Case of Renal Aspergillosis after Heart Transplant: Diagnosis and Treatment

M. Mahdavi, G. Mortaz-Hejri
H. Shahzadi, H. R. Pouraliakbar,
A. Amin, M. Hesami, B. Naghavi*

Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

ABSTRACT

Invasive aspergillosis (IA) is a severe complication after heart transplantation (HTx), with a high mortality rate. Invasive pulmonary aspergillosis (IPA) is the most common presentation. We herein describe a unique case of Renal aspergillosis (RAsp) diagnosed on month 10 post-HTx with no known risk factors for IPA in cardiac transplant recipients. The diagnosis of RAsp was made based on radiographic findings, renal biopsy, and tissue cultures. The patient initially received combined antifungal therapy (caspofungin and voriconazole) without radical or partial nephrectomy, followed by voriconazole maintenance monotherapy with favorable clinical outcomes.

KEYWORDS: Heart transplant; *Aspergillus*; Invasive aspergillosis; Fungal infection

INTRODUCTION

Invasive aspergillosis (IA) has emerged as a significant cause of morbidity and mortality in solid organ transplant (SOT) patients, including heart transplant recipients (HTRs) [1, 2]. Lung infection is the most common presentation and involvement of other sites of the body with IA including the central nervous system, myocardium, mediastinum, skin, prostate, digestive tract and paranasal sinus have been reported [2]. Renal aspergillosis (RA) is a rare complication in SOT but not reported in HTRs hitherto [2, 3, 4]. We hereby describe a patient with dysuria 10 months after heart transplant (HTx) who was diagnosed with invasive kidney aspergillosis based on CT guided biopsy.

CASE PRESENTATION

A 14-year-old boy with cardiomyopathy following myocarditis who underwent orthotopic HTx presented with dysuria 10 months after HTx. His organ was from a donor who was a brain death patient following a road traffic accident. After transplantation the patient was discharged in excellent condition and his immunosuppressant regimen included prednisolone, mycophenolate mofetil, and tacrolimus. The patient had a 2-week history of dysuria, fatigue and anorexia. He had no history of recent travel and intravenous drug use, and he used to work in a fruit shop and has been in direct contact with fresh fruits, also he had a bird at home. On physical examination he was ill and vital signs included a blood pressure of 110/70 mmHg, an oral temperature of 37.3°C, heart rate of 88 beats/min, respiratory rate of 18 breath/min, and oxygen saturation of 96% at room temperature. Heart sounds were normal and clear breathing sounds were noted. Laboratory testing demonstrated a hemoglobin of 12.1 mmol/L, thrombocyte count of 254*109/L, and white blood cell count of 9300/µL with 82.1% neutrophils, 10.9% lymphocyte, 7% mixed monocytes and eosinophils. Erythrocyte sedimentation rate (ESR) and High-sensitivity C-reactive protein (hs-CRP) were significantly increased. Urine analysis showed more than 100/hpf white blood cells (WBC), 20/hpf red blood cells (RBC) and a few/hpf bacteria. Cytomegalovirus (CMV) antigen

*Correspondence: Batool Naghavi, MD,
Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Vali-Asr Avenue, Tehran, Iran
ORCID: 0000-0002-4714-9844
Tel: +98-913-245-4720
E-mail: naghavirhc@gmail.com

