

Aspergillus Terreus-related Ureteral Obstruction in a Diabetic Patient

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INTRODUCTION

Urinary tract aspergillosis is uncommon and predominantly occurs following kidney transplantation and other situations, such as acquired immunodeficiency syndrome, uncontrolled diabetes mellitus, chronic steroid therapy, and intravenous drug use.¹ Aspergillosis of the urinary tract may occur in 3 patterns: hematogenous disseminated aspergillosis with renal parenchymal involvement, *Aspergillus* casts of the renal pelvis leading to formation of fungal ball, and ascending infection from the lower tract.² A fungus ball causing

An *Aspergillus* fungal ball is a rare cause of ureteral obstruction attributed to indwelling catheters, stents, antibiotics, anastomotic leaks, obstruction, and immunosuppressive therapy and other immunocompromised states. We describe a case of unilateral ureteral obstruction caused by *Aspergillus terreus* following ureteroscopic lithotripsy and ureteral stenting in a 45-year-old diabetic man. The patient was successfully treated with endoscopic removal of the fungal mass and oral voriconazole. We also review briefly the clinical features, treatment, and outcome in 9 previously reported diabetic patients with ureteral obstruction due to aspergillosis. Obstructive uropathy related to *Aspergillus* mass may be suspected in diabetic patients with a history of manipulation, impaired kidney function, and persistent passage of a soft mass in urine. Direct microscopy and culture of multiple urine and ureteral washing are necessary for early diagnosis. Antifungal therapy and endoscopic removal of the mass are needed to reduce morbidity.

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ureteral obstruction is very rare and only about 50 cases have been reported.³ Almost 15 cases of ureteral obstruction by *Aspergillus* bezoars have been diagnosed.⁴ Herein, we describe a case of unilateral ureteral obstruction caused by *Aspergillus terreus* in a diabetic patient. We also review 9 reported diabetic cases of urinary tract aspergillosis.⁵⁻¹²

CASE REPORT

A 45-year-old man with well-controlled diabetes mellitus presented with mild pain in the left lumbar region, occasional dysuria, passing whitish

soft mass, and lower abdominal pain aggravation prior to passing of such a mass per urethra. Three months prior to hospital admission, he had undergone ureteroscopic lithotripsy for removal of a calculus and placement of a ureteral stent (double J catheter) for three weeks. Due to pyuria and symptoms related to ureteral obstruction, the catheter was removed earlier and antibiotic administration was continued.

Computed tomography scan of the abdomen and pelvis showed dilatation of the left pyelocalyceal system and ureter in the pelvic inlet (Figure 1). Intravenous pyelography showed no excretion of the contrast media from the left calyces or the renal pelvis into the ureter (Figure 2). The ultrasonographic features revealed multiple floating echogenic debris within the pyelocalyceal system of the left kidney. Uretroscopy and retrograde pyelography were performed and ureteral irrigation and insertion of ureteral stent (double J catheter) were done. Initial laboratory evaluation showed an increased serum level of creatinine and blood urea nitrogen. Kidney failure occurred due to ureteral obstruction. In a second ureteroscopic examination, multiple debris was observed in the ureteral orifice of the calyces (Figure 3). The stent was removed and the drainage fluid and the removed double J catheter were sent to laboratory. Direct microscopy examination of the whitish soft mass revealed hyaline septate hyphae with branching at acute angles (Figure 4). A growth of mold was yielded after 24 hours incubation at 27°C, and the isolate was identified presumptively as *Aspergillus terreus*.

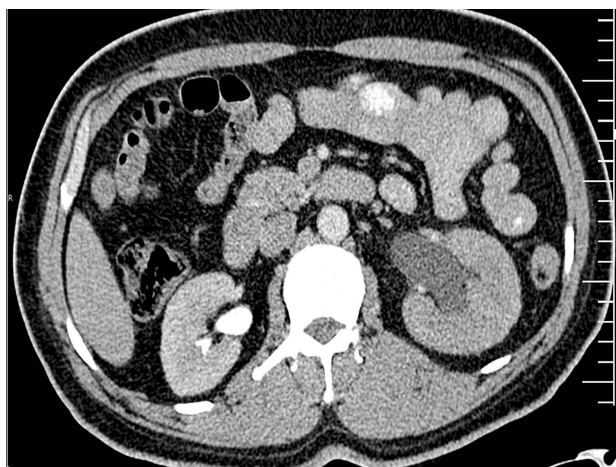


Figure 1. Computed tomography of the abdomen and pelvic showing dilatation of the left pyelocalyceal system and ureter. Dilatation of the left ureter is in the pelvic inlet.



