Sudden Death in Middle Aged Woman with Invasive Pulmonary Aspergillosis

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Abstract

Invasive pulmonary aspergillosis is an opportunistic infection occurring in a background of severe immune depression and usually presented as acute non-specific pneumonia that rapidly becomes life-threatening. The development of massive haemoptysis is a major risk. This article described an unexpected death from fatal massive haemoptysis from invasive aspergillosis as the patient started to be recovered and appear well.

Keywords: Aspergillosis; Opportunistic Infection; Immune Depression; Massive Haemoptysis

Introduction

Aspergillus species are ubiquitous in nature and can affect lung in many ways: Allergic bronchopulmonary aspergillosis, invasive aspergillosis, Subacute invasive pulmonary aspergillosis and chronic pulmonary aspergillosis [1].

Invasive aspergillosis most commonly involves the lungs and optimal management involves early diagnosis and early initiation of antifungal therapy. Patient can be presented with fever, chest pain, shortness of breath, cough, and/or hemoptyis [2].

Case Report

45 year old Saudi female with history of SLE on hydroxychloroquine 400 mg daily and prednisolone 5 mg daily. Presented to ER by epigastric pain, diarrhoea 3 motions per day and generalized body aches associated with infrequent cough for past 2 days not preceded by flu symptoms without contact to sick people for last month, without history of recent travel and without contact to animals.

In ER patient was conscious, oriented, cooperative but appear ill with temperature 38°C, HR 100 beat/minute, RR 16 cycle/minute, Bp 110/70 mmhg and SO2 81% RA. Chest examination unremarkable. Abdominal Examination lax and soft without tenderness or palpable mass or organomegally. Laboratory investigations WBC 0.6 Hb 16.4 Plt 85 Cr 1.2 sGOT 1400 sGPT 340 lipase 476 amylase 124 LDH 1700 and chest x ray heterogeneous opacity obliterating right heart border with right diaphragmatic hump (Figure 1).

Figure 1: Heterogeneous opacity obliterating right heart border with right diaphragmatic hump.

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Patient admitted in ICU isolation started on ceftriaxone, azithromycin, oseltamivir, steroid pulse therapy and other supportive measures with swabbing for seasonal influenza and MERS-cov which came later +ve for influenza A and ECHO done with normal study.

**Through next week**

Throat swab revealed *Klebsiella pneumoniae* and chest examination right sided crepitation and laboratory investigations showed; MRSA -ve, blood culture -ve, urine culture -ve, *Salmonella* and *Brucella* -ve, normal level of C3 and C4, - ve HCV, - ve HBV, - ve HIV (asked by infectious disease team), - ve Rheumatoid factor, - ve Anti ds DNA, - ve anticardiolipin antibody (asked by rheumatologist) CBC showed steady decreased in HB 12.8 and improved WBC 5.6 but decreased Plt 44 So occult blood in stool requested by gastrologist and reported -ve with partial improvement in liver function sGOT 400 sGPT 200 and preserved renal function. Serial CXR show increased in opacity on right side (Figure 2) and HRCT chest done figure 3. CT brain came with impression of 2ry fahr disease and Abdominal us unremarkable except for fatty liver.

![Figure 2: Serial chest x rays show increased in the right opacity.](image)

![Figure 3: High resolution CT chest.](image)

**At 7th day**

Patient deteriorate and put on NIMV although lab panel improved (WBC 6.4 Hb 11 Plt 70 sGPT 42 sGOT 49 alb 2.5 Cr 1.2 LDH 500) with coughing of brownish plug in night while off of NIMV figure 4 and chest x ray show increased infiltration on right side with some less infiltration on left side figure 5.

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More deterioration so intubated with mechanically Ventilation and sputum culture came +ve for heavy *Aspergillus* growth so diagnosis of invasive pulmonary aspergillosis established with antifungal started. After this patient progress smoothly with regression of fever and improvement of ventilator parameters and all laboratory investigations normalized except for Hb decrease with again - ve occult blood in stool. MRI brain reported as right fronto-parietal lesions with double halo sign mostly of infectious origin tuberculoma or small abscesses. Chest x ray gradually improved figure 6. CT abdomen reported as bilateral calcified gluteal nodules with right phlebolith with lower chest cuts showed patches of consolidation more on right.
At 12th day

Antibiotics (imipenem, moxifloxacin and vancomycin), oseltamivir and steroid stopped and antifungal with oseltamivir continued by committee of consultant rheumatologist, pulmonologist and infectious disease but weaning was difficult possibly from steroid induced myopathy.

2 days later

Patient developed fever with increased chest x ray opacity figure 7 so diagnosis of VAP established and antibiotics started again (linezolid, imipenem and colistin) with septic screen requested.

Last 2 days

Urine culture revealed *Klebsiella pneumonia* sensitive to linezolid and imipenem so colistin stopped And patient swabbed again for H1N1 and MERS-COV (came later - ve) and patient look hopeful without any inotropic support or sedation with fio₂ 40% PEEP 5 P S 12 and SO₂ was 97%, HR 88, temp 36.8 Bp 130/80 with chest x ray less better figure 8 and weaning trial advised but unfortunately sudden attack of massive hemoptysis at PM shift with about 1200 ml fresh blood from ETT patient arrested and not revive.

