

Case Report

A pulmonary aspergillosis case with fatal course in a patient with SIRS clinic

Nedim Çekmen^{*a}, Sonay Açiksöz^a, Hacer Serdaroğlu^a, Özcan Erdemli^a

Abstract

A 77-year-old male patient with a history of tuberculosis applied to emergency service with complaints of confusion, shortness of breath, tachycardia, hypothermia and hypotension. A bronchoalveolar lavage culture was collected because a fungus ball was seen on repeat chest X-ray and thoracic CT of the patient. *Aspergillus fumigatus* grew and voriconazole treatment was started, but the patient was lost from multiple organ failure (MOF). In diagnosis of patients with SIRS clinic, causative factor may be aspergillus located in an old tuberculosis cavity, and this may have a fatal course in an old patient having previous pulmonary and systemic diseases.

KEYWORDS: Pulmonary Aspergillosis, Systemic Inflammatory Response Syndrome, Multiple Organ Failure, Morbidity, Mortality.

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Aspergillus spp are ubiquitous fungi acquired by inhalation of airborne spores and may cause life-threatening infections especially in immunocompromised hosts. *Aspergillus* spp are commonly isolated from the soil, plant debris, and the indoor environment, including hospitals. *Aspergillus* can effect different organ systems. The most frequently involved organs are the lungs. Pulmonary aspergilloma (PA) is an infectious disease originating from colonization of *Aspergillus fumigatus* in lung cavities and it is frequently and concomitantly present with pulmonary diseases such as tuberculosis cavity, sarcoidosis, cavitory neoplasia, bronchiectasia, lung abscess, bronchial cyst and pulmonary infarct.¹⁻³ *Aspergillus* cause three different groups of diseases in lungs including allergic, colonized and invasive pulmonary aspergillosis (IPA). Demonstrating specific hyphae in tissue specimens histopathologically is diagnostic for aspergillus. If it is not treated, mortality of invasive aspergillosis reaches up to 100%. Long term antifungal therapy is generally required.¹⁻⁴

Although IPA is seen in neutropenic patients or in immunocompromised patients due to any reason, it may rarely appear in immun-

competent patients.⁴ This paper presents an IA case with fatal course determined on the follow up of a patient in systemic inflammatory response syndrome (SIRS) clinic. The patient had no immunodeficiency condition in the clinic's intensive care unit (ICU).

Case Report

A 77-year-old male patient with previous history of tuberculosis, followed up with diagnoses of Chronic Obstructive Pulmonary Disease (COPD), Hyperthyroidism and *Diabetes Mellitus* (DM) for 10 years referred to emergency service with complaints of confusion, shortness of breath, tachycardia, hypothermia and hypotension. He was admitted to ICU with pre-diagnoses of acute respiratory failure and SIRS. The patient was intubated and connected to ventilator. There was a decrease in respiratory sounds, being more marked on the right lung, coarse rales, prolongation of expiration and bilateral biphasic expiratory ronchi on physical examination. An obstructive pattern was seen on the pulmonary function test of the patient's history. Other system findings were normal. Glasgow Coma Score was 6, Acute Physiology and Chronic Health Evaluation (APACHE II): 34, Multiple organ dysfunc-

^a Güven Hospital, Department of Anesthesiology and Intensive Care, Şimşek Sok, Kavaklıdere, Ankara, Turkey.