Figure 2. **Top,** Intravenous urography (5 minutes) shows no excretion to the pyelocalyceal system from the left kidney. Drainage of the right kidney is normal. **Bottom,** Intravenous urography (3 hours) shows no excretion to the pyelocalyceal system from the left kidney. Drainage of the right kidney is normal.

(Figure 4). The diagnosis was confirmed later by polymerase chain reaction assay, DNA sequencing, and comparing with reference data obtained from GenBank database using the BLAST.

Antifungal susceptibility Etest (AB Biodisk, Solna, Sweden) of isolated *Aspergillus* showed low minimum inhibitory concentrations of voriconazole (0.023 $\mu\text{g}/\text{mL}$), posaconazole (0.032 $\mu\text{g}/\text{mL}$), itraconazole (0.032 $\mu\text{g}/\text{mL}$), and caspofungin (0.5 $\mu\text{g}/\text{mL}$). The patient was treated initially with oral itraconazole, 400 mg/d, for 1 week, and then the dosage was diminished to 200 mg/d due to

intolerance. The oral itraconazole was replaced with oral voriconazole, 400 mg/d, after 25 days because of continuing kidney impairment. The treatment with voriconazole continued for 3 months. After 6 months of antifungal therapy and endoscopic treatment, kidney function and perfusion completely recovered. Several ultrasonographic studies and computed tomography scans of the abdomen and pelvis showed no caliectasis (Figure 5) or ureteral

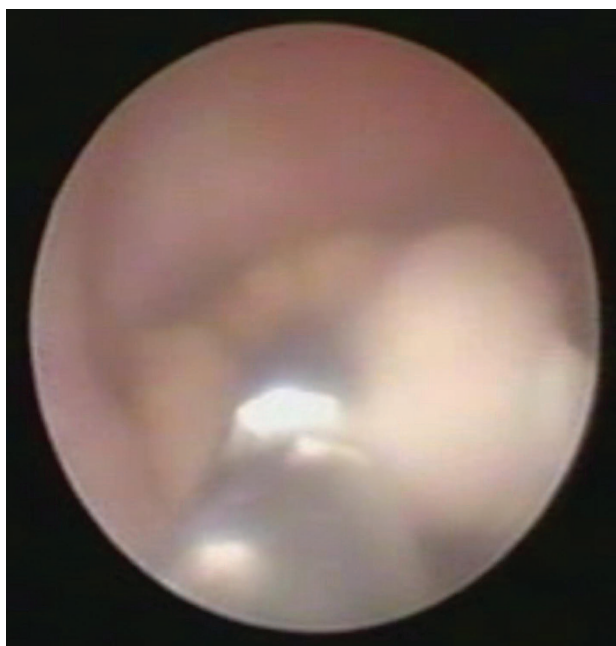


Figure 3. Intra-ureteral fungus ball on ureteroscopic examination.

