

Invasive Mediastinal *Aspergillus* in Immunocompetent Male with Invasion of Left Atrium and Hilar Structures

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Abstract

Aspergillus is described as mould characterised by septate hyphae about 2-4 μ in diameter, it is ubiquitous in nature and spreads by inhalation of spores. It causes opportunistic infections in almost six forms namely Allergic bronchopulmonary aspergillosis, *Aspergillus* sinusitis, Cutaneous aspergillosis, Aspergilloma, Chronic pulmonary aspergillosis, Invasive aspergillosis. Invasive aspergillosis of mediastinum in an immunocompetent patient has rarely been reported. We present a case of a young male who had presented with chest pain, cough and breathlessness was later diagnosed as fulminant mediastinal aspergillosis. Incisional biopsy with histology report and endotracheal cultures helped in diagnosing mediastinal aspergillosis. Despite initiation of the right antifungal therapy and best supportive measures, patient died of septic shock and multiorgan dysfunction. This case report highlights the need for higher suspicion in such cases of mediastinal masses and early tissue biopsy which can help in reducing mortality.

Keywords: *Aspergillus*, galactomannan, heart, mediastinum, pulmonary veins, voriconazole

INTRODUCTION

Invasive pulmonary aspergillosis is known to occur predominantly in immunocompromised patients, like hematologic malignancies with ongoing chemotherapy, bone marrow, organ transplantation patients, and patients on concomitant immunosuppressive therapy.^[1] Very few case reports have been published where extension of invasive pulmonary aspergillosis to the mediastinum and proximal pulmonary arteries has been reported.^[2-4] Case reports of invasive pulmonary aspergillosis invading to the mediastinum and abetting the left atrium in an immunocompetent patient very scarcely have been reported. The present case report explains about rare occurrence of fulminant mediastinal aspergillosis in immunocompetent young male who was admitted with complaints of chest pain, cough and breathlessness. The diagnosis was difficult due to vague presentation features and inconclusive pathological evidence which consumed time. In spite of initiation of the right therapy with antifungals and other supportive measures, the patient died of multiorgan dysfunction and septic shock.

CASE REPORT

A 29-year-old male patient presented emergency room with complaints of breathlessness for 4 months, cough with white

sputum for 2 months, loss of weight and appetite for 5 months. He had shooting pain in the right side of chest for 2 weeks. His vital signs revealed blood pressure of 110/70, respiratory rate of 28/min, and oxygen saturation (SpO₂) of 90% on room air. Chest X-ray revealed cardiomegaly, pleural effusion with fissural extension, and underlying collapse on the right side with fibrotic bands in right perihilar region [Figure 1]. Total leucocyte count (TLC) count was 10,730 cells with neutrophilic predominance with other investigations within normal limits. Pleural tap of 300 ml fluid revealed exudative effusion and intercostal drain (ICD) insertion was performed. Diagnosis of lower respiratory tract infection was made and treated with intravenous antibiotics (ceftriaxone/sulbactam and levofloxacin), nebulizations, and other supportive measures. Pleural fluid analysis revealed sugars 75 mg/dl, proteins <2 g/dl, and adenosine deaminase (ADA) 4.8 u/l.

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Pleural fluid cytology showed white blood cells of 950 cells predominantly lymphocytic (95%) with reactive mesothelial cells. Two-dimensional Echo showed left atrial wall thickening with infiltration or thrombus and pulmonary vein obstruction with good left ventricle function [Figure 2]. Contrast-enhanced computed tomography (CT) chest showed homogeneous poorly enhancing soft tissue in subcarinal region indenting left atrium with partial narrowing of right inferior pulmonary vein ostium extending along the interatrial groove [Figure 3]. The encasing mass also led to partial narrowing of the right main pulmonary artery and azygous arch.