* Corresponding Author

E-mail: nedimcekmen@yahoo.com

tion syndrome (MODS): 8, and pulse: 122/min., arterial blood pressure: 82/41 mmHg, respiratory rate: 30/min., temperature: 35°C, Leukocyte: 27600/mm³, C-reactive protein (CRP): 52 mg/L, and remaining values were normal. He was also compatible with thyrotoxicosis [free thyroxine (FT4) = 8.5 ng/dL (NR = 0.8-2.0), thyrotropin (TSH) < 0.05 µIU/mL (NR = 0.3-4.0), thyroid receptor antibodies (TRAb) = 0.9 IU/mL, (NR < 1.8)]. Thyroid ultrasonography revealed a solid, hyperechoic nodule of 8.5 mm diameter in the right lobe. The patient was diagnosed as having Hyperthyroidism associated with Graves' thyrotoxicosis. Treatment with propranolol and methimazole was initiated. Pneumonic infiltration and increase in ground glass density were seen at the middle zone of right lung on chest X-ray (Figure 1). There was no pathology belonging to cardiac ischemia on ECG, except for diastolic dysfunction in *Echocardiography* (ECHO). He was 38.4°C at 2th day, but no growth occurred on all cultures collected. So, Ampicilline-Sulbactam and Levofloxacin were given as empirical therapy. *Acid resistance bacteria* (ARB) were studied 3 times for excluding active tuberculosis and result came to be negative. No response could be obtained from the patient. Treatment of patient was substituted by Piperacilline/Tazobactam, Trimetoprim/Sulfametaxazol and Claritromycin at 7th day, when his temperature did not decrease, had more severe clinical course and showed no regression of pneumonic infiltration. A bronchoscopy was performed due to a fungus ball seen on thoracic computed tomography (CT) (Figure 2). Lumens of the trachea and bronchi have become narrow and there were diffuse white-colored plaques. The thin-walled necrotic lesion, located in tuberculosis cavity at the middle lobe of right lung on thorax CT and having infiltration around was interpreted as crescent sign. Histopathological examination of biopsy specimens taken by bronchoscopy from the bronchiectatic lobe or segment bronchi showed areas of mixed active inflammation and fibrous scarring with microscopic abscess cavity and central bronchiectasis with dense

peribronchial inflammation, fibrosis, and fungus ball and septate hyphae of *Aspergillus fumigatus* in hematoxylin-eosin-stained section (Figure 3). *Aspergillus fumigatus* grew on bronchoalveolar lavage (BAL) culture collected, and voriconazole treatment was started with loading dose of 1x400 mg i.v., and maintenance dose was given as 2x200 mg i.v. The patient's disease became more severe on 18th day of therapy and he was lost due to multiple organ failure (MOF).

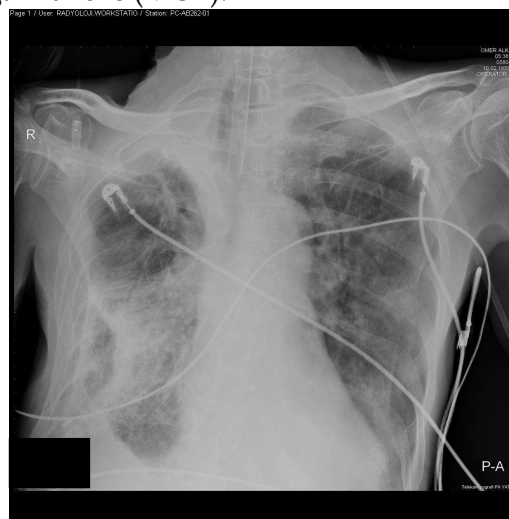


Figure 1. Chest X-ray showing extensive infiltrates and atelectasis of the right middle lobe in the right lung



Figure 2. CT scan of the thorax, showing extensive infiltrates with a loculated pleural effusion and moderate bronchiectasis, with areas of mucoid impaction, pleural thickening, atelectasis and crescent sign of the right middle lobe in the right lung

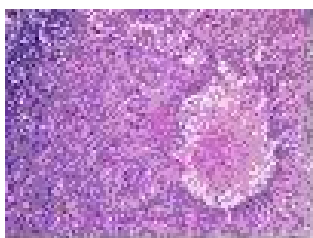


Figure 3. Fungus ball and septate hyphae of *Aspergillus fumigatus* are seen in hematoxylin-eosin-stained section

Discussion

Invasive fungal infections have started to be determined as cause of gradually increasing infection rates in non-immunosuppressed patients and patients admitted in ICU. There is a pulmonary involvement in 90% of *Aspergillus* infections, and in 70% of cases lungs are the only localization.^{2,3} It is chronic and silent, but may rarely have fulminating and fatal course. Diffuse or localized cavity or infiltrative lesion may be seen on chest X-rays.⁴ Early diagnosis and therapy of the infection having high mortality is important in cases such as SIRS, because clinical condition of the patient may show more severe course if diagnosis is delayed, and the patient may be lost from MOF. While mortality is 100% in untreated cases, this ratio has decreased to 34% in cases taking amphotericin-B therapy. Mortality is between 20%-100% in major organ involvement or in disseminated cases.⁴⁻⁶

Beginning of PA is clinically insidious, and first symptoms are generally fever, cough, respiratory failure, chest pain, weight loss and hemoptysis. Local finding may not be present in physical examination, or findings of respiratory distress and consolidation are determined.⁴ Our patient had confusion, shortness of breath, hypothermia and hypotension. The patient was admitted to ICU with the pre-diagnosis of acute respiratory failure and SIRS.

