

Urinary tract mycosis masquerading as renal papillary necrosis post-COVID: A case report

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ABSTRACT

Urinary tract mycosis is more often seen in hospitalized patients than in community-acquired ones. Funguria is common but becomes invasive and life-threatening in immunosuppressed patients such as with diabetes mellitus, post-transplant, chronic antibiotic usage, cancer chemotherapy, and long-term steroids. In the last 2 years, the world has witnessed one of its worst pandemics with the COVID-19 infection, killing millions of people. Deaths have been due to the virus or secondary complications thereafter. Secondary fungal infections, especially those caused by mucormycosis, have been on the rise, the majority of which have been reported from India. The rhino-cerebral-pulmonary form is the most common, followed by isolated case reports of gastrointestinal, cutaneous, and musculoskeletal mucormycosis. Isolated renal and urinary tract mycosis in COVID-19 is an extremely rare association. We report a case of a middle-aged man with fairly well-controlled diabetes who received steroids for COVID-19 infection and, about 8 weeks later, presented with non-invasive mixed mycosis of the urinary tract that was managed conservatively without any surgical intervention.

Key words: COVID-19, Diabetes, Immunocompromised, Mixed mycosis

Mucormycosis refers to rare infections caused by fungi of the order *Mucorales*, which are characterized by the production of aseptate hyphae and asexual spores. Isolated urinary tract mucor mycosis is extremely rare. Mucor mycosis and aspergillosis can cause invasive infections in immunosuppressed individuals [1-3]. Fungal infections have been described in immunocompetent hosts as well [4-6]. Seventy-one individual cases were detected through PubMed bibliographic database searches published between 2010 and April 2022 [7]. India and Asia had the largest number of reported cases (50% and 70%, respectively). Renal mucormycosis had a 44% mortality rate in the analyzed cases. Immunosuppressive agent therapy, followed by tissue transplantation (kidney and liver), and diabetes were the most remarkable risk factors in patients.

Our case report also reiterates the fact that a high index of suspicion, early initiation of antifungal therapy, and nephrectomy may decrease mortality due to mucormycosis and aspergillosis as both are angioinvasive and associated with a high mortality rate of 65% in unilateral and nearly 100% in bilateral mucormycosis patients without surgical intervention [8].

CASE PRESENTATION


A 43-year-old gentleman, an IT professional, was admitted in April 2021 with a COVID-19 infection. He was hospitalized for nearly 2 weeks in the hospital. His computerized tomography (CT) chest revealed multiple central and pre-dominantly peripheral patchy ground glass opacities (CORADS 6). The patient was treated with injection methylprednisolone, remdesivir, low-molecular-weight heparin, and steroid inhalers. He was also known to have Type 2 diabetes, which was fairly well controlled with oral hypoglycemic agents. He did not undergo any instrumentation during this admission. He was discharged on oral steroids for another 10 days. On June 14th, the patient experienced right-sided loin pain with fever and vomiting. He noticed a fleshy, soft tissue coming out of the urine. A week later, he had a similar episode of loin pain, fever, and another bit of tissue. This time he collected the tissue, took pictures of the same, and shared them with his doctors (Fig. 1a).

On July 22nd, he came to the endocrinology clinic with yet another episode and was advised admission. He was suspected to have renal papillary necrosis. On examination, he had a body mass index of 24 kg/m², was febrile, and had normal blood pressure of 130/80 mmHg (on Tab Losartan 25 mg) but mild tachycardia.

He gave his laboratory tests and urine culture, and he was promptly admitted and hydrated with intravenous fluids.

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Ultrasound abdomen revealed bilateral acute renal parenchymal disease with right renal hydronephrosis. A CT of the abdomen showed features of pyelonephritis. However, the urine culture came back negative.