The patient underwent cervical mediastinoscopy and biopsy of 4R lymph node station under general anesthesia [Figure 4]. The frozen section was remained inconclusive. The patient's condition improved and was discharged at request on day 5 of admission with ongoing antibiotics and advised to come back for video-assisted thoracoscopic surgery (VATS) procedure due to financial reasons. He underwent VATS and incisional biopsy after 10 days under general anesthesia with one lung

ventilation and epidural analgesia. Thoracotomy findings showed hard mass encasing heart and hilar structures infiltrating left atrium [Figure 4]. Biopsy for histopathological examination and immunohistochemistry was sent and the patient was extubated and received noninvasive ventilation and oxygen (O₂) support postoperatively. The patient developed tachypnea on postoperative day 4 and was shifted back to surgical intensive care unit. Procalcitonin levels were raised (1.69 ng/ml), and D-dimer levels were within normal limits. Arterial blood gas showed partial pressure 54.5 and SpO₂ of 90% on bilevel positive airway pressure with O₂ support of 10 L. In view of respiratory distress and O₂ desaturation, he was intubated and connected to ventilator support on postoperative day 5. ET culture and sensitivity, Gram stain, fungal stain, acid-fast bacilli stain, and ET culture sensitivity were sent, and Gram-negative coverage was continued. X-ray postintubation showed left lower lobe pneumonia with basal crept bilaterally. Blood culture was negative and endotracheal secretion culture grown pseudo hyphae, hyaline septate with acute branching

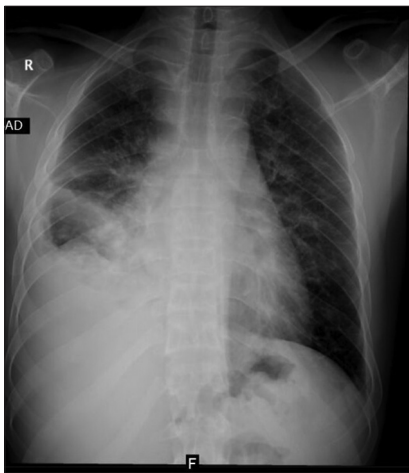


Figure 1: X-ray chest showing cardiomegaly, right pleural effusion with underlying collapse, and fibrotic bands in the right perihilar region

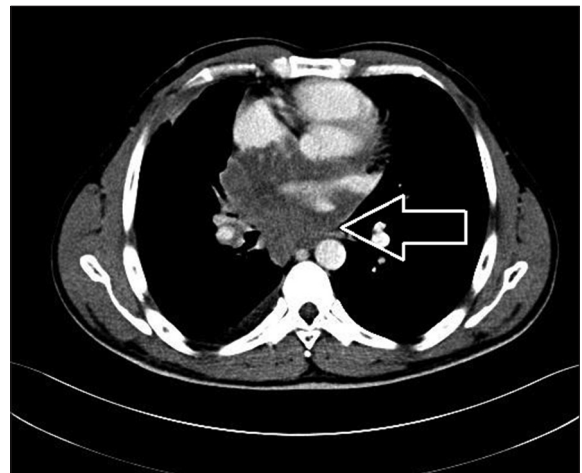


Figure 2: Contrast-enhanced computed tomography chest showed homogeneous poorly enhancing soft tissue indenting left atrium



