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Case Report

Prompt diagnosis and treatment of cutaneous mucormycosis: a challenging complication in post-renal transplant patients

Kailash N. Singh[1], Ankit Grover[1]*, Sandeep Guleria[2]

[1]Department of Nephrology, Indraprastha Apollo Hospital, New Delhi, India
[2]Department of Transplant Surgery, Indraprastha Apollo Hospital, New Delhi, India

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***Correspondence:**
Dr. Ankit Grover,
E-mail: angrover@gmail.com

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ABSTRACT

A 52 years old male cadaveric renal transplant recipient developed cutaneous mucormycosis, presenting with febrile toxicity and a rapidly growing black lesion. Diagnosis was confirmed by biopsy and treatment began with liposomal amphotericin B. Owing to the high mortality associated with mucormycosis, isavuconazole, a non-nephrotoxic antifungal, was added to Amphotericin B. The patient underwent surgical debridement and his condition subsequently stabilized, accompanied by improved renal function. He was discharged on a combination of isavuconazole and other medications, with good wound healing and a creatinine level of 1.6 mg/dl at one-month follow-up. This case highlights prompt diagnosis and treatment and maintenance with isavuconazole as a viable alternative for mucormycosis in transplant patients with renal impairment.

Keywords: Amphotericin B, Acute tubular injury, Isavuconazole, Mucormycosis, Renal transplant

INTRODUCTION

Solid organ transplant (SOT) recipients face a higher risk of fungal infections due to diabetes, neutropenia and immunosuppressive medications. Up to 20% of kidney transplant recipients develop invasive fungal infections.[1] Mucormycosis is a rare fungal infection in patients with renal transplants, with an incidence of 0.4–0.5 per 1,000 patients.[2] The mortality rate of mucormycosis ranges from 38% to 56.5% and can be as high as 100% when dissemination occurs.[1]

Mucormycosis diagnosis is difficult and frequently delayed due to a dulled immune response. Prompt initiation of treatment is crucial and is associated with improved survival outcomes. Medical therapy and surgery (for localized disease) form the basis of treatment. Amphotericin B has been the drug of choice. Here we report a case of cutaneous mucormycosis in a renal transplant patient, diagnosed timely and treated with Amphotericin B and isavuconazole, a novel non-nephrotoxic broad-spectrum antifungal azole.

CASE REPORT

A 52 years old male with chronic kidney disease Stage 5 was on maintenance haemodialysis for a year before undergoing an ABO-compatible deceased donor renal transplant in January 2024 at our center. Induction immunosuppression (IS) with rATG and methylprednisolone and maintenance IS with tacrolimus, mycophenolate mofetil (MMF) and prednisolone were administered. Post-surgery, the patient showed a good recovery, with a creatinine level of 1.8 mg/dl and a urine output of 5 l/day at discharge on postoperative day 7 (Table 1). Prophylactic valganciclovir, trimethoprim/ sulfamethoxazole and clotrimazole oral drops were provided along with maintenance triple drug IS.

After one month, the patient presented with febrile toxicity, a blackish indurated lesion on the back with surrounding erythema (Figure 1a) and leakage from the surgical site. The back lesion rapidly enlarged to 10 cm within two days, with skin blackening and surrounding erythema. Laboratory findings revealed a total leukocyte

count (TLC) of 18,200/cumm and a creatinine level of 2.4 mg/dl. IV antibiotics (meropenem, colistin and teicoplanin) were initiated and empirical liposomal amphotericin B (5 mg/kg) was started. MMF and tacrolimus were withheld and Immunosuppression switched to IV hydrocortisone. Skin biopsy confirmed mucormycosis (Figure 2a).

CT imaging of the PNS, brain, orbits, chest and abdomen showed no mucormycosis dissemination. Extensive lesion debridement was performed (Figure 1b) and isavuconazole 200 mg was administered three times daily for 2 days, followed by 200 mg once daily, as an adjunct to antifungal therapy. He had a worsening graft function with a rising creatinine (4.8 mg/dl), urine output 2.5–3 l/day, Graft biopsy performed and revealed acute tubular injury and mild tubulitis without C4d positivity (Figure 2b). Colistin was discontinued due to suspected nephrotoxicity.

