



REVIEW ARTICLE

AN AUTOPSY CASE REPORT OF DISSEMINATED INVASIVE ASPERGILLOSIS AFTER CHEST TRAUMA

Anjali Solanki, *Raveendra Sandhu, Manita Duggal and Rohit Kathpalia

Kalpana Chawla Government Medical College, Karnal, India

ARTICLE INFO

Article History:

Received 18th April, 2016
Received in revised form
20th May, 2016
Accepted 15th June, 2016
Published online 16th July, 2016

Key words:

Disseminated invasive aspergillosis,
Aspergillus flavus, Autopsy.

ABSTRACT

We present a case of disseminated invasive aspergillosis involving lung, heart and both kidneys in a 62-year old male who developed bronchopneumonia after chest trauma. Though endotracheal aspiration demonstrated presence of *Aspergillus flavus* during his hospital stay but invasive status and extent of dissemination was established only by autopsy and histopathological examination. This case report discusses the predisposing factors, pathogenesis, clinical presentation, diagnostic difficulties and course of disseminated aspergillosis. Moreover, this autopsy report emphasizes the significance of the postmortem examination to know extent of the disease in such cases and to gain insight into the pathogenesis of aspergillus infection.

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Citation: Anjali Solanki, Raveendra Sandhu, Manita Duggal and Rohit Kathpalia, 2016. "An autopsy case report of disseminated invasive Aspergillosis after chest trauma", *International Journal of Current Research*, 8, (07), 34407-34410.

INTRODUCTION

Disseminated invasive aspergillosis is a life-threatening infection, caused by a saprophytic fungi belonging to the genus *Aspergillus*. These fungi commonly exist in soil, on decaying plants and in the atmosphere. Although the main entry of the mold into the human body generally occurs via the inhalation of the conidia, an inoculation of conidia through the damaged skin is not an infrequent way of gaining access to infection. Subsequently to the primary infection, a hematogenous dissemination may occur due to the several factors, especially the immunosuppression of the host and accompanying chronic diseases. (Samdanci *et al.*, 2012) Invasive aspergillosis has been reported in patients with profound neutropenia or patients with hematological malignancies, patients receiving chemotherapy, bone marrow and organ transplant recipient and those receiving high doses of corticosteroids. However, invasive aspergillosis is rarely found in immunocompetent patients. (Raja and Singh, 2006) We report a fatal case of disseminated invasive aspergillosis caused by *Aspergillus flavus* in a 62-year old male who was hospitalized initially due to chest trauma.

*Corresponding author: Raveendra Sandhu,
Kalpana Chawla Government Medical College, Karnal, India.

Case report

A 62 year old male was admitted to our hospital with right sided rib fracture having open wound. After three days of admission, he developed high grade fever, persistent cough and progressive breathlessness. Chest radiography was performed which revealed right upper lobe consolidation. Based on his symptomatology and chest radiography findings, a diagnosis of pneumonia was made and antibiotics were started. However his condition worsened with time and patient was referred to higher centre where he was treated in intensive care unit. He was put on ventilator where he had cardiac arrest after two days and could not be revived. Salient features of general physical examination at the time of admission were: febrile (103^o F), pulse rate of 134/ min and blood pressure of 80/60 mm Hg. Respiratory rate was 42/ min and crepts were heard in right upper zone. Abdomen was soft and there was no free fluid or organomegaly. Hematological examination revealed Hb of 12.1 gm% which decreased to 7.4 gm% during hospital stay. Initial leucocyte count were 17000/cmm which increased to 24000/cmm with absolute neutrophilia. Chest X-ray demonstrated consolidation in upper lobe of right lung and pyothorax. Endotracheal aspiration was performed which showed presence of *Aspergillus flavus* by microscopic examination and culture. Blood, urine and pleural fluid cultures were sterile. HIV serology was negative. An autopsy was

performed after his demise to establish the cause of death. He had second, third and fourth ribs fractured on the right side with partial healing. On opening the serous cavities, purulent exudates was noted in both pleural cavities and 80 ml of fluid in pericardial cavity. Peritoneal cavity was within normal limits. Lungs were heavy, weighed 1850 gm and firm to feel. Overlying pleura was dull and adherent to right lung (Figure 1).



