the left ureteropelvic junction (yellow arrow) and mild to moderate left hydronephrosis, as well as enhancement of the renal pelvic wall suggesting inflammation/infection (yellow circle).

C. Sagittal sequence abdominal CT without intravenous (IV) contrast obtained 2 hours later demonstrating delayed nephrogram on the left secondary to the obstructing calculus at the ureteropelvic junction and mild hydronephrosis. Two discrete foci of debris within the anterior pelvis in the lower pole and in the proximal ureteropelvic junction region were initially thought to be due to clot but could likely have been due to fungal growth.

D. Abdominal x-ray demonstrating left ureteral stent placement and previously obstructing left ureteropelvic junction calculus overlying the central left kidney (yellow oval).

The white blood cell count on admission was 16,400/mm³ (16.4 x 109/L) with an instrument absolute neutrophil count of 13,200/mm³ (13,200/µL) and monocyte number of 1,400/ mm³ (1,400/µL), hemoglobin 12.3 g/dL (7.62 mmol/L), hematocrit 35.2% (0.352), platelets 318,000/mm³ (318.0 x 109/L), and lactate 11.7 g/dL (1.3 mmol/L). Automated chemistry was significant for serum bicarbonate of 17 mEq/L (17 mmol/L), creatinine of 1.7 mg/dL (150.3 µmol/L), and estimated glomerular filtration rate (eGFR) of 40 mL/min (decreased from 111 mL/min 3 days prior). Urinalysis on the following day revealed 20-50 white blood cell count (WBC), 20-50 red blood cell (RBC) count, 30 mg/dL (0.3 g/L) protein, a large amount of blood, small quantity of ketones, moderate bilirubin, moderate esterase, and negative nitrites. Blood culture on admission was negative; however, urine cultures were positive for *Candida albicans* growing <10,000 colony-forming units (CFU)/mL the following day.

Pelvic computed tomography (CT) with rectal contrast did not reveal any evidence of an anastomotic leak. A contrast-enhanced CT of the abdomen and pelvis (Figure B and C) displayed a 7 mm x 10 mm diameter obstructing calculus at the left ureteropelvic junction, a nonobstructing 5 mm diameter calculus in the mid-left kidney, and mild to moderate left hydronephrosis. Enhancement of the renal pelvic wall was nonspecific but suggested inflammation or infection. These findings had changed from a contrast-enhanced CT of the abdomen and pelvis obtained 20 days prior. The initial CT showed a 9 mm diameter calculus within an infundibulum or lower pelvis on the left kidney, but there were no signs of inflammation or infection noted at that time (Figure A).

The patient was taken to the operating room by urology for placement of a left nephroureteral stent. Upon placement of the stent and dislodgement of the stone, a significant purulent hydronephrotic drip was noted. The patient originally was started on piperacillin-tazobactam in the emergency department but

Published online June 23, 2022.

switched to levofloxacin based on the findings during the procedure. Levofloxacin was the chosen agent because it covered every organism that had grown in his urine over the prior 3 weeks, following this discovery. The following day, blood cultures came back positive for *Candida albicans*, at which time intravenous micafungin 100 mg daily was initiated and the levofloxacin was discontinued. Ophthalmology was consulted for an ophthalmology exam, and cardiology was consulted for an echocardiogram to rule out chorioretinitis with/without vitritis and infective endocarditis, which were both negative. The patient responded well to the antifungal, as blood cultures the following day were negative for *Candida*. After consulting with infectious disease, he was discharged 2 days later on oral fluconazole for a total of 14 days of antifungal treatment.

The patient was seen for a follow-up 15 days later and had recovered well. In a second follow-up 2 weeks later, he returned for extracorporeal shockwave lithotripsy and removal of the nephroureteral stent without complications. Ultrasound and x-ray (Figure D) imaging 5 months later identified no focal renal abnormalities.

DISCUSSION

Fungal pyelonephritis can be caused by either ascending or hematogenous infection.[1,7] Hematogenous infection usually presents bilaterally, while ascending infection presents unilaterally and tends to involve the renal pelvis and medulla, as seen in our patient.[7] Therefore, it is reasonable to conclude that our patient's candidemia resulted from an ascending urinary tract source.

Multiple factors contribute to the pathogenesis of candiduria as a source of candidemia, which may explain its rarity, complexity, difficult management, and high mortality. Our patient had diabetes mellitus, obstructive uropathy, an indwelling catheter, prior antibiotic use, and a recent history of colovesicular fistula[7-9] Previous reports on fungal pyelonephritis have identified diabetes mellitus, urinary tract abnormalities, and catheterization as major risk factors for this disease.[4,13,14] However, this case may have had an additional layer of complexity due to his colovesicular fistula, its repair, and the interplay with his preexisting renal calculus.

This patient's bladder was colonized due to his various risk factors. His renal calculus then obstructed the ureter, inhibiting the kidney's ability to flush out the pathogen and likely causing subsequent pyelonephritis.[9] This, along with his indwelling catheter, allowed the fungus to form a biofilm, ascend to the kidney, and further disseminate into the circulatory system.[15] Removal of the obstruction, stenting of the ureter to maintain patency, close monitoring of the fistula repair, and targeted antifungal treatment were vital to the resolution of the infection and recovery.

Here we describe a case of fungal pyelonephritis due to obstructive uropathy with a rare interplay of a colovesicular fistula and repair as a possible etiological contributor. Despite the commonality of *Candida albicans* colonization in hospitalized patients, the complications from disseminated *Candida* infection remains an issue for hospital-related mortality rates, care costs, and hospitalization duration. This particular patient had numerous risk factors for developing ascending fungal pyelonephritis, which further increased his risk of life-threatening complications and required careful consideration when assembling our treatment plan. Due to the the patient's diligent compliance and direct response from the health care team, he was successfully treated.

CONCLUSION

Although fungal pyelonephritis and fungemia are relatively rare, they should be included in the differential diagnostic measures—esspecially in those who have risk factors such as diabetes, in-dwelling urinary catheters, or structurally compromised urinary system anatomy. Interestingly, the precise pathophysiological role of the patient's recent colovesicular fistula and repair remains unknown. By presenting this case, we aim to remind clinicians of possible risk factors for fungal pyelonephritis, detail the events leading up to the patient's diagnosis of fungal pyelonephritis and steps taken toward treatment, and contribute insight for future health care professionls when educating patients on possible outcomes of this pathology. Ultimately, we hope to inform future clinical decision-making and potential expectations for disease course.

Funding/Support: None declared.

Financial Disclosures: None declared.

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Published online June 23, 2022.