DJ stenting was done prophylactically by the urology team. During the procedure, they noticed white cottony material in the right pelvis, which was extracted with a grasper and sent for a KOH stain and fungal culture. KOH was positive for fungal septate hyphae. The culture grew *Aspergillus fumigatus*. His diabetes was managed with insulin in combination with oral drugs. He passed two more bits of soft tissue during the hospitalized period (Fig. 1b). Antifungal therapy was started with Posaconazole, and the patient was discharged on July 30th.

On August 23rd, he again developed loin pain, but on the left side, and passed two bits of tissue. This time the histopathology showed an entangled mass of broad aseptate hyphae suggestive of mucormycosis (Fig. 2). He was immediately recalled, readmitted, and started on injection Amphotericin 150 mg in 5% dextrose. While on amphotericin therapy, he passed a few more grayish-white fragments. Microscopy revealed eosinophilic fungal balls composed of branching septate hyphae of *Aspergillus* with focal inflammatory infiltrates. A repeat CT was done to rule out renal tissue damage. The DJ stent was in-situ, and there was no hydronephrosis. The right ureter was dilated with no radio-opaque calculus.



Figure 1: (a and b) Tissue passed in urine

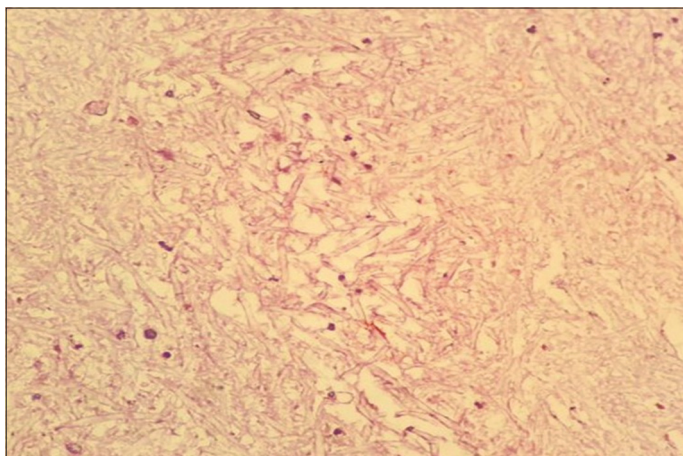


Figure 2: The hyphae of the *Mucorales* are distinct. The hyphae are broad (5–15 micron diameter), irregularly branched, and have rare septations. This is in contrast with the hyphae of ascomycetous molds, such as *Aspergillus*, which are narrower (2–5 micron diameter), exhibit regular branching, and have many septation

The patient was again readmitted on September 9th, with thrombophlebitis of the right internal jugular vein. His central venous catheter was removed. Blood sugars were well maintained on insulin and oral drugs. Blood cultures were negative. Blood-borne virus screens for HIV, HBsAg, and HCV were negative. After 3 weeks of completing Amphotericin, he was put back on Posaconazole 300 mg per day for 3 months. DJ stents were removed on October 6th, 2021. This time, the findings were of normal mucosa. After the stent removal, a small bit of tissue came again; this was also shown to be from *Aspergillus*. He remains symptom-free to date. He maintains good glycemic control, which is monitored on a periodic basis.

DISCUSSION

Urinary tract mycosis seldom occurs in immunocompetent hosts. The common pre-disposing factors are uncontrolled diabetes, hospitalization, immunosuppressive therapy following organ transplantation, parenteral drug abuse, HIV infections, repeated instrumentations [1], antibiotic therapy, etc. The fungal infections are commonly caused by *Candida* species in hospitalized patients. Fungal infections can be non-invasive, where they colonize the urinary tract and form fungal balls that may cause obstructive symptoms [2-4]. Life-threatening invasive forms can be due to hematogenous spread or retrograde infection from the lower urinary tract. Both small and large arteries show hyphal invasion, leading to thrombosis and renal infarction [5].