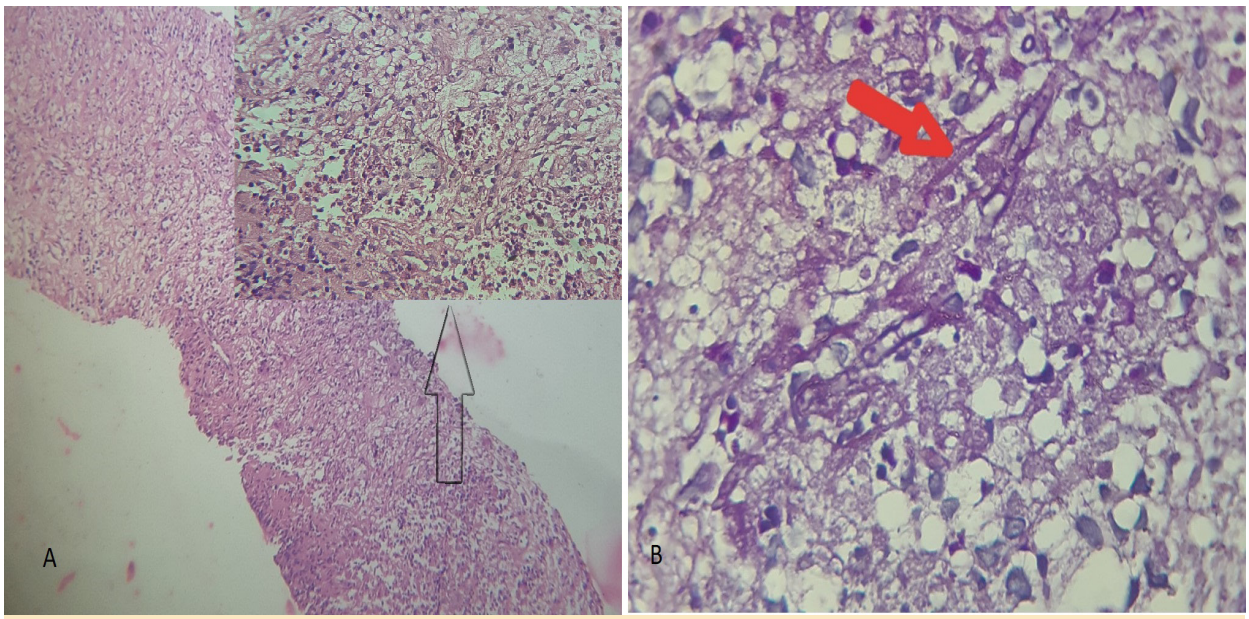

Figure 1: Pathology specimen of renal tissue reveals active inflammation with aggregation of foamy macrophages (A), High-power photomicrograph of a small area shows scattered *Aspergillus* organisms in the necrotic tissue (B).

was negative and metabolic profile was normal. Chest X-ray and echocardiogram data were unchanged from the previous results. The patient was hospitalized and intravenous ceftriaxone was started. Urine and blood cultures showed no microbial growth after four days of incubation, but hematuria and pyuria persisted. Therefore, the patient underwent renal ultrasonography which showed a cystic mass with heterogenic and capsular pattern in the lower pole of the left kidney, no stone and hydronephrosis were seen. Abdominopelvic MRI revealed cystic lesion (50*70mm) in the lower pole of the left kidney that was suggestive of abscess formation or pyelonephritis and less likely in favor of tumor lesions. On suspicion of lymphoma, CT scan guided renal mass biopsy was performed. Renal mass biopsy showed infiltrated renal tissue with mixed inflammatory cells accompanied by some fungal structures including branched and septated hyphae with necrotic derbies (Fig 1). Cultures of tissue specimens indicated *Aspergillus fumigatus*. Diagnosis of RA was made and antifungal therapy was initiated with caspofungin and voriconazole. Immunosuppressant medication was decreased judiciously by keeping tacrolimus level at about 5 ng/ml. Serum *Aspergillus galactomannan* antigen assay was requested which was positive. Symptoms promptly resolved immediately and 8 weeks later urine analysis was normal. The CT scan showed a significant reduction in lesion size and endomyocardial biopsy (EMB) revealed no evidence of rejection. The patient was discharged with oral voriconazole and immunosuppressant drugs. The patient received voriconazole therapy for 5 months and has been off voriconazole for 5 years and there have been no clinical signs of relapse of fungal infection at this time.

