Case Report

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Aspergillus nidulans Fungal Infection in Lungs of an HIV Immunocompromised Patient: A Case Report

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Abstract

Pulmonary aspergillosis is a life-threatening fungal infection, particularly in immunocompromised patients. We report here a case of a 62-year-old male patient with a history of diabetes and human immunodeficiency virus, who developed *Aspergillus nidulans* fungal infection in the lungs identified by fungal culture and confirmed by MALDI TOF. The patient's *Aspergillus nidulans* fungal infection in the lungs was successfully managed with voriconazole (6mg/kg twice a day on day 1 and 4mg/kg twice a day from day 2 onwards) based treatment.

Keywords: *Aspergillus Nidulans*; Fungal Infection; Immunocompromised; HIV; Voriconazole.

Introduction

Pulmonary aspergillosis is a life-threatening fungalinfection,particularlyinimmunocompromised patients, i.e., human immunodeficiency virus (HIV) infected patients (Holding J et al, 2000). Lungs are the most common affected site by aspergillosis infection with a variety of distinct manifestations including thick-walled cavitary disease of the upper lobes, diffuse unilateral or bilateral infiltrates, ulcerative tracheobronchial disease, and obstructive bronchitis. Other much less commonly affected sites are blood, sinuses, skin, ear, bone, brain and heart [1]. Risk factors for aspergillosis include neutropenia, corticosteroid use, hematologic neoplasms, diabetes mellitus, underlying lung disease, and HIV (Holding J et al., 2000).

Aspergillosis is the most common cause of mortality in immunocompromized patients, being responsible for over one third of the associated deaths. *Aspergillus fumigatus* is by far the most frequent fungus causing these infections, however, *Aspergillus nidulans* has also been recognized (Dotis J et al., 2002).

We report here a case of an immunocompromized patient with *Aspergillus nidulans* fungal infection in the lungs who was successfully managed with voriconazole based treatment.

Case Report

A 62-year-old male presented with complaints of intermittent high grade fever with rigors, dry coughing, dyspnoea on exertion, loss of appetite and weakness since 4 days. Patients had a history of type 2 diabetes mellitus from last 8 years and HIV diagnosed 6 years back. He was receiving anti-retroviral therapy (ART) with a combination of Tenofovir + Emtricitabine + Efavirenz (TDF+FTC+EFV) since 6 years. His absolute CD4 counts ranged from 450 to 500 cell/µl in last 3 consecutive evaluations. He had uncontrolled diabetes mellitus since 2 to 3 months.

At the time of presentation, his hematological parameters were: hemoglobin (Hb): 10.1 gm/dl, total WBC count: 6800/mm^3, differential count polymorph: 63%, lymphocyte: 31%, eosinophil: 2%, monocyte: 4%, and platelet count: 128000/mm^3; peripheral smear findings were normal. Erythrocyte sedimentation rate (ESR) 1 hour was 7mm and for 2 hours was 13mm. His chest X-ray chest showed minimal cardiomegaly (Figure 1).

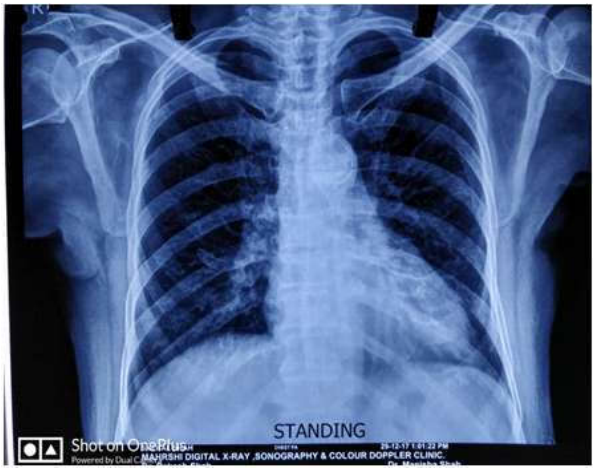

Fig. 1: Chest X-ray showing minimal cardiomegaly

The patient was initially treated with amoxycillin + clavulanic acid (625mg) 1TID for 7 days with supportive management. After 1 week follow-up, the patient presented with chief complaints of high grade fever since 1 day, loss of appetite, weakness, dry coughing, and weight loss of 2 kg in 15 days. His vitals were normal, Hb was low (9.1 gm/dl), total WBC count was 17900/mm^3; peripheral smear finding showed leukocytosis.