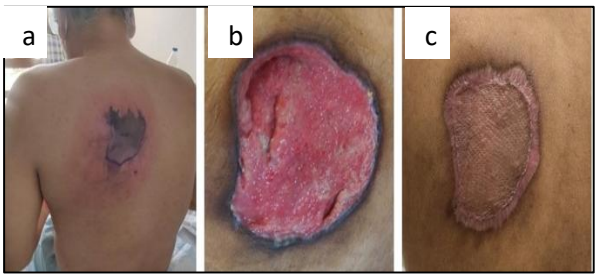

Figure 1: (a) Blackish indurated lesion with erythema, (b) Extensive debridement of lesion, (c) After skin grafting.

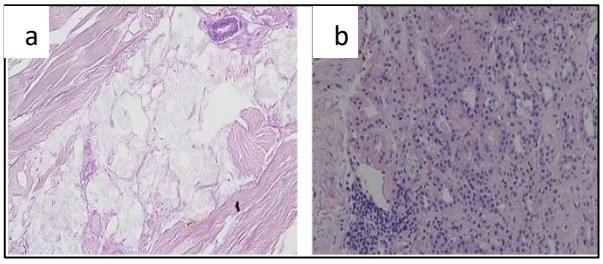

Figure 2: (a) Histopathology of mucormycosis, (b) Acute tubular injury with mild tubulitis.

The patient's condition initially stabilized but worsened with a spike in fever. Urine cultures revealed CRE (Klebsiella) at a concentration of greater than 10^5 CFU/ml and ceftazidime-avibactam and aztreonam were initiated. The patient responded well, becoming afebrile within five days and showing improved renal function. Amphotericin B was discontinued after three weeks and the patient was discharged following the removal of a DJ stent with a creatinine level of 2.2 mg/dl. At discharge, the patient was prescribed tacrolimus, Wysolone, ceftazidime-avibactam and isavuconazole (200 mg OD for three months). Regular wound care was advised. On one-month follow-up, the patient maintained good urine output and a creatinine level of 1.6 mg/dl. Skin grafting was performed on the debrided site by a plastic surgeon after 45 days. Antifungal isavuconazole was continued for a total of 3 months as maintenance therapy, along with optimization of the tacrolimus dose according to drug trough levels (Figure 1c).

Table 1: Post-transplant laboratory parameters.

	POD-0	POD-3	POD-5	POD-7
Urine output (ml/day)	1290	3080	4300	5550
Urea (mg/dl)	158	118	112	100
Creatinine (mg/dl)	5	4.7	3.1	1.8
Na^+ (mEq/l)	140	136	134	132
K^+ (mEq/l)	4.4	3.8	3.6	4.1
Hb (g/dl)	9.6	8.7	8.6	8.8
TLC (cells/cu.mm)	5550	6500	6200	6600
Platelet (/mcl)	281000	246000	250000	223000
Tac level (mcg/ml)		10.7	10.2	

DISCUSSION

Invasive fungal infection is more common in diabetic patients receiving SOT.[3] Immunosuppression is another significant risk factor, particularly with the use of potent T-cell-depleting agents, such as ATG.[4] Our patient was non-diabetic and the likely cause of mucormycosis seems to be an immunosuppressant state. Early diagnosis and treatment are crucial for preventing tissue necrosis and the spread of aggressive mucormycosis. 37.8% non-Aspergillus fungal infections occur within the first 6 months and 33.3% two years after the transplant.[5] In our case, we made a timely diagnosis and promptly started the patient on isavuconazole, as disseminated mucormycosis is reported to cause up to 100% mortality.[1] Traditionally, AmB and its liposomal formulations (lipAmB) have been used to treat IFI. In contrast, posaconazole has been suggested for Patients Who Are Intolerant or refractory to AmB.[6] However, the role of posaconazole becomes questionable in post-transplant patients owing to its drug interactions with posaconazole. Surgical debridement, managing immunosuppression and controlling diabetes have resulted in a 40% reduction in mortality over the past decade.[6] Antifungal use is limited due to lipAmB's renal

toxicity and insufficient data supporting posaconazole as a first-line, non-nephrotoxic option. Isavuconazole can be safely used in patients with impaired renal function without any renal toxicity and minimal interactions with tacrolimus drug levels.

CONCLUSION

Early diagnosis and prompt initiation of treatment, including debridement and antifungals, remains the mainstay of treatment for Mucormycosis. With the advent of the novel antifungal agent isavuconazole, it demonstrated favorable outcomes in our renal transplant patient with post-transplant cutaneous mucormycosis. Isavuconazole offers comparable efficacy to amphotericin B, while exhibiting significantly lower nephrotoxicity and fewer drug interactions, making it a suitable alternative for broader use in such cases.

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