Ortotopik Kalp Transplantasyonu Sonrasında Gelişen Pulmoner Aspergillus İnfeksiyonu

PULMONARY ASPERGILLUS INFECTION AFTER ORTHOTOPIC HEART TRANSPLANTATION

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Özet

Bu yazıda, kalp transplantasyonu sonrasında pulmoner aspergillus absesi gelişen 56 yaşında bir erkek hastayı sunuyoruz. Hasta kalp transplantasyonu sonrasında sorunsuz erken postoperatif dönemi takiben taburcu edildi; ancak postoperatif 60. günde nefes darlığı gelişti. Teleradyogramda ve bilgisayarlı toraks tomografisinde sağ akciğerde kistik bir yapı gözlendi. Bunun üzerine 2 mg/kg/gün dozunda Amfoterisin B başlandı ve bronkiyal aspirasyon kültürü almak için bronkoskopi planlandı. Bronkoskopi işleminin sonunda hasta ventriküler fibrillasyona girdi ve bunu takibeden arrest neticesinde kaybedildi. Kalp transplantasyonu yapılan bir hastada akciğerde kistik oluşumların gelişmesi aspergillus infeksiyonuna bağlı olabilir. Bu tip infeksiyonlar uygun tedavi ile bile mortal seyredebilirler. Bu hastalarda bronkoskopi yüksek risk taşır, bu nedenle tedaviye başlamak için non-invaziv işlemler yeterli olmalıdır.

Anahtar kelimeler: Kalp transplantasyonu, aspergillus, bronkoskopi

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Summary

We present a 56-year-old male patient, who had pulmonary aspergillus abscess after his heart transplantation. He was discharged after an uncomplicated hospital stay, but on postoperative 60th day he presented with dyspnea. On chest X-ray and thorax computerised tomography there was a right lung cavern. We started Amphotericin-B 2 mg/kg/day. We proposed bronchoscopy to perform a bronchial aspiration culture. Shortly after termination of the procedure, the patient had ventricular fibrillation and was lost following cardiac arrest. A lung cavern in a heart transplant recipient may be due to an aspergillus infection, which may cause death even under appropriate treatment. Bronchoscopy may carry high risk in these patients, so non-invasive diagnostic tools should suffice to start treatment.

Keywords: Heart transplantation, aspergillosis, bronchoscopy

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Introduction

After solid organ transplantations fungal infections are encountered less than bacterial and viral infections, but they cause the worst outcome (lethality 26%) [1]. As many as 32% of heart recipients and 35% of heart-lung recipients have been reported to develop clinically significant fungal infections [2]. The occurrence of fungal infections in these patients is determined by several factors such as the epidemiological exposures, the state of immunosuppression, the technique of the transplantation procedure, and the efficacy of the antifungal prophylaxis. Lungs can be reservoirs of the pathogenic fungi. Aspergillus and candida species are responsible for more than 80% of fungal infections in thoracic organ transplant recipients [3]. In recent studies estimates of the frequency of invasive aspergillosis is 2-13% in heart transplant recipients. In this paper we report the first aspergillosis case in our heart transplant series of 15 patients.

Case

On July 2001, we had performed orthotopic heart transplantation in a 56 years old male patient who had an ischemic cardiomyopathy previously. Early postoperative period was uneventful and we started the immunosuppressive therapy with cyclosporine 350 mg/day, azathioprine 150 mg/day, and prednisone 65 mg/day. We measured the blood cyclosporine levels each day to adjust the dose to achieve a blood level between 250 and 300 ng/mL. On postoperative 15th day we decreased the dose of azathioprine to 100 mg/day since he had neutropenia. After that, white blood cell (WBC) count increased up to 7.5x10^{3}/dL. Percentage of neutrophils and lymphocytes were 65.6% and 14.4%, respectively. We tapered the dose of prednisone down to 20 mg/day. We had performed several myocardial biopsies. We had found either grade I or II International Society of Heart Lung Transplantation (ISHLT) grades in these biopsies. On postoperative 25th day he was discharged without any complaints. On postoperative 45th day he visited our out-patient clinic for routine follow-up. Blood cyclosporine level was 300 ng/mL, and WBC count was 12.4x10^{3}/dL, routine blood and urine tests were within normal