DISCUSSION

Invasive fungal infections with *Aspergillus* are an important cause of morbidity and mortality in patients who had undergone heart transplantation with an overall incidence of 6.5% [2]. Invasive pulmonary aspergillosis (IPA) is the most common clinical anifestation and usually occurs < 3 months (early-onset aspergillosis) after HTx [2, 3]. Late-onset Aspergillosis (> 3 months) after transplantation is more complicated and disseminates in unusual sites compared with early-onset aspergillosis [2, 5]. Risk factors for IA include delayed

chest closure, excessive blood loss, reoperation, steroid-resistant rejection, renal failure particularly hemodialysis, CMV infection, diabetes mellitus, anti-thymocyte globulin and prolonged use of broad-spectrum antibiotics [6, 7]. Targeted anti-fungal prophylaxis in HTx recipients was administrated only to patients with risk factors and was maintained for approximately 20 days after resolution of risk factors [2, 8]. Our case had no risk factors whereas he had a high environmental exposure to *Aspergillus* spores at work and home. Kidney is an atypical site for IA after HTx, which was involved in our patient. The serum *Aspergillus galactomannan* antigen assay has moderate accuracy for the microbiologic diagnosis of IA in immunocompromised patients [9]. Both CT and MRI are useful in diagnosing, localizing and differentiating renal lesions, however up to now imaging manifestations of RA have not yet been described [4]. Percutaneous lung biopsy has high accuracy with up to 100% sensitivity and specificity in the diagnosis of IPA [10]. We performed CT guided renal mass biopsy for rapid diagnosis and it helped to initiate anti-fungal therapy including caspofungin and voriconazole as soon as possible. Although amphotericin B is the most frequently used anti-fungal medication [6], voriconazole is recommended as the drug of choice for primary therapy in IA with a minimum duration of 12 weeks. Combination therapy with voriconazole plus an echinocandin (caspofungin, micafungin, or anidulafungin) led to higher survival in serious life threatening patients with IPA [5, 6, and 11]. Radical or partial nephrectomy followed by adjuvant antifungal treatment can be effective for reducing the risk of dissemination and mortality [4]. Our case was cured only with antifungal treatment without surgical resection. In conclusion, kidneys can be involved with IA after HTx and percutaneous renal biopsy is a good modality for early diagnosis. Renal aspergillosis can be treated without the need for surgical resection.

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REFERENCES

1. Montoya JG, Chaparro SV, Celis D, *et al*. Invasive Aspergillosis in the Setting of Cardiac Transplantation. *Clin Infect Dis* 2003;**37**(s3):S281-92.
2. Muñoz P, Cerón I, Valerio M, *et al*. Invasive aspergillosis among heart transplant recipients: A 24-year perspective. *J Heart Lung Transplant* 2014;**33**:278-88.
3. Kabbani D, Goldraich L, Ross H, *et al*. Outbreak of invasive aspergillosis in heart transplant recipients: The role of screening computed tomography scans in asymptomatic patients and universal antifungal prophylaxis. *Transpl Infect Dis* 2018;**20**:e12808.
4. Meng X-C. Renal aspergillosis after liver transplantation: Clinical and imaging manifestations in two cases. *World J. Gastroenterol* 2014;**20**:18495.
5. Shakerian B, Razavi N, Mandegar MH. Fatal Case of Pulmonary Invasive Aspergillus after Heart Transplant with a Rapidly Progressive Course. I*nt J Org Transplant Med* 2018;**9**(3):140-3.
6. Barchiesi F, Mazzocato S, Mazzanti S, *et al*. Invasive aspergillosis in liver transplant recipients: Epidemiology, clinical characteristics, treatment, and outcomes in 116 cases. *Liver Transpl* 2015;**21**:204-12.
7. Rabin AS, Givertz MM, Couper GS, *et al*. Risk factors for invasive fungal disease in heart transplant recipients. *J Heart Lung Transplant* 2015;**34**:227-32.
8. Muñoz P, Valerio M, Palomo J, *et al*. Targeted Antifungal Prophylaxis in Heart Transplant Recipients. *Transplantation* 2013;**96**(7):664-9.
9. Pfeiffer CD, Fine JP, Safdar N. Diagnosis of Invasive Aspergillosis Using a Galactomannan Assay: A Meta-Analysis. *Clin Infect Dis* 2006;**42**:1417-27.
10. Hoffer FA, Gow K, Flynn PM, Davidoff A. Accuracy of percutaneous lung biopsy for invasive pulmonary aspergillosis. *Pediatr Radiol* 2001;**31**:144-52.
11. Marr KA, Schlamm HT, Herbrecht R, *et al*. Combination Antifungal Therapy for Invasive Aspergillosis: A Randomized Trial. *Ann Intern Med* 2015;**162**:81.