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

Alan de Jesús Martínez-Salas a,*, Jorge Eduardo Aquino-Matus b, Cesar Emmanuel López-Vejar b, María Esther Gutiérrez Díaz Ceballos b, Alejandro Noyola-Guadarrama b

a Hospital Santa Coleta, Mexico City, Mexico
b Hospital Angeles Pedregal, Mexico City, Mexico

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**ABSTRACT**

Invasive bladder Aspergillus infection 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 cystotomy. Pathological findings reported Aspergillus species. The patient was successfully treated with 4-week oral Isavuconazole. The first bladder Aspergillus was published in 1978. The most recent case was published in 2020. Aspergillosis infection is extremely rare disease, treatment with Isavuconazole 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. 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 low-grade fever (ranging between 37.2 and 38.0 °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/mm³) with neutrophilia (80%), and elevated serum creatinine (1.4 mg/dL) with an estimated glomerular filtration rate (eGFR) of 53 mL/min/1.73 m² (CKD-EPI equation). The urinalysis reported abundant leucocytes, erythrocytes, and bacteria.

Renal ultrasound showed bilateral pyelocaliceal dilatation. Bladder imaging was not satisfactory because of severe pain upon transducer placement. Abdominal computed tomography with contrast (due to eGFR) showed bilateral pelvis and ureteric dilatation, and a dysmorphic bladder with a tumor with possible extravasal 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.
**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 m²).

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.3

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.4 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.2

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.5

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.

References

1. González-Vincent M, Lassaletta A, López-Fino MA, Romero-Tejada JC, de la Fuente-Trabado M, Díaz MA. Aspergillus “fungus ball” of bladder after hematopoietic transplantation in a pediatric patient: successful treatment with intravesical voriconazole and surgery. Pediatr Transplant. 2008 Mar;12(2):242–245. https://doi.org/10.1111/j.1399-3046.2007.00871.x.
2. Hameed T, Jain SK, Ansari FM, Dua A. Isolated fungal balls in urinary bladder presenting as acute retention of urine, 2020 Jan 4. Case Rep Urol. 2020:4601474. https://doi.org/10.1155/2020/4601474.
3. Latgé JP, Chamilos G. Aspergillus fumigatus and aspergillosis in 2019. Clin Microbiol Rev. 2019 Nov 13;33(1):e00140–18. https://doi.org/10.1128/CMR.00140-18. PMID: 31722890; PMCID: PMC6860006.
4. Sakamoto S, Ogata J, Sakazaki Y, Ikegami K. Fungus ball formation of Aspergillus in the bladder. an unusual case report. Eur Urol. 1978;4(5):388–389. https://doi.org/10.1159/0000474000.
5. Wu X, Venkataramanan R, Rivosecchi RM, et al. Population pharmacokinetics of intravenous Isavuconazole in solid-organ transplant recipients. Antimicrob Agents Chemother. 2020 Jan 27;64(2):e01728-19. https://doi.org/10.1128/AAC.01728-19. PMID: 31767725.