Figure 3: *Aspergillus* mass seen in sagittal view

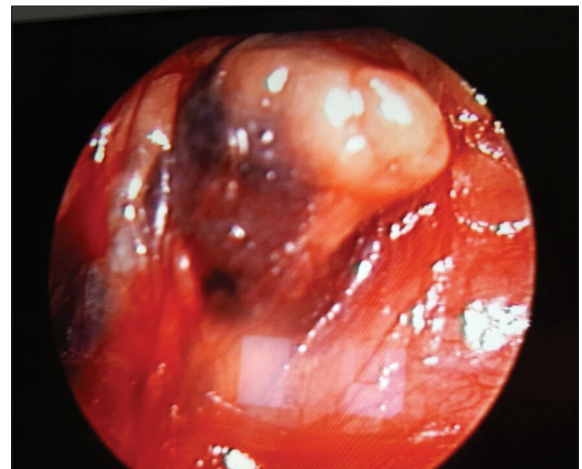


Figure 4: Cervical mediastinoscopy and biopsy of enlarged lymphnode

hyphae. He was started on voriconazole 200mg BID therapy. [Figure 5]. HPE report revealed several epithelioid granulomas accompanied by numerous multinucleated giant cells and areas of necrotising inflammation were found, few scattered acute branching fungal hyphae were noted amidst the inflammation and within the giant cells [Figure 6]. On special Periodic-acid-Schiff (PAS) and Grocotts-methenamine-silver (GMS) staining septate, elongated, slender forms of fungal organisms morphologically resembling *aspergillus* were noted [Figures 7 and 8]. Diagnosis of acute respiratory distress syndrome with invasive aspergillosis was made and treated accordingly with low tidal volume strategy [Figure 5]. The patient's condition worsened and developed septic shock with refractory hypoxemia. Serum creatinine increased to 3.1 mg/dl developing acute kidney injury and was started on renal replacement therapy in view of hyperkalemia and acidosis. The family refused to take any further treatment and left against medical advice. He expired on day 8 after suffering a cardiac arrest.

DISCUSSION

Aspergillus fumigatus is known to cause broad spectrum of diseases. Common manifestations of pulmonary aspergillosis include a benign form namely aspergilloma and a fatal form namely invasive aspergillosis.^[4] The causative factors for invasive pulmonary aspergillosis include prolonged neutropenia for more than 3 weeks, chronic granulomatous disease, high corticosteroid, posttransplantation (especially lung and bone marrow recipients), leukemia patients, cytotoxic therapy recipients, and AIDS.^[5] In aspergilloma stage, the mycelia reside in a localized cavity or on bronchial mucosa and rarely invasion into the pulmonary parenchyma occurs. When endobronchial proliferation occurs, it leads to transbronchial extension into the pulmonary parenchyma when it is termed as invasive. Further extension leads to thrombosis, emboli, hemorrhagic transformation in the vasculature.^[6,7] There have been reports of invasive aspergillosis due to accidental drowning and necrosis of the spinal cord due to disseminated aspergillosis.^[8,9]

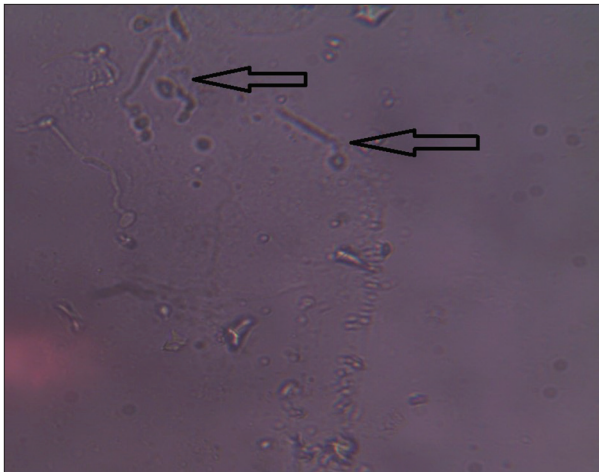


Figure 5: Endotracheal secretions showing *Aspergillus* with branching hyphae and pseudohyphae

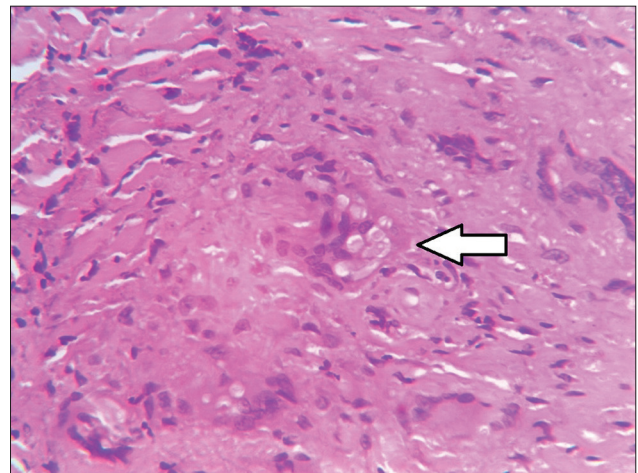


Figure 6: Histopathological examination showing multinucleated giant cells and fungal elements

