Case Report

Subacute invasive pulmonary aspergillosis in a nondiabetic immunocompetent female suffering from allergic broncho pulmonary aspergillosis

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Abstract

A 55-year-old female presented with recent exacerbation of the chronic cough, dyspnea, and copious expectoration. The symptoms worsened during the winter months. In the past, she was misdiagnosed with pulmonary tuberculosis. A computed tomography scan revealed bronchiectasis changes, high attenuated mucus, and hypereosinophilia. The diagnosis of Allergic Bronchopulmonary Aspergillosis (ABPA) with subacute invasion was confirmed through bronchoscopy and fungal culture. Treatment with oral voriconazole significantly improved lung function and quality of life. This case highlights the importance of considering invasive pulmonary aspergillosis in patients with exacerbations of asthma and bronchiectasis. Early diagnosis and appropriate treatment are essential for improved outcomes in such cases.

Keywords: Aspergillus, asthma, exacerbation, HAM, invasive aspergillosis

Introduction

Subacute invasive pulmonary aspergillosis (SAIA) is a locally invasive form of chronic pulmonary aspergillosis that typically occurs in patients with some degree of immunosuppression. It has a slightly rapid progression of symptoms with a radiological pattern of nodules and consolidation. In some cases, patients having pre-existing cavities possibly containing one or more aspergillomas may develop SAIA during the disease progression.[1] Allergic bronchopulmonary aspergillosis is another pulmonary manifestation of *Aspergillus fumigatus* due to a hypersensitive response to the fungal spores.[2] Here, we describe a case of SAIA in a patient with ABPA, which is rarely observed.

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Case Report

A 55-year-old female presented to the outpatient department with a recent severe exacerbation of chronic cough and dyspnea. The episodic cough started almost a decade earlier. Cough was associated with copious expectoration and was more severe during winter. Dyspnea gradually progressed over the last 5 years.

Three years ago, the patient was diagnosed with pulmonary tuberculosis (TB) based on a chest X-ray and received 9 months of antitubercular therapy (ATT). Although there was slight relief in the cough following ATT, overall symptomatology remained the same. After completing ATT, the patient sought the opinion of another physician, who advised a computed tomography (CT) scan of the thorax. The scan revealed bronchiectasis changes in bilateral upper lobes (right > left) and the left lower lobe of the lungs. Symptomatic treatment with inhaled steroids and antibiotics was advised. There used

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to be a frequent exacerbation of cough and dyspnea. During the past year, this led to hospitalization on more than one occasion. She was taking prescribed inhalation steroids during disease exacerbations.

During the past 7-10 days, the severity of the cough increased with purulent expectoration and difficulty in breathing. The modified medical research council scale calculated severity as Grade 3.[3] There was no history of hemoptysis during the current exacerbation.

On examination, the patient was afebrile, conscious, and able to speak slowly. Her pulse rate was 112 beats per minute, and SpO_2 was 91% at room air. Auscultation of the chest revealed bilateral coarse crepitations with rhonchi. On X-ray, bilateral infiltrates were visible, along with a hand-in-glove appearance in the left upper lobe [Figure 1]. No significant bacterial growth was observed on the sputum aerobic culture. Microchip-based real-time polymerase chain reaction (Molbio Diagnostics, India) was negative for M tuberculosis. Blood investigation showed leucocytosis with hypereosinophilia (absolute eosinophil count = 2,200 cells/μL) and elevated Serum IgE (6,000 ng/mL). The blood glucose levels were within normal limits, with HbA1C <6%. Following these findings, a CT scan of the thorax was performed, which showed central bronchiectasis with a predominance in the bilateral upper lobe, along with mucus plugs and high attenuated mucus. In the left lung, "halo sign" was noted in the lower lobe, suggesting an invasion of lung parenchyma [Figure 2]. Based on the CT scan, a provisional diagnosis of subacute invasive aspergillosis was made.