High-resolution computed tomography (HRCT) thorax showed scattered discrete and confluent fluffy ground glass opacities in both lungs, more marked in mid-lower zones along with few mildly enlarged discrete mediastinal nodes (Figure 2). The patient was admitted to hospital and a combination of antibiotics- pipracillin + tazobactum and moxifloxacillin were administered with supportive medication. Bronchoscopy and bronchoalveolar lavage (BAL) investigations were performed.

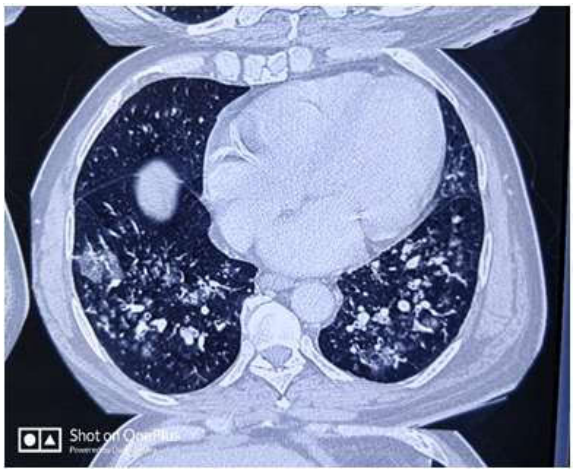

Fig. 2: HRCT thorax showing few mildly enlarged discrete mediastinal nodes in both lungs

Bronchoscopy showed signs of infective etiology. BAL for fungal culture identified *Aspergillus nidulans* infection with moderate colony counts which was confirmed by MALDI TOF mass spectrometry. Drug sensitivity is provided in Table 1.

During hospitalization, patient had complaints of low grade fever, weakness, severe dry coughing at night time and loss of sleep. His laboratory parameters were - HB: 8.2 gm/dl, total WBC count: 13600/mm^3, differential count polymorphs: 78%, lymphocyte: 17%, eosinophil: 3%, monocyte: 3%, and platelets: 181000/mm^3. His Piperacillin-tazobactum and Moxifloxacillin antibiotics were switched to Meropenem and Doxycycline with antifungal Voriconazole 6mg/kg BID on day 1 and 4mg/kg BID from day 2 day onwards. Patients' condition improved gradually, and he stabilized. His Hb was low (7.7 gm/dl) and red blood cell concentrate was given daily for 3 days (Table 2). The patient was discharged with hemodynamically stable condition and advised to continue voriconazole until follow-up (Table 2).

After 1 week, the patient was heomodynamically stable without any complaints. CBC, LFT, and uric acid levels were within the normal range, expect

Table 1: Drug sensitivity for fungus

Drug	Resistant / Susceptible	MIC Value (µgm/ml)
Posaconazole	Susceptible	0.06
Amphotericin B	Resistant	4.0
Itraconazole	Susceptible	0.12
Voriconazole	Susceptible	0.12
Caspofungin	Susceptible	0.03

Table 2: Hematological parameters

Heamatological parameter	Baseline	After 1 week	Week1 + Day 3	Week1 + Day 6	Week1 + Day 8
HB(gm/dl)	10.1	9.1	8.2	7.9	7.7
TC(cmm)	6800	17900	13600	9100	5400
Polymorph%	63	85	78	67	67
Lymphocyte%	31	12	17	26	28
Eosinophil%	2	2	2	3	2
Monocyte%	4	1	2	4	3
Platelet Count (cmm)	128000	155000	181000	216000	232000

Hb; iron correction was done. Patient continued taking Voriconazole 4mg/kg twice daily with his existing ART regimen. Follow-up examination after 2 more weeks showed improved appetite, no cough and hemodynamically stable condition with voriconazole being continued.

HRCT thorax done after a further 2 weeks showed 2-3 scattered discete nodules in both lower lobes and very faint subtle ground glass opacities in both lungs. Few subcentimeter sized discrete mediastinal nodes were observed (Figure 3). HRCT showed significant (near complete) regression of previously noted lung opacities, and reduction in size of the nodes were also seen.

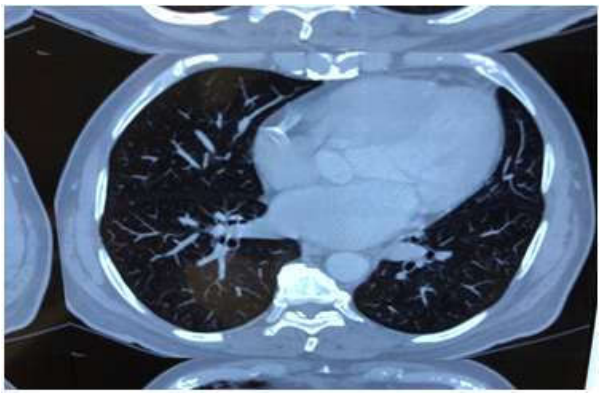

Fig. 3: Follow-up HRCT thorax showing lung opacities and reduction in size of the nodes

The patient was advised to continue Voriconazole (200mg) 2-0-1 for 15 days and then stop Voriconazole but to continue ART with strict diabetes control.