Figure 1. Right pyothorax with right lung consolidation

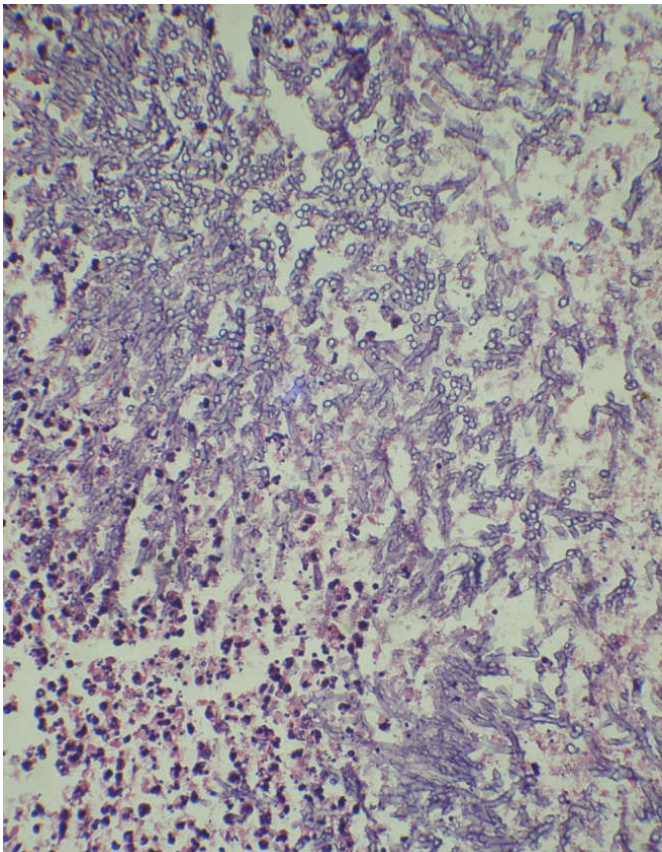


Figure 2. Histopathological examination of right lung showing bronchopneumonia and invasion by septate, acute angle branching hyphae confirming to the morphology of *Aspergillus* (H & E stain X 400)

Cut surface showed consolidation of right lung, more marked in upper lobe with formation of cavity. Microscopic examination of these areas showed confluent necrotizing bronchopneumonia with infiltrate rich in neutrophils and presence of fungal hyphae with angioinvasion (Figure 2).



Figure 3. Fungal microabscesses in the ventricular Endocardium

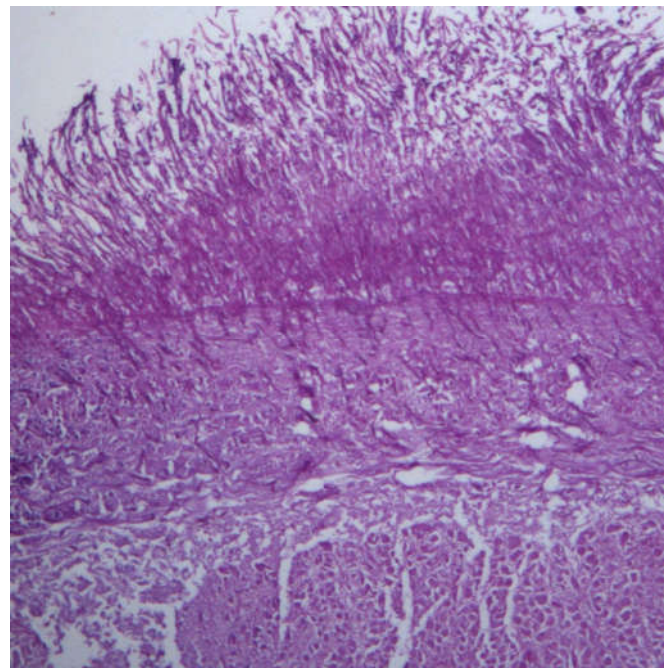


Figure 4. Endocardial invasion by *Aspergillus* (PAS stain X 100)

These fungal profiles were thin, septate with acute angle branching confirming to the morphology of *Aspergillus*. Other areas showed diffuse pulmonary edema. Both kidneys together weighed 360 gm. Capsular surface of both kidneys showed hemorrhagic areas measuring 0.5x0.3 cm to 1.6x 1.3 cm which on histopathological examination revealed dense neutrophilic infiltration and presence of fungal profiles consistent with morphology of *Aspergillus*. Heart weighed 320 gm. Petechial hemorrhages were noted over pericardial surface. Few small whitish nodules were present over the endocardial surface in the ventricles (Figure 3) which showed similar septate, acute angle branching fungal profiles microscopically (Figure 4). In addition, all the coronary arteries revealed extensive atherosclerosis. Liver weighed 1400 gm, capsular and cut surface was unremarkable. Histology showed sinusoidal dilatation with presence of inflammatory cells. There was no evidence of fungal infection. Spleen weighed 150 gm and showed red pulp congestion. Final autopsy diagnosis in this 62 year old male was kept as disseminated invasive aspergillosis involving lung, heart and kidneys.

