



## Localized genitourinary tract *Aspergillus* infection in an immunocompetent patient: Bladder and epididymal aspergillosis

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### ABSTRACT

Invasive bladder *Aspergillus* has only been reported in six publications so far.

A 74-year-old male, presented to the emergency department with fever, abdominal pain, and right testicular enlargement. Abdominal computed tomography concluded a bladder tumor and testicular ultrasound reported right epididymitis. Cystoscopy showed a bladder fungal mass, which was extracted with cystostomy. Pathological findings reported *Aspergillus* species. The patient was successfully treated with 4-week oral Isovucanazole.

The first bladder *Aspergillus* was published in 1978. The most recent case was published in 2020. *Aspergillus* infection is extremely rare disease, treatment with Isovucanazole is efficient.

### 1. Introduction

Invasive *Aspergillus* infection of the kidney and the upper urinary tract is extremely rare, and almost exclusively diagnosed in immunocompromised patients, such as organ transplant, hematologic malignancies, and immunosuppressive therapies, infection of lower urinary tract is even less common, as bladder aspergillosis has only been reported in 6 publications so far, all of them in male patients.<sup>1,2</sup> We present a case of invasive localized bladder and epididymal *Aspergillus* infection in an immunocompetent patient.

### 2. Clinical case

A 74-year-old male with no relevant medical background (diabetes or hypertension) underwent an uneventful transurethral resection of prostate (TURP) due to benign prostatic hyperplasia in another hospital four months before. Upon hospital discharge he referred intermittent hematuria, mixed incontinence, urinary urgency, incomplete bladder emptying, frequency (between 15 and 20 times per day), nocturia and intermittent low-grade fever (ranging between 37.2 and 38.0 °C), as well as right testicular pain and enlargement.

He was admitted to the Emergency Department because of low-grade fever (37.8 °C), and abdominal pain. On examination, the bladder was palpable and fixed upon suprapubic palpation, with severe pain upon

suprapubic superficial palpation, the right testis was enlarged, painful and indurated.

Blood analysis showed leukocytosis (11,000/mm<sup>3</sup>) with neutrophilia (80%), and elevated serum creatinine (1.4 mg/dL) with an estimated glomerular filtration rate (eGFR) of 53 mL/min/1.73 m<sup>2</sup> (CKD-EPI equation). The urinalysis reported abundant leucocytes, erythrocytes, and bacteria.

Renal ultrasound showed bilateral pyelocaliceal dilation. Bladder imaging was not satisfactory because of severe pain upon transducer placement. Abdominal computed tomography with no contrast (due to eGFR) showed bilateral pelvic and ureteric dilation, and a dysmorphic bladder with a tumor with possible extravesical extension into the bladder dome (Fig. 1). Testicular ultrasound reported right epididymitis.

The patient was hospitalized and started on intravenous antibiotic treatment with Ertapenem. Diagnostic work-up included a cystoscopy in which abundant mucous, detritus, and an intravesical whitish mass, was observed. Resection with bipolar resectoscope was not possible, and due to the intravesical mass characteristics a mini-suprapubic cystostomy was performed, extracting a whitish, gelatinous mass, macroscopically compatible with a fungal mass (Fig. 2).

Histopathological examination identified the bladder mucosa infiltrated by abundant hyaline filamentous fungi of the Ascomycota phylum, with septate hyaline hyphae compatible with *Aspergillus* species (Fig. 3). Urine cultures taken during cystoscopy reported mixed *Candida*

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Fig. 1. Abdominal computed tomography showing a bladder mass involving the bladder dome, with heterogeneous content. A. Coronal section B. Axial section.



Fig. 2. Fungal ball appearance. A. Cystoscopy showing a whitish mass, occupying almost all bladder capacity. B. Macroscopic appearance of fungal ball after extraction from bladder.