Diagnosis is generally made radiologically. Differential diagnosis includes chronic pulmonary diseases such as tuberculosis, actinomycosis, histoplasmosis, and lung cancer. These diseases may appear with persistent segmental or lobar consolidation or masses with or without an internal low-attenuation area. When

fungus ball formed, opacity belonging to ball is seen inside the cavity. When fungus ball does not fill the cavity completely, air remains between wall and ball, and this image is named air-crescent sign.³⁻⁷ Bronchoscopy with BAL is generally helpful in the diagnosis of IPA, especially in patients with diffuse lung involvement. In addition to obtaining samples for fungal stain and culture, it may also be useful in detecting *Aspergillus* antigens in the BAL fluid, and excluding other infections.^{1,3} Existence of previous tuberculosis in the private history of our patient has made us think that aspergillosis may present in diagnosis. *Aspergillus fumigatus* was determined on bronchoalveolar lavage culture obtained. Thorax CT was consistent with fungus ball and air-crescent sign located in tuberculosis cavity at the middle lobe of right lung seen on chest X-ray (Figure 1).

Although no complete consensus could be obtained in treatment of Aspergilloma up to now, conservative approaches with antifungal agents and surgical approach forms the base of therapy. Although antifungal drugs are available as the first choice in treatment of PA, eradication is rare due to the presence of residual lesions, and therefore, recurrence is potentially possible in case of a new immunosuppression.^{4,5,8} Surgical management is successfully provided by surgical excision of infected tissues in presence of *Aspergillus* sinusitis, cerebral mycetoma, infected prosthetic valve and localized pulmonary infection.^{4,8} Our patient did not have any hemoptysis, and his poor general condition and his respiratory functions being at the boundary determined our selection for conservative approach. Amphotericin-B deoxycholate, the most frequently used drug in invasive aspergillosis and the oldest one in Polyene group drugs, is an approved standard drug, and efficiency and safety of newly developed antifungal agents are determined by comparing them with it. Infusion-related toxicity or nephrotoxicity develops in 80% of cases. Two randomized controlled study on conservative approach to Aspergilloma have shown that voriconazole is better than amphotericin-B considering survival

and side effects.⁴ This also was effective for choosing voriconazole for our patient. The patient's complaints partially regressed with voriconazole therapy, but he was lost due to MOF resulted from gradually worsening septic clinic.

First findings such as fever, shivering, hyperventilation, hypothermia, skin lesions and change of conscious suggesting an infection as the cause of SIRS show the existence of complications such as hypotension, bleeding, leucopenia, thrombocytopenia, organ failure (cyanosis, acidosis, oliguria, anuria, icterus, congestive heart failure).⁹ The patient had hypothermia, tachycardia, hypotension, tachypnea and change of conscious, which were consistent with SIRS clinic.

Many factors such as underlying disease, requirement for invasive mechanical ventilation, high APACHE II score, presence of arrhythmia, development of ventilator-related pneumonia (VİP), hypoalbuminemia, hypotension requiring inotropic agent, advanced age, concomitant diseases and duration of stay in ICU influence mortality in cases with respiratory failure and in patients thought to have SIRS.⁹⁻¹² Most of these indicated factors were

present in our patient. Because our patient had an advanced age, APACHE II of 34, MODS score of 8, existence of an endocrine problem such as thyrotoxicosis, requirement for inotropic agents due to long term diastolic function disorder, presence of hypoalbuminemia, existence of previous COPD, DM and previous history of tuberculosis, we think that determination of PA infection observed in SIRS picture aggravated his sepsis and caused his death. Vasilyev et al ⁸ has reported that the lowest survival rate (46%) has been in sepsis group, which develop acute respiratory failure.

Because mortality dramatically decreases when urgent diagnosis is made and treatment is given, diagnosing whether the cause of SIRS is an infection is of great importance in SIRS patients. Despite advances in therapy, the invasive forms of aspergillosis are often associated with significant morbidity and mortality. Therefore, in diagnosis of patients presenting with SIRS clinic it should also be considered that causative factor may be aspergillus located in an old tuberculosis cavity, and this may have a fatal course in an old patient having previous pulmonary and systemic diseases.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

All authors contributed to the medical management of the patient and preparation of the manuscript. All authors have read and approved the content of the manuscript.

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