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Renal Allograft Mucormycosis: Report of Two Cases

NASSER TAYYEBI MEYBODI, SAKINEH AMOUIAN*, NA'MA MOHAMMADIAN-ROASHAN

Department of Pathology, Emam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

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Introduction

Mucormycosis infection, as a sporadic worldwide infection, is often seen in immunosuppressed patients and those with hematologic malignancies and diabetes mellitus. This opportunistic pathogen, which widely exists in our environment, enters the body via respiratory system, gastrointestinal tract and skin wounds.[2] Mucormycosis infection can be isolated or disseminated and may rarely involve kidney alone.[3] Rhinocerebral mucomycosis is the most common form and its isolated form rarely involves organs such as lung, gastrointestinal tract, and brain. Also disseminated form has been reported in these patients.[1]

With respect to the potential role of mucormycosis infection in allograft rejection, it is crucial to consider it as a differential diagnosis in cases with graft rejection, so that prompt treatment can rescue the patient and the kidney allograft. We report two cases of renal mucormycosis infection in kidney recipients, which were both diagnosed by histopathological examinations, following nephrectomy due to rejection.

Case Reports

Case 1

The patient was a 31-year-old man from Mashhad, who was a known case of end-stage renal disease, resulted from bilateral hydronephrosis due to ureteropelvic junction obstruction, and had received cadaveric kidney transplantation in July 2003. Two months later, he was admitted with nausea, vomiting, flank pain, dysuria, and terminal hematuria. On physical examination, he had pain in allograft site and tenderness on the incisional line. Laboratory tests results were as follows: negative blood culture, Hb: 9 mg/dL, white blood cell count: 12 000/μL, Neutrophils: 68%, blood urea nitrogen: 25 mg/dL, and plasma creatinine: 5 mg/dL. Urinalysis revealed WBC 20 to 25 WBC/HPF and 12 to 20 RBC/HPF. Urine culture was negative. Further evaluations with ultrasonography and renal scan were indicative of acute rejection. In September 2003, the patient underwent operation. The graft was swollen and had color changes in the lower pole; subsequently, nephrectomy was done.

In macroscopic examination, the outer layer of the kidney was congestive and multifocal bleeding was seen on the necrotized incisional surface. In microscopic view, extensive necrosis of kidney with disseminated mucormycosis invasion and obstructive infectious thrombosis, accompanying a large amount of fungal elements in renal artery wall, other small arteries, and the adjacent tissues were seen (fig. 1). The patient was discharged with good general condition.

FIG. 1. Extensive mucormycosis hyphae, without transverse septum, having lateral right angle branch (×100)

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**Corresponding Author: Department of Pathology, Emam Reza Hospital, Mashhad, Iran.*
Tel: ++98 511 854 3031, Fax: ++98 511 859 3038,
E-mail: s_amouian@mums.ac.ir

Case 2

A 58-year-old woman from Sabzevar (current citizen of Mashhad), was referred with fever and chills, oliguria, and incisional inflammation, 9 months after kidney transplantation. She had been a known case of polycystic kidney disease and undergone living-unrelated kidney transplantation in October 2002. Also, she had been treated for hyperacute rejection in the first post-transplant hours and also for urinary tract infection and acute rejection one month later.

Laboratory tests results were as follows: negative blood culture, white blood cell count: 13000/μL, Neutrophils: 68%, blood urea nitrogen: 28 mg/dL, and plasma creatinine: 5.5 mg/dL. Urinalysis showed 20 WBC/HPF and 15 RBC/HPF. Urine culture was negative. Diagnostic workup for acute rejection was done and the patient underwent operation with acute rejection diagnosis. Thick purulent secretions were evacuated and nephrectomy was done.

In macroscopic examination, the kidney had irregular external surface, creamy color, covered by fibrin, with necrotized surface of the incision. Amorphic necrotic elements were seen in calyces sections (fig. 2). In microscopic examination, fungal elements invasion with broad hyphae, without transverse septum, and with right angled branches were seen in small and major kidney arteries (fig. 3), accompanying with intensive coagulative necrosis in parenchyma (fig. 4). Obstructive infectious thrombosis, accompanying by a large amount of fungal hyphae, invading the artery and adjacent tissue were seen in renal artery wall (Both samples were sent to laboratory fixed in formalin, so that it was impossible to culture the fungi). The patient was discharged with good general condition.