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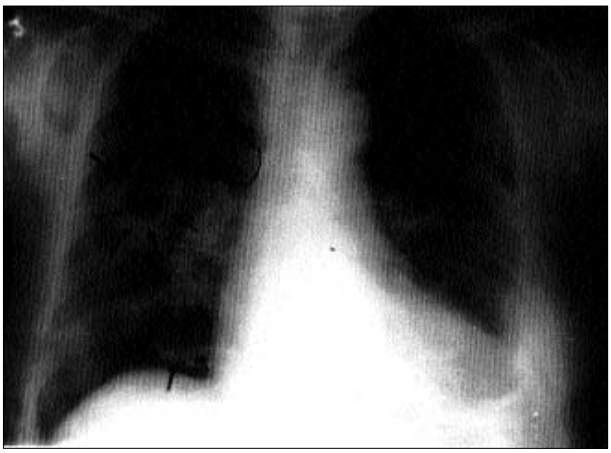

Figure 1. Teleradiogram of the patient.

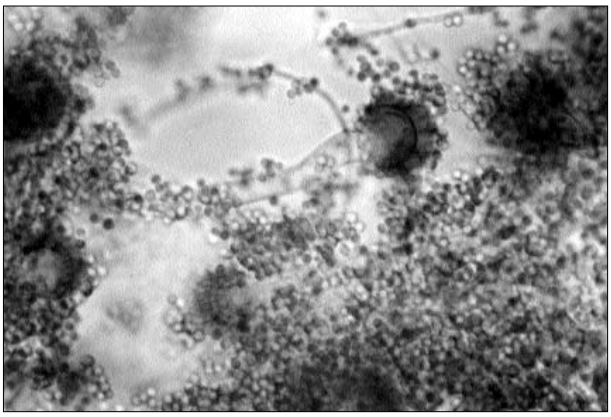

Figure 3. Microscopic view of the broncho-alveolar lavage material showing aspergillus fumigatus (Gram stain, X100 magnification).

limits; cultures of throat, urine, blood and sputum did not reveal any organism. He had no complaints at that time and we let him go home. On postoperative 60th day he presented with dyspnea. Respiratory sounds could not be auscultated over right middle lobe. His physical examination did not reveal any other pathologic findings. On echocardiographic examination cardiac functions were within normal limits; left ventricular ejection fraction was 59%. His body temperature was 38.5°C, WBC count was 2.7x10^3/dL, percentage of neutrophils and lymphocytes were 82.9% and 6.8%, respectively. On teleradiogram there was an image on right lung looking like a cavern (Figure 1). We did thorax computerised tomography (CT), which revealed a 35x35 mm-sized cystic cavitary lesion at the middle lobe of the right lung (Figure 2). We did sputum and fine needle aspiration biopsy cultures but could not cultivate any organism. We started Teicoplanin 3 mg/kg/day, Amphotericin-B 2 mg/kg/day, and metronidazole 1 g/day; then we planned bronchoscopy for definitive diagnosis. Under local anesthesia we performed bronchoscopy, which revealed clear airways and increased amount of secretions. Shortly after termination of the procedure, the patient had ventricular fibrillation and cardiac arrest. We applied cardiopulmonary

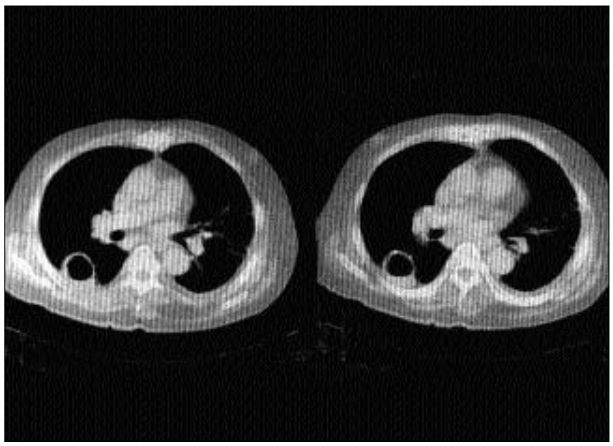

Figure 2. Computerised tomography of thorax.

