Mucormycosis Extending From the Surgical Wound to the Transplanted Kidney: Case Report and Literature Review

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Abstract

Mucormycosis is an opportunistic, life-threatening infection in organ transplant recipients. We report a case of surgical wound mucormycosis that extended to a transplanted kidney. The patient was a 59-year-old man who underwent a donation-after-cardiac-death kidney transplant 10 years after receiving a liver transplant. On day 10 after the kidney transplant, he presented with cutaneous and subcutaneous tissues necrotizing at his right lower abdominal surgical wound. The necrotic tissue biopsy and laboratory culture showed different causes, while a polymerase chain reaction quickly identified the causative fungus at the species level. Although the combination therapy consisted of immunosuppressant withdrawal, intravenous Liposome AmB, and aggressive surgical debridement; unfortunately, the cutaneous mucormycosis invaded his transplanted kidney, and the patient was given a graft nephrectomy and subsequent hemodialysis.

We review the literature and conclude that mucormycosis in organ transplant recipients is a rare and extremely severe complication. Polymerase chain reaction provides a rapid and accurate diagnostic technique for species identification. Early effective antifungal therapy combined with aggressive surgical intervention and judicious withdrawal of immunosuppressants appears to be indispensable for a favorable outcome.

Key words: Kidney transplant, Mucormycosis, Polymerase chain reaction, Nephrectomy

Introduction

Mucormycosis is an invasive fungal infection caused by organisms of the Mucorales affecting immunocompromised individuals. It often progresses rapidly, with a devastating clinical course carrying a high morbidity and mortality rate. However, the clinical manifestations vary owing to different involved sites such as rhino-cerebral, pulmonary, cutaneous, and gastrointestinal, so that diagnosis and treatment of mucormycosis remains challenging for clinicians. Hopefully, a polymerase chain reaction (PCR) can identify the Mucorales at the species level, which renders a promising diagnostic alternative.

We describe a rare case of mucormycosis that progressed from the surgical wound to the allograft kidney with PCR identifying it in a donation after cardiac death (DCD) kidney transplant recipient and review the literature.

Case Report

A 59-year-old Chinese man with a history of primary hepatic cellular carcinoma underwent a orthotopic liver transplantation 10 years ago and received immunosuppressive therapy consisting of tacrolimus and mycophenolate mofetil at a local hospital. Shortly after this, he developed end-stage renal disease and underwent hemodialysis for nearly 10 years.

On September 20, 2010, the patient received a DCD kidney transplant with the permission of the Ethics Committee of our hospital. He had been given anti-thymocyte globulin (50 mg/d, from day 0) for 5 days as induction therapy and ensuing maintenance
therapy with tacrolimus (6 to 9 mg/d), mycophenolate mofetil (1.5 g/d), and prednisone (30 mg/d). Allograft function recovered slowly. On day 4, the drainage tube was removed, and little light-yellow exudates were seen inside the wound on the following days. On day 7, the volume of the exudates increased and several stitches were removed. Three days later, tissue inside the wound gradually liquefied and was covered with grey inanimate tissue. The grey tissue increased and turned black and necrotic several days later. Immediately, bacterial and fungal cultures, and pathology of the necrotic tissue were done, and only coagulase-negative staphylococcus was detected. The infection invaded the skin around the wound and showed dry, gangrenous changes, although the necrotic tissue culture and biopsy were negative on day 18.

Wound infection of mucormycosis was considered on day 23 and immunosuppressants were discontinued along with empirical introduction of caspofungin. Meanwhile, repeated debridement and causative examinations were done. The tissue culture yielded Mucorales twice, while histopathology showed aspergillosis. Liposomal amphotericin B (AmB) with an initial dosage of 25 mg/d followed by 50 mg/d was administered. The patient underwent debridement 6 times until day 32 (Figure 1). Then, the lesion seemed limited gradually. However, the patient insisted on being discharged from our hospital and continued treatment at his local hospital. More than half a month later, we discovered that the nonfunctioning transplanted kidney was removed owing to a graft biopsy, also manifesting mucormycosis and finally, he returned to hemodialysis.