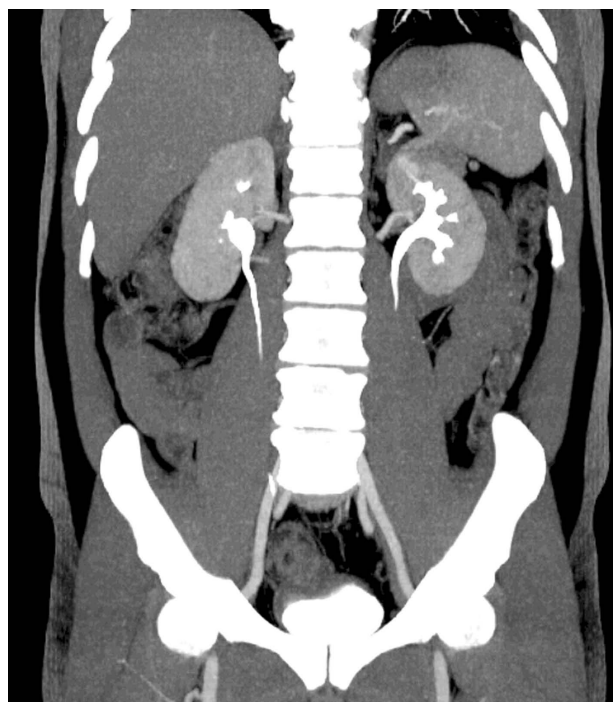


Figure 5. Computed tomography of the abdomen and pelvic after 6 months of starting and 2 month after cessation of oral voriconazole showing excretion to the pyelocalyceal system from the left kidney and complete relief of the hydronephrosis.

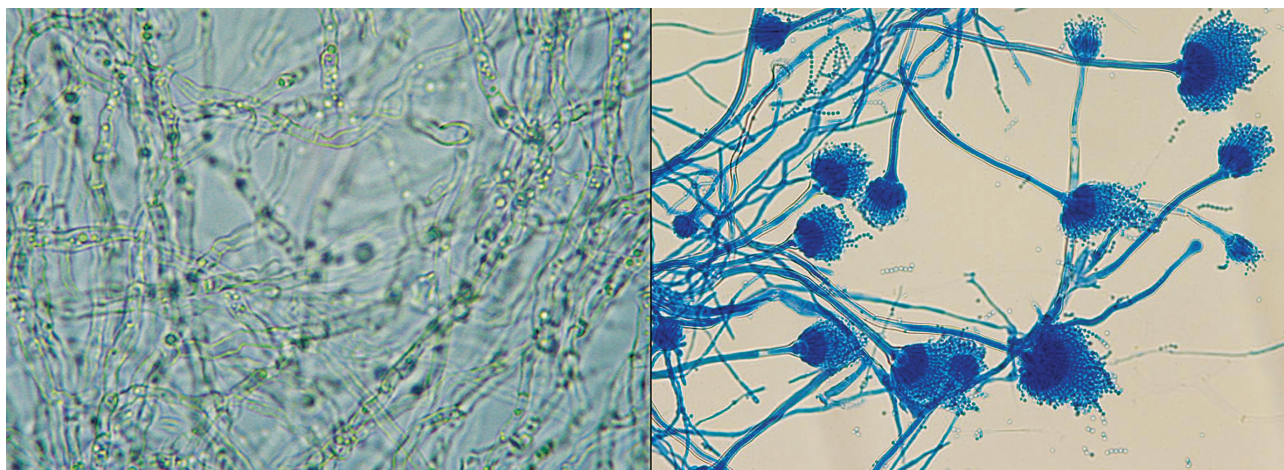


Figure 4. **left,** A direct examination of the removed fungus ball showing septate hyphae and branching at acute angles, suggestive of *Aspergillus* (KOH Preparation, $\times 100$). **Right,** Biserial conidial head and conidiophore of *Aspergillus terreus* (Lactohenol aniline blue preparation).

dilatation. Hydronephrosis passing whitish mass in urine ceased and several urine analyses and the cultures were negative for fungi.

DISCUSSION

Uncontrolled diabetes mellitus leads to defective phagocytic function, glycosuria, and renal injury, all promoting antegrade colonization of the renal pelvis. In our patient, diabetes was well controlled, but few other predisposing factors included prior antibiotic therapy, urinary calculi, ureteroscopic lithotripsy, and stent placement, all of which probably promote fungal colonization.