resuscitation for about an hour, but we lost the patient. On post-mortem cytological examination of broncho-alveolar lavage material we found aspergillus fumigatus (Figure 3).

Discussion

The aspergillus species rarely cause infection in healthy individuals but pose a great risk for transplant recipients. It is the most common non-candida fungal infection occurring in these patients, and the fatality rate for invasive aspergillosis exceeds 80% [3]. Furthermore not uncommonly, aspergillus infection can occur concomitantly with candida infection during the intermediate post-transplant period (22-90 days after transplantation). Sixty-six percent of fungal infections occur in the first 3 months after transplantation; this is most likely due to intensive immunosuppressive regimen in that period [4].

Classically, the major risk factors for invasive pulmonary aspergillosis (IPA) include severe or prolonged neutropenia (absolute neutrophil count < 500/dL) and prolonged high-dose corticosteroid therapy [5]. In the absence of an effective host immune response, the spores mature into hyphae that can invade the pulmonary structures, particularly blood vessels. This results in pulmonary artery thrombosis, haemorrhage, lung necrosis and systemic dissemination.

In the immunocompromised or neutropenic host, IPA is the most common manifestation of an aspergillus infection, although local infections also occur in the sinuses, skin, or intravenous catheter site. A definite diagnosis of IPA is difficult to establish because there is no single diagnostic test that is either universally applicable or sensitive and specific enough. Some non-invasive tests can support the diagnosis, like detection of aspergillus antigen in serum and positive aspergillus culture from an extra-pulmonary site [6]. A probable diagnosis of IPA is possible for patients with the characteristic clinical picture of sudden onset of shortness of breath, pleuritic chest pain, hemoptysis, pulmonary infiltrates and high-grade fever while on broad-spectrum antibiotics, and IPA appears on radiographs as multiple ill-defined 1-2 cm nodules that gradually coalesce into larger masses or areas of consolidation [7]. An early computed tomography finding is the rim of ground-glass opacity surrounding the nodules (halo

sign) [8]. This sing is non-specific and has also been described in patients with tuberculosis, mucormycosis and Wegener's granulomatosis. Cavitation is usually a late finding. The intracavitary mass composed of sloughed lung and the surrounding rim of air may be seen as the "air crescent sing". Pleural effusion is unusual and adenopaties are rare. A definitive diagnosis of IPA was established for patients with similar clinical presentation by bronchoscopy with broncho-alveolar lavage demonstrating aspergillus organism on cytological examination and/or on culture or by histology or culture from surgery or autopsy.

Patients with IPA were treated with intravenous Amphotericin-B 1-1.5 mg/kg/day during neutropenia, and with Itraconazole thereafter until resolution of CT scan lesions, usually for 4-6 moths. The most prominent disadvantage of Amphotericin-B is its nephrotoxic effect. The treatment of aspergillosis with Amphotericin-B in solid organ transplant recipients results in a higher incidence of nephrotoxicity because of concomitant use of cyclosporine [9]. Liposomal Amphotericin-B has far fewer side effects and can be much more safely used in patients with solid organ transplants, despite concomitant use cyclosporine.

In conclusion, aspergillus is an important cause of infection in heart transplant recipients, especially during early period. It carries high mortality even under appropriate treatment. For this reason, this infection should always be kept in mind, and a suspect of diagnosis from clinical and radiological signs should let the physician start the treatment immediately. This may help to prevent deaths due to aspergillus infections in transplant recipients. Since bronchoscopy carries high risk in these patients, we do not recommend it anymore.

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