DISCUSSION

Aspergillus is a spore-forming saprophytic thermotolerant fungus, usually found in soil, organic debris, dust and decaying vegetable matter. There are approximately 200 species of ubiquitous *Aspergillus* in the world and *A. fumigatus* is the most commonly isolated pathogen in this group. The conidia are released into the atmosphere and can easily reach the lung alveoli due to their small size (2-3 µm). The most frequent site of human infection is the lung, followed by the liver, spleen, heart, bones, central nervous system, sinuses, ear, eye, oesophagus, urinary tract and lymph nodes. (Soubani and Chandrasekar, 2002; Stevens *et al.*, 2000) Aspergillosis manifests usually in three forms: pulmonary aspergillosis (bronchopulmonary allergy or aspergillosis), a local form of disease; invasive aspergillosis, a complication of chronic lung disease; and disseminated aspergillosis. Marked neutropenia is the most common risk factor for disseminated aspergillosis. Nevertheless, patients with acute haematological malignancies receiving chemotherapy, bone marrow and organ transplant recipient and those receiving high doses of corticosteroids are at risk of developing disseminated invasive aspergillosis. Other predisposing factors include congenital or acquired immunodeficiency, diabetes, chronic granulomatous disease, cytomegalovirus infection, alcoholism and parental antibiotic therapy. (Raja and Singh, 2006) Invasive aspergillosis is an uncommon entity in immunocompetent individuals who do not have any of the above mentioned predisposing factors. In the index case, the patient had presented with rib fracture. The origin of the aspergillosis could be the wound infection by the mold which would have probably gained access from the atmosphere. The germination of the conidia that leads to invasion plays an important role in the pathogenesis of the disease. The immunity of the host is essential to prevent fungal dissemination. In our case, right lung might be primarily involved, however, prolonged hospitalization with ventilator support in terminal stage along with broad spectrum antibiotic therapy might have led to the dissemination of *Aspergillus* to other organs. A diagnosis of bronchopneumonia was established based on the clinical features of fever, cough and

dyspnoea along with evidence of consolidation by chest radiography. Furthermore, worsening symptoms of patient despite broad-spectrum antimicrobial therapy and antemortem isolation of *Aspergillus flavus* by endotracheal aspiration indicated fungal pneumonia. This case highlights the fact that aspergillosis can occur in any patients even in the absence of an immunocompromised state, corticosteroid or cytotoxic therapy and neutropenia.

The diagnosis of invasive aspergillosis remains difficult even today; a high degree of suspicion is imperative in patients with risk factors. Unfortunately, there is no single test available to establish definitive diagnosis of aspergillosis infections. However, features currently regarded as diagnostic tools in invasive aspergillosis include: 1) histopathologic evidence of disease; 2) positive culture; 3) positive CT scan or magnetic resonance imaging; 4) detection of *Aspergillus* antigen in serum; 5) polymerase chain reaction; and 6) chest X-ray.⁵ The demonstration of the presence of septate, acute, branching hyphae in the lung tissue specimen along with a positive *Aspergillus* culture from the same site provides the most robust diagnosis.³ Though the diagnosis of pulmonary aspergillosis was made during the lifetime of patient, extent of dissemination could be established only by autopsy and histopathological examination of organs. In an autopsy study of intensive care unit (ICU) patients, disseminated aspergillosis involving non-contiguous organs was demonstrated in 2.7% of the autopsies. Furthermore, similar to our patient, in each case, sputum and bronchoalveolar lavage (BAL) cultures had been positive for *Aspergillus fumigatus* after ICU admission but this was considered as mere colonization. (Dimopoulos *et al.*, 2003) It is often difficult to ascertain invasion by aspergillus before autopsy. Although aspergillosis could be treated with different kinds of antifungal drugs like amphotericin B and itraconazole, it can be fatal in a high ratio in immunocompromised patients. Hence an empirical antifungal treatment should be favoured for recovery of the patient in the presumption of aspergillosis. (Patterson, 2001) In conclusion, though disseminated invasive aspergillosis is rare in immunocompetent patients but it can be fatal if not suspected and treated appropriately in early stage. Clinical suspicion of this condition in the patients who have resistant infections despite extended spectrum antibiotic therapy even in the absence of any risk factor, is imperative for early diagnosis to revert the course of disease and to attain favorable outcome. Furthermore, if the disease is fatal, post-mortem pathological examination is essential to determine the extent of dissemination and to provide insight into the pathogenesis of *Aspergillus* infection.

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