Our patient had no history of urinary tract infection or passage of mass per urethra prior to instrumentation and placement of the double J catheter. Ascending infection is possible and occurs mainly in patients with nephrostomy tubes, other permanent indwelling devices, and stents.¹³ A case of unilateral renal aspergillosis following intracorporeal pneumatic lithotripsy was described in a type 2 diabetic man.¹⁴ The authors suggested that *Aspergillus* was introduced into the urinary tract during the instrumentation and probably occurred as a result of inadequate sterilization of the equipment.¹⁴ Many such patients have more than one risk factor. Pre-existing urinary stasis is suggested as a critical factor in such cases.¹⁵

Active antifungal agents against *Aspergillus* species are amphotericin B, itraconazole, voriconazole, caspofungin, and posaconazole. Systemic antifungal therapy with amphotericin B is not recommended due to the limited concentration in the renal parenchyma and nephrotoxicity,^{13,16} even though local irrigation with amphotericin B has also been used for the urinary bladder and renal pelvic infections.¹ Oral voriconazole in combination with endoscopic removal mass measures to relieve urinary stasis were quite effective. Some have suggested that a large fungus ball can be managed effectively by endourological methods.^{9,11,17}

The clinical features, treatment, and outcome in 9 previously reported diabetic patients with ureteral obstruction due to renoureteric aspergillosis are summarized in the Table. Fifty-five percent of the patients were male and 64% had unilateral involvement. In addition, 46% of the patients had at least one predisposing factor in addition to diabetes mellitus. In the present case, the initial nonenhanced computed tomography findings did

Clinical Features, Treatment, and Outcome in Reported Cases of Diabetic Patients With Ureteric Obstruction Resulted From Urinary System Aspergillosis*

Study	Year	Age, y	Sex	Predisposing Factor	<i>Aspergillus</i> Species	Localization	Acute Kidney Failure	Medical Treatment	Surgical Treatment	Outcome
Comings et al ⁵	1962	27	Female	Diabetes, Addison disease	<i>A fumigatus</i>	Unilateral	Yes	None	Nephrectomy	Recovery
Salgia and Mani ⁶	1985	48	Male	Diabetes	<i>A glaucus</i>	Unilateral	No	Amphotericin B	None	Recovery
Baird and Lancaster ⁷	1987	34	Male	Diabetes	<i>A flavus</i>	Unilateral	Unknown	Amphotericin B, flucytosine	Ureteral stent insertion	Recovery
Irby et al ⁸	1988	39	Male	Diabetes, intravenous drug use	Not reported	Unilateral	Unknown	Amphotericin B	Nephrectomy	Recovery
Halpern et al ⁹	1990	35	Male	Diabetes	Not reported	Bilateral	Yes	Amphotericin B	Endoscopic removal	Recovery
Kueter et al ¹⁰	2002	40	Male	Diabetes, intravenous drug use	<i>A flavus</i>	Bilateral	Yes	Amphotericin B	Ureteral stent insertion	Recovery
Smaidone et al ¹¹	2006	50	Female	Diabetes	<i>A flavus</i>	Bilateral	Yes	Voriconazole	Percutaneous nephrostomy, endoscopic removal	Recovery
Yoon et al ⁴	2010	60	Female	Diabetes, intravenous drug use, steroid therapy	<i>A nidulans</i> group	Unilateral	Yes	Amphotericin B, voriconazole	Percutaneous nephrostomy	Recovery
Ahuja et al ¹²	2009	45	Female	Diabetes	Not reported	Unilateral	Yes	Amphotericin B, itraconazole	Percutaneous nephrostomy	Recovery
present case	2011	45	Male	Diabetes	<i>A terreus</i>	Unilateral	Yes	Itraconazole, voriconazole	Endoscopic removal	Recovery

*A part of this table was adapted from the reference 4.

not raise suspicion of fungus ball. Therefore, the patient was initially misdiagnosed as having of remnant ureteral calculi and bacterial infection. This finding has been also described earlier.^{10,18}

In conclusion, obstructive uropathy related to *Aspergillus* mass may be suspected in diabetic patients with a history of manipulation, impaired kidney function, and persistent passage of a soft mass in urine. Direct microscopy and culture of multiple urine and ureteral washing are necessary for early diagnosis. Antifungal therapy, endoscopic removal of the mass, and controlling of diabetes mellitus are needed to reduce morbidity in renoureteral aspergillosis.

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CONFLICT OF INTEREST

None declared.

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