Discussion

Aspergillosis may refer to several types of diseases such as allergic disease, invasion of the upper or lower airways, skin infection, or extrapulmonary disease, which may be due to tissue invasion and hematogenous dissemination, which can lead to disseminated infection (Dias C et al, 2018). Aspergillosis occurs uncommonly among people with HIV infection, and is associated with a short survival (Holding J et al. 2000). Invasive aspergillosis is associated with a high mortality rate ranging from 30% to 90 % (Brakhage A, et al. 2005). The estimated annual incidence of aspergillus infections is 12–34 infections per million population in the United States (Richardson M et al., 2008). Of the total aspergillus infections, 35% patients are affected by aspergillus nidulans (King J et al., 2016). The incidence of aspergillosis is higher among people with severe immunosuppression (Holding J et al, 2000). Pulmonary aspergillosis occurs primarily in patients with severe immunodeficiency (Kousha M et al., 2011).

We report here a case of an immunocompromized patient with history of diabetes and retrovirus illness with pulmonary *Aspergillosis nidulans*, who was successfully managed with Voriconazole based therapy.

The Center for Disease Control and Prevention recommend Voriconazole for the treatment of invasive fungal infection (CDC, 2018). Studies have demonstrated the treatment of *Aspergillus nidulans* infection with Voriconzaole (Ulusoy et al., 2011; Yun et al., 2010). Other effective treatments for invasive aspergillosis include Amphotericin, Posaconazole, Isavuconazole, Itraconazole, Caspofungin, and Micafungin. Voriconazole has been successfully used as salvage and primary therapy, either alone or in combination with surgical debridement, and has been shown to be superior to Amphotericin in cases of disseminated aspergillosis (Patterson et al., 2016).

Ulusoy and colleagues reported the first case of peritonitis due to *Aspergillus nidulans* and its effective treatment with Voriconazole. The patient was initially treated with intravenous liposomal Amphotericin B (1 × 120mg/day) therapy 2 days after removal of the catheter. Antifungal susceptibility testing for A. *nidulans* was performed, and susceptibility to Voriconazole was detected; thus, liposomal amphotericin B was terminated and treatment with voriconazole (2 × 200 mg/day) was initiated on day 21 of therapy. No side effects were detected during treatment of voriconazole. The patient's laparoscopic peritoneal lavage sample was negative for fungal culture and Voriconazole treatment was stopped (Ulusoy S et al., 2011).

Amphotericin B has been the standard agent used for the treatment of invasive aspergillosis, particularly for life-threatening and severe infections. A recent investigation demonstrated that Voriconazole was more effective with *A. nidulans* (Yoon et al., 2010).

A recent clinical trial in patients with invasive aspergillosis, revealed that voriconazole, as opposed to Amphotericin B led to better responses and improved survival, with fewer severe side effects. In this randomized, unblinded trial, patients received either intravenous Voriconazole (two doses of 6mg/kg on day 1, then 4mg/kg BID for at least seven days) followed by 200mg orally BID or intravenous Amphotericin B deoxycholate (1 to 1.5 mg/kg/day). At week 12, there were

successful outcomes in 52.8% of the patients in the Voriconazole group (complete responses in 20.8% and partial responses in 31.9%) and 31.6% of those in the Amphotericin B group (complete responses in 16.5% and partial responses in 15%). The survival rate at 12 weeks was 70.8% in the Voriconazole group vs. 57.9% in the Amphotericin B group (hazard ratio, 0.59; 95% confidence interval, 0.40 to 0.88). Voriconazole-treated patients had significantly fewer severe drug-related adverse events, but transient visual disturbances were common with Voriconazole (occurring in 44.8% of patients) (Herbrecht R et al., 2002). In the current patient, no such events were observed. Overall, the patient had successful outcome and tolerated the treatment well.

Conclusion

Patients with HIV infection/AIDS are susceptible to *Aspergillus nidulans* infection, which can lead to disseminated disease. Voriconazole based therapy can be a useful option to successfully manage these patients.

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