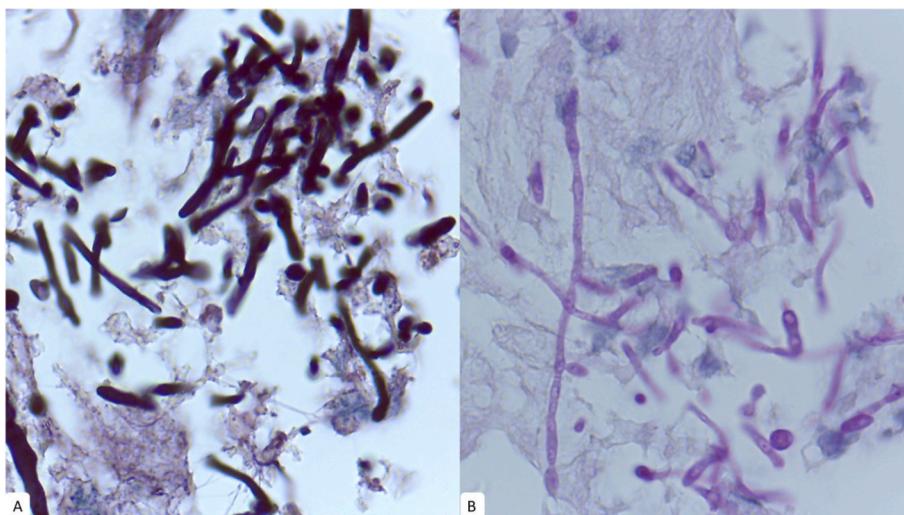


Fig. 3. High power images showing the presence of a hyaline, saprophytic, filamentous fungi of the Ascomycota phylum, characterized by multiple hyaline septate hyphae, compatible with *Aspergillus* species. A. Grocott methenamine silver stain B. Periodic acid-Schiff (PAS) stain.

species and bacterial development. Additionally, serum galactomannan antigen test, HIV, Diabetes Mellitus, and hematologic pathologies work-up resulted negative.

Antibiotic treatment was suspended and Isavuconazole was started. The patient was discharged on postoperative day 6 with transurethral silicone 18 Fr foley catheter and instructed to complete 4-weeks of oral Isavuconazole. During follow-up a cystoscopic evaluation was performed immediately after the last day of Isavuconazole, identifying normal mucosal macroscopic appearance. Histopathological analysis of random bladder biopsies showed absence of *Aspergillus* species. Right epididymitis also resolved. Lower urinary tract symptoms and fever disappeared. Kidney function improved with a serum creatinine of 0.7 mg/dL (eGFR of 97mL/min/1.73 m<sup>2</sup>).

### 3. Discussion

*Aspergillus* species is an ubiquitous environmental fungus of the *Ascomycota* Phylum found in plants, soils, decaying organisms, and in environmental aerosols. They produce asexual conidia that are highly resistant and can spread through surfaces and air. It is via these conidia that *Aspergillus* can enter the lower respiratory tract, where most of *Aspergillus* infections may occur. The most common invasive *Aspergillus* species are *Aspergillus fumigatus* (90%), *A. flavus* and *A. niger* species.<sup>3</sup>

The first case of urinary bladder aspergillosis was described in 1978 in a male patient with Diabetes Mellitus and a previous abdominal surgical intervention, which was successfully treated with transurethral evacuation of bladder clots and fungal masses, and postoperative intravesical Amphotericin B and oral Nystatin for 25 days.<sup>4</sup> The most recent case was described by Hameed and colleagues in 2020, in a male patient unaware of Diabetes Mellitus diagnosis who was admitted with urinary retention due to an intravesical bladder fungal mass which was treated with transurethral evacuation. No evidence of upper urinary tract involvement.<sup>2</sup>

In our case treatment with Isavuconazole was discussed among the attending specialists and was decided based on several assumptions. First, the patient's immune status was unknown and was assumed to be immunocompromised. Second, the patient had at least two possible sites

of *Aspergillus* infection (bladder and right testes), and a disseminated disease was a possibility. Third, preliminary pathology findings were inconclusive of a specific fungus, therefore, the possibility of Mucorales infection existed. Previous reports of Isavuconazole treatment have been described in both Mucorales and *Aspergillus* infections, especially in the case of immunocompromised patients.<sup>5</sup>

### 4. Conclusion

Lower genitourinary tract aspergillosis is an extremely rare disease, especially in immunocompetent patients. Certain possible risk factors should be considered, such as male gender, immunocompromised status, and history of previous intravesical catheter or transurethral surgery. Persistent lower urinary tract symptoms without improvement despite antibiotic and medical treatment in the presence of an unknown atypical bladder mass should raise suspicion of fungal infections. When possible, transurethral resection or evacuation of fungal mass should be performed and systemic antifungal treatment, with Isavuconazole or other antifungal drugs should be individualized.

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