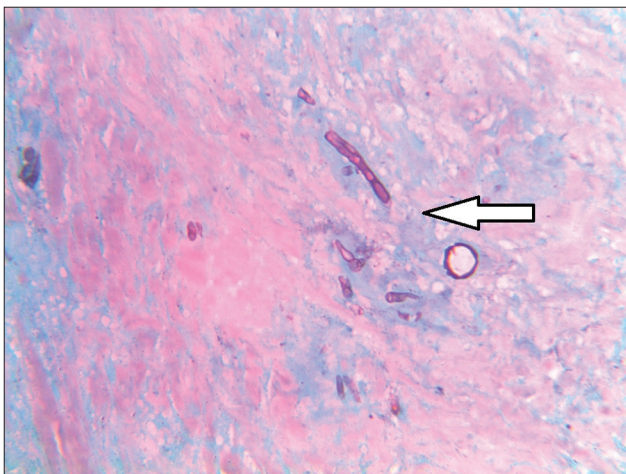


Figure 7: Grocotts-methenamine-silver staining showing septate, elongated, slender forms of fungal organisms

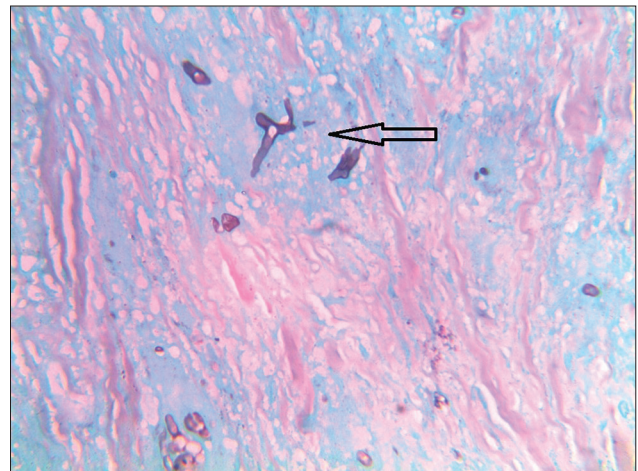


Figure 8: Histopathological examination showing *Aspergillus* elements

In our case, the absence of past medical history, absence of leukocytopenia, and inconclusive mediastinoscopy biopsy lead to lesser suspicion of a fungal infection. Exudative picture of pleural fluid with normal ADA and negative cultures lead to a stronger suspicion of malignancy. Eventually, biopsy specimen from the VATS showed abundant fungal hyphae leading to breakthrough in diagnosis. Reporting of endotracheal secretion with fungal stain as well as cultures suggestive of *Aspergillus* growth leads to conclusive diagnosis of invasive mediastinal aspergillosis.

Diagnosing mediastinal aspergillosis requires a high index of suspicion in those subsets of patients who are having risk factors as mentioned above or those having recurrent fevers despite treating with broad-spectrum antibiotic therapy. Fungal isolates from respiratory secretions obtained from a febrile granulocytopenic patient most often indicate invasive pulmonary aspergillosis, and its presence should not be dismissed as a contaminant.^[10] The galactomannan, a principal ingredient of *Aspergillus* hyphae cell membrane, is released into the blood when *Aspergillus* invades the blood vessel.^[11] Median sensitivity of galactomannan in proven cases of aspergillosis is 71% and specificity is 89% respectively. In probable cases, it was 61% and 93%, respectively.^[12] According to a study in stem cell transplant recipients, mean number of days for diagnosis of aspergillosis with galactomannan preceded fever by 3.5 days, positive chest high-resolution CT by 6 days, positive chest radiograph by 8 days, positive cultures by 9 days, and a definitive diagnosis by 14 days, respectively.^[13] We did not perform galactomannan due to lesser suspicion of aspergillosis. Mortality due to invasive pulmonary aspergillosis is high ranging from 30% to 50%, in spite of adequate treatment.^[14] The prognosis of aspergillosis with cardiac involvement is very poor, usually due to the delayed diagnosis.^[15]

CONCLUSION

This case report highlights the need for higher degree of suspicion in recognizing the clinical features of extrapulmonary aspergillosis early and providing early and aggressive appropriate antifungal treatment even in immunocompetent patients who are not responding to broad-spectrum antibiotics.

Immunocompetent host can develop fatal invasive aspergillosis. Therefore, invasive aspergillosis should not be excluded from

the differential diagnosis on the basis of immunocompetency alone.

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Conflicts of interest

There are no conflicts of interest.

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