**Discussion**

Mucormycosis is a rare opportunistic infection that complicates immunosuppressed solid-organ transplant recipients and chronic debilitating diseases. Its infestation usually causes a rapidly progressive disease process. Vessel thrombosis and tissue necrosis are 2 major hallmarks of mucormycosis. *Rhizopus oryzae* (belonging to a class of Zygomycetes in the order Mucorales) is the most-common species responsible for mucormycosis.

According to literature, old age, previous liver transplant with long-time immunosuppression, potent induction therapy for a kidney transplant, and delayed graft function, in this case, were thought to be risk factors for developing mucormycosis.

A cutaneous form of mucormycosis, including surgical wound infection, is much easier to discern. However, it can mimic several other infections that usually would be found in transplant recipients, which still pose diagnostic and therapeutic challenges for clinicians. Because of the rarity of the disease in kidney transplant recipients, introduction of therapy is often delayed. Moreover, the infection may invade from the original infected site to adjacent organs or tissues, which could increase mortality of this severe complication (as in our patient, the infection extended to allograft kidney). It is imperative to recognize the diagnosis promptly and use appropriate therapy. Usually, the diagnosis is based on clinical manifestation and examination, laboratory tests, and a biopsy. However, in this case, the necrotic tissue culture and biopsy not only were initially negative, but different results displayed the diagnostic difficulty and indeterminacy of these routine methods. What is needed is a rapid and accurate method to reliably identify Mucorales.

In our case, genomic fungal DNA was extracted from a mycelium that grows on Sabouraud dextrose agar; the fungal species was identified by sequencing of the internal transcribed spacer. Ribosomal DNA (rDNA) was amplified using universal internal transcribed spacer rDNA primers internal transcribed spacer 4 and internal transcribed spacer 5. A BLAST analysis was performed on the

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**Figure. 1.** Situation of the infected wound on day 28 (before the 5th debridement): The tissue shows gangrenous changes and the necrotic area gradually enlarged.

2. Creeping stolon was highly differentiated and rhizoids developed. Sporangióphore was straightened and grew densely at the opposing side of the rhizoid with no branch.
sequenced region of 603bp, and the 603bp DNA sequence was submitted to the GenBank. The fungus was identified as a *Rhizopus oryzae* species (Accession No.: HQ 625026), as assessed by sequencing of the internal transcribed spacer of the rRNA gene. We hypothesized that use of PCR for directly identifying *Mucor* spp. from the debrided necrotic tissues would reduce the time to obtain the microbiologic identification of the fungi, which may provide a promising diagnostic alternative to the species level, while sensitivity and specificity must be further assessed.\(^\text{10}\)

The therapeutic principle of mucormycosis in transplant recipients currently consists of withdrawal of immunosuppressants, aggressive surgical resection or debridement, and appropriate antifungal therapy.\(^\text{2}\) Immune drug discontinuation, concomitant with intravenous nutrition and gammaglobulin, can improve the immunocompromised state of organ transplant recipients in a relatively short time.

Early surgical intervention may play an important role.\(^\text{8, 9}\) There is consensus that surgical resection of an infected tissue or organ, over and above antifungal therapy, improves outcomes. In some life-threatening cases, saving lives is the most important thing regardless of allograft function. Debridement or radical resection should be used as soon as possible.

Intravenous AmB remains the criterion standard for treatment of mucormycosis.\(^\text{11}\) Lipid formulations of AmB may alleviate potentially severe adverse effects.\(^\text{12, 13}\) Recent therapeutic advances have revealed that posaconazole may be useful. It is an extended-spectrum, orally administered, triazole, with proven activity in vitro against Mucorales, both in an immunosuppressed mouse model of mucormycosis and in humans as salvage therapy against mucormycosis.\(^\text{13, 14}\)

Mucormycosis is an extremely rare and potentially lethal complication after kidney transplant. A PCR may facilitate an early diagnosis. Combination therapy consists of immunosuppressant withdrawal, appropriate antifungal agents, and aggressive surgical resection—these can result in a better prognosis for the patient.

**References**