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**Discussion**

*Aspergillus* species are ubiquitous in nature and can affect lung in many ways; Allergic bronchopulmonary aspergillosis, invasive aspergillosis, Subacute invasive pulmonary aspergillosis and chronic pulmonary aspergillosis [1].

**Invasive pulmonary aspergillosis**

Inhalation of infectious conidia is a frequent event but Tissue invasion is uncommon occurring most frequently in the setting of immunosuppression including steroid therapy [2] and when there is a high amount of airway exposure as in the setting of construction [3].

While Invasive aspergillosis most commonly involves the lungs it can disseminate beyond the respiratory tract to multiple different organs, including the skin, brain, eyes, liver, and kidneys. and most commonly are caused by *A. fumigatus* complex, followed by *A. flavus*, *A. niger*, and *A. Terreus* [4].

Patients can present with fever, chest pain, shortness of breath, cough, and/or hemoptysis and the classic triad that has been described in neutropenic patients with pulmonary aspergillosis is fever, pleuritic chest pain, and hemoptysis [1].

Invasive Pulmonary aspergillosis typically manifests as single or multiple nodules with or without cavitation, patchy or segmental consolidation, or peribronchial infiltrates with or without tree-in-bud patterns [5].

Optimal management involves early diagnosis and early initiation of antifungal therapy and the duration of antifungal therapy is dependent upon the location of the infection, the patient’s underlying disease, the need for further immunosuppression, and the response to therapy with the minimum duration of therapy is 6 to 12 weeks [6].

While three classes of antifungal agents are available for the treatment of aspergillosis: polyenes (amphotericin B lipid formulation), azoles (voriconazole, isavuconazole, posaconazole), and echinocandins (caspofungin, micafungin, and anidulafungin). Voriconazole is the main therapy for most patients and the preferred monotherapy by most of expert but For initial therapy of severe invasive aspergillosis combination therapy of voriconazole and an echinocandin is recommended and For patients who are intolerant of voriconazole due to severe reactions, a lipid formulation of amphotericin B or isavuconazole is recommended. In patients with refractory or progressive invasive aspergillosis altering the antifungal regimen (ideally changing the class of antifungal), reducing immunosuppression when feasible and surgical resection of necrotic lesions in some cases should be considered [6,7].

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Allergic bronchopulmonary aspergillosis (ABPA)

It is a complex hypersensitivity reaction in response to colonization of the airways with *Aspergillus fumigatus* that occurs almost exclusively in patients with asthma or cystic fibrosis [8] characterized pathologically by mucoid impaction of the bronchi, eosinophilic pneumonia, and bronchocentric granulomatosis [9].

Diagnostic criteria include positive *Aspergillus* skin test or detectable IgE levels against *Aspergillus fumigatus*, elevated total blood eosinophil count (generally > 500 cells/microL), elevated total serum IgE (generally > 1000 IU/mL), precipitating IgG antibodies (precipitins) to *Aspergillus*, and also specific IgE and IgG antibodies to *Aspergillus* on immunoassay, Central bronchiectasis, Expectoration of golden-brown plugs in the sputum [10-12].

While Oral corticosteroids are the mainstay for the treatment of ABPA, Itraconazole may be added in patients experiencing recurrent exacerbations despite adequate steroid therapy but The role of itraconazole monotherapy for ABPA is still not established and omalizumab could possibly have steroid-sparing alternative [13].

Chronic pulmonary aspergillosis

Includes several disease manifestations including aspergilloma, *Aspergillus nodules*, chronic cavitary pulmonary aspergillosis and Subacute invasive pulmonary aspergillosis and Almost all cases of chronic pulmonary aspergillosis are caused by *Aspergillus fumigatus*, although patients have been described with *A. niger* or *A. flavus* infection [1,4].

All patients with chronic pulmonary aspergillosis have either prior pulmonary damage or disease such as pulmonary tuberculosis, nontuberculous mycobacterial infection, allergic bronchopulmonary aspergillosis, lung cancer (following successful treatment), prior pneumothorax with associated bulla formation, chronic obstructive pulmonary disease, and fibrocavitary sarcoidosis [14-16].

The cardinal test for chronic pulmonary aspergillosis is a positive *Aspergillus* immunoglobulin (Ig)G antibody test from the serum. Elevated inflammatory markers, such as C-reactive protein and/or erythrocyte sedimentation rate, are very common in patients with chronic pulmonary aspergillosis but are not specific [17].

Subacute invasive pulmonary aspergillosis (chronic necrotizing pulmonary aspergillosis)

Occurs in immunocompromised patients with hyphal invasion of tissue is observed histologically and progressive features over one to three months. This manifestation typically occurs in patients with diabetes mellitus, malnutrition, alcoholism, advanced age, prolonged glucocorticoid use or other modestly immunosuppressive agents, chronic obstructive pulmonary disease, connective disease, radiation therapy, nontuberculous mycobacterial infection, or human immunodeficiency virus (HIV) infection [1].

Such patients usually have a single thin-walled cavity or area of cavitating pneumonia/consolidation and may have detectable *Aspergillus* antigen (galactomannan) or *Aspergillus* IgG antibodies in blood [6].

Conclusion

Fatal massive hemoptysis in patient with invasive aspergillosis is an unavoidable annoying event that should be taken in consideration even in clinically appeared good patients.

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