Mucormycosis in the Urinary Bladder—the Devil Is in the Details

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Abstract
Mucormycosis is a fungal infection involving rhinocerebral, pulmonary, cutaneous, gastrointestinal and disseminated forms with high morbidity and mortality with rare involvement of the urinary bladder. Diagnosis is made by examining under a microscope, identifying broad, nonseptate, irregular and ribbon-shaped hyphae. Timely diagnosis and starting antifungal drugs are key to successful treatment.

Keywords Urinary bladder · Mucormycosis · Aspergillosis

Introduction
Mucormycosis in the urinary bladder is extremely rare with only one case reported in the literature [1].

Mucormycosis of the urinary bladder is usually associated with renal mucormycosis. Risk factors for mucormycosis are diabetes mellitus, chronic kidney disease, malignancies, immunosuppressive therapy and recently COVID-19 infection [2].

It is caused by fungi of the order Mucorales which includes several species. It causes infection in immunocompromised patients [3].

We present a case of a 55-year-old diabetic patient with fever, difficulty in urination and deranged creatinine and ultimately diagnosed with urinary bladder mucormycosis.

Case Summary
A 55-year-old gentleman presented with low-grade fever, dysuria, flank pain and obstructive urinary symptoms. He was a known diabetic on oral hypoglycaemic drugs. He has no history of dyspnoea, chest pain, facial pain, recent COVID-19 infection or intake of any immunosuppressive therapy. On clinical examination, abdomen was normal, and the renal angle was nontender. Blood investigation results were as follows: haemoglobin 12.5 g/dl, TLC 11,500/mm3, urea 35 mg/dl, creatinine 2.5 mg/dl, and electrolytes were normal. Ultrasound and noncontrast CT scan abdomen were suggestive of right mild hydronephrosis with a thickened urinary bladder filled with internal echoes (Fig. 1a, b). Cystoscopy was planned because of hydronephrosis and echoogenic contents in the urinary bladder which revealed creamy yellow necrotic material in the urinary bladder (Fig. 2). Evacuation of necrotic material was done and sent for histopathology. Ureteric orifices were normal, and no mass was seen in the urinary bladder. The histopathologic examination of the necrotic material was suggestive of mucormycosis and occasional aspergillosis hyphae (Fig. 3). He was started on posaconazole and improved.

Discussion
Mucormycosis is an infection due to fungi (order Mucorales) of species Rhizopus, Mucor, Cunninghamella, Apophysomyces, Lichtheimia and Rhizomucor [4].

These are angioinvasive fungi, which invade kidneys haematogenously as part of a multi-organ disease, although isolated renal involvement is also reported [1, 3].

Mucor is a ubiquitous fungus that reaches the human body through spores entrapped in nasal turbinates or through ingestion, inhalation and interrupted skin. This infection is seen commonly in diabetics, immunocompromised patients
Fig. 1 (a) Noncontrast CT scan showing right mild hydronephrosis (red arrow), (b) urinary bladder mildly distended (orange arrow)

Fig. 2 (a) Cystoscopy showed yellowish-white material (red arrow) in urinary bladder, (b) cystoscopy showed normal ureteric orifice (yellow arrow) and necrotic mass

Fig. 3 (a) Photograph showing broad hyphae of Mucor, thin hyphae of Aspergillus and broad hyphae of Mucor (H & E 100×), (b) hyphae of Mucor revealing obtuse angle branching (GMS 400×), (c) broad hyphae of Mucor (blue), thin hyphae of Aspergillus (black) (PAS stain 400×)
such as allograft recipients, HIV patients, patients with malignancy and intravenous (IV) drug abusers [1, 5].

The virulence factor involved in the pathogenesis of Mucorales are high-affinity iron permease (FTR1), spore coat protein (Cot H) and ADP-ribosylation factor which allows fungi to tolerate a low iron environment, impairing host defences and growth of Mucorales [6].

Neutrophils are the mainstay to mount a response against *Mucor*, hence patients with neutropenia or dysfunction in neutrophils (steroid use, diabetes mellitus) result in fulminant fungal infection [7].

On basis of location, mucormycosis can be divided into rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and uncommon presentations [8].

Having an index suspicion and timely diagnosis is required for successful treatment of mucormycosis.

In genitourinary organs, mucormycosis is reported in kidneys, although involvement of other organs is reported occasionally. It can present with flank pain, fever, acute kidney injury and lump. Diagnosis is by clinical suspicion, radiology, smear examination, culture, cytopathology and direct examination under a microscope. When culture is not available or cannot be done, histopathology is the mainstay of diagnosis [9].

Examination with stains haematoxylin and eosin (H&E) or Grocott methenamine-silver (GMS) or periodic acid-Schiff (PAS) stains show typical broad, nonseptate, irregular, ribbon-shaped (typically 6- to 25-µm diameter) and irregular branching at 45–90°. Histopathology from tissue shows necrosis and angioinvasion with neutrophils as the predominant inflammatory response. A granulomatous response may be seen in delayed stages [10].

Treatment can be medical as well as surgical as per the condition of the patient. Amphotericin B (liposomal) is the first-line treatment with posaconazole and isavuconazole as alternatives.

Espejo et al. reported a case of bladder mass detected and managed medically. They described the presence of a fungal mass in a patient with DM and CKD (chronic kidney disease) [1].

In a case series by Devana et al., 15 patients with isolated renal mucormycosis were described. Ten underwent unilaterally nephrectomy and 2 underwent bilateral nephrectomy, whereas 2 were managed medically for mucormycosis [2].

Our patient complained of low-grade fever and difficulty in urination with deranged creatinine. Investigations suggested right mild hydronephrosis with no renal changes of mucormycosis with echogenic contents in the urinary bladder. The patient was taken up for cystoscopy and stenting. On cystoscopy, elongated, creamy yellow material was seen in the urinary bladder. Histopathology suggested mucormycosis in the urinary bladder. He was started on oral posaconazole and improved considerably. Follow-up investigation revealed normal kidneys and normal creatinine (1.1 mg/dl).

## Conclusions

Isolated urinary bladder mucormycosis is extremely rare. Mucormycosis is a rare opportunistic fungal infection with high morbidity and mortality with rare bladder involvement. It can also remain asymptomatic; timely diagnosis and starting antifungal drugs are key for successful treatment.

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