In hospitalized patients, the outcome of mycosis depends on the underlying risk factors. Funguria and fungal urinary tract infections are the most commonly caused by *Candida* species but may also be caused by *Cryptococcus neoformans*, *Aspergillus* species, and the endemic mycoses. In addition to microscopic identification, a colony count of 10,000–15,000 cfu/mL is the suggested cutoff value for the diagnosis of fungal urinary infection. A fungal ball can originate from the agglutination of a necrotic tissue nucleus, mucous debris, and foreign debris. A fungal ball can be obstructive or non-obstructive. If the fungal ball blocks the ureters, the infection manifests as acute-onset fever, flank pain, nausea, vomiting, dysuria, and hematuria [2-4]. Direct microscopy or culture of floccules in urine can help in diagnosing the condition. Histopathology helps with the rest.

In patients with diabetes, there is a higher incidence of asymptomatic bacteriuria, a two-fold increase in funguria, especially *Candida* infection, and a high incidence for both with antibiotic therapy. Treatment is indicated in symptomatic patients and in those at risk for fungal sepsis. The antifungal agents used for funguria are mainly fluconazole and amphotericin B deoxycholate because other drugs have extremely low concentrations in urine.

Our patient described here is a healthy individual with fairly well-controlled diabetes and no history of previous urinary infections or previous instrumentation. He was treated for COVID infection with both antivirals and antibiotics with nearly 2-week course of steroids. What led to dual fungal colonization of the urinary tract is difficult to explain. The patient at no time

was showing toxic symptoms. He, however, had a fever and pain whenever he would pass out a fungal ball. Two different fungal organisms, i.e., *Aspergillus* and Mucormycosis, were isolated in two different culture plates, suggesting the possibility of concomitant infection. Invasive aspergillosis is a life-threatening condition involving the lungs in immunosuppressed individuals. Aspergillosis limited to the urinary tract is rare [1-3]. *Aspergillus* colonization of the urinary tract has been reported in patients with concomitant urinary infections. A direct microscopic examination of the urine sample can diagnose these infections early. Treatment can be challenging. Most of the currently known antifungals, such as voriconazole, posaconazole, itraconazole, amphotericin B formulations, and echinocandins, show poor urinary concentrations. Posaconazole, an extended-spectrum triazole antifungal agent, has great activity against *Aspergillus* and *Mucorales*. Guidelines recommend posaconazole as salvage therapy for invasive pulmonary aspergillosis, but whether it could be used in invasive urinary tract aspergillosis remains uncertain. Newer anti-*Aspergillus* drugs, notably voriconazole, offer less toxic therapeutic options and are quite successful in combination with surgical drainage. In our patient, posaconazole was very effective, and the patient has remained symptom-free to date.

Renal mucormycosis has been described post-renal transplantation. The mode of spread can be homogenous or retrograde from the lower urinary tract. As mucor is angioinvasive, it can lead to thrombosis and necrosis of the renal parenchyma [9,10]. Mortality can be as high as 50%, and in the literature review, the patients could be saved only after a transplant nephrectomy. The key to a successful outcome is early recognition, prompt institution of surgical debridement of all infected tissue, and appropriate antifungal therapy [8-10].

In disseminated mucormycosis, the lung is more commonly involved, followed by the kidneys in 20% of patients. Isolated renal mucormycosis has also been described. The patient may present with flank pain, fever, hematuria, or even renal failure following occlusion of the renal artery and its branches [11]. Treatment would involve systemic antifungals and nephrectomy in select cases. Our patient had evidence of non-invasive dual fungal colonization in the form of fungal balls. As he had no toxic symptoms and no evidence of tissue damage, he could be managed conservatively with systemic antifungals alone.

CONCLUSION

This case highlights the importance of early diagnosis, early intervention, and control of risk factors with close follow-up.

Non-invasive forms of mycosis can be managed with a conservative approach. A nephrectomy is life-saving in the invasive category. A high index of suspicion is required in hospitalized patients for funguria or colonization of the urinary tract. Whether the mixed mycosis described in this case report has any bearing with the COVID-19 infection is something for readers to ponder.

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