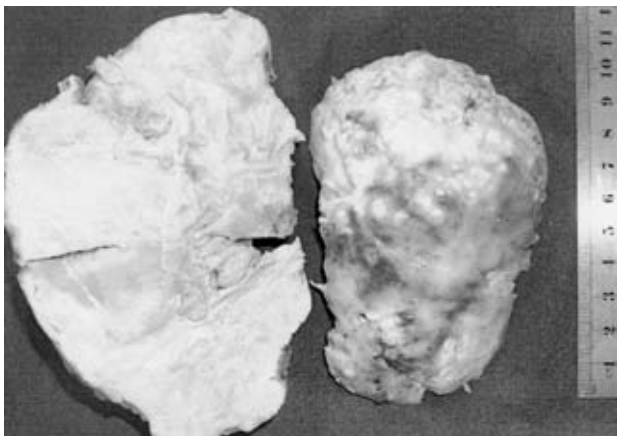

Fig. 2. Multifocal necrosis in external and internal kidney views

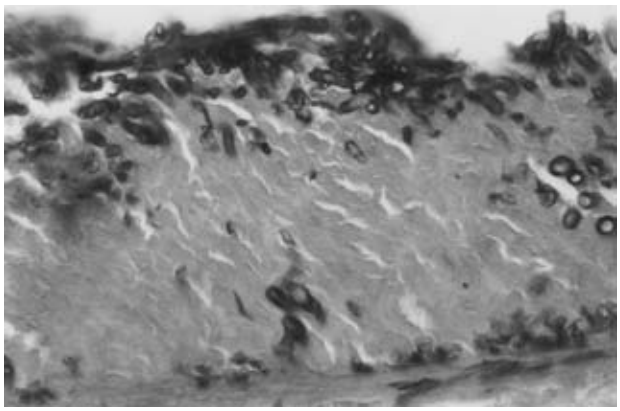

Fig. 3. Fungal elements invasion in transplanted kidney artery walls (× 40)

Fig. 4. Fungal elements and coagulative necrosis of kidney parenchyma (×40)

Discussion

Mucormycosis (Zygomycosis) is an opportunistic upper respiratory tract and lung infection caused by mucorales fungi, and its most common pathogen species is rhizopus oryzae. The infection is transmitted by spores in the air.[3] It can enter the body through gastrointestinal tract and wounded skin.[2] Different clinical forms of mucormycosis infection have been described, among which rhinocerebral mucormycosis is the most common form. Mucormycosis may rarely involve the kidney alone. Rhiozopus Oryzae often invades blood vessels and disseminates through the hematogenous route. Urinary system involvement can be asymptomatic or can manifest as signs and symptoms of kidney infection, such as pain, dysuria, gross hematuria, or acute renal failure. Kidney involvement has been seen in 50% of the patients who have died of disseminated mucormycosis. Several vessel thromboses may lead to segmental or subtotal kidney infarction. Involvement can be unilateral or bilateral. Microscopically, necrotizing purulent inflammation is seen accompanying by

thrombosis of arcuate and interlobar arteries. Fungal hyphae are usually wide (20 to 50 μm or more) with irregular margins and different shapes. Although most of them seem to be without transverse septum, they are, in fact, pauciseptate with few transverse septa. Of course, transverse septa can be hardly seen in the tissue samples. Peripheral branches have a lateral right angle branching shape. Hyphae septum in hematoxylin-eosin staining is basophyl or amphophil. We can detect the organisms using Grocott methenamine-silver staining or using antibody attached to fluorescent elements.[3] Mucormycosis can be seen in three different forms in a patient with kidney disease. The first form is primary isolated infection of kidney. Primary mucormycosis of kidney is rare and can result in disseminated infection. The most common predisposing factors are AIDS, drug addiction, and diabetes mellitus, which must be considered in every single patient with flank pain, fever, and sterile urine without clinical response to antibiotic therapy.[3-5]

The second type of mucormycosis infection in patients with kidney disease is the involvement of other organs of kidney recipients. Mucormycosis infection in lung, gastrointestinal system,[6] nose, sinuses, and brain[7] has been reported in immunocompromised patients with renal transplantation.

The third form, to which our reported cases belong, is mucormycosis infection in transplanted kidney, which is very rare and, to our best knowledge, has been reported in 5 cases, so far.[8] In these cases, patients have normal diuresis after transplantation and level of serum creatinine is also normal. However, from the third postoperative day to the second month they are affected with decreased urinary flow, increased creatinine, and flank pain, with no significant microscopic finding in urine, urine culture, and blood culture.[8] Afterwards, severe pain, decreased blood pressure, and hematogenic shock will occur. In one case, isolated mucormycosis of renal artery is reported to lead to renal artery rupture, hematoma formation around transplanted kidney and posterior peritoneum, and immediate death.[9] In another patient, biopsy of transplanted kidney had been done before surgical operation showing necrotic tissue of kidney and intensive fungal infiltration, which was confirmed in culture.[9] Our patients had been referred with rejection signs, flank pain, and hematuria two to nine months after transplantation and nephrectomy was performed for both of them.

Mucormycosis in transplanted kidney is a very rare and fatal infection. It seems that living-unrelated kidney transplantation is a probable risk factor in developing countries. Fungal colonization can take place during transplantation.[9]

Mucormycosis infection diagnosis in transplanted kidney usually takes time, because culture of the organism is difficult to perform, and there is no available diagnostic serological test for its diagnosis.[8] Thus, in every single patient with rejection signs, flank pain, and without any specific changes in microscopic urine exam, urine culture, or blood culture, mucormycosis must be considered even if no specific changes in microscopic urine exam, urine culture and blood culture is seen. Early treatment with anti fungal agents can result in a better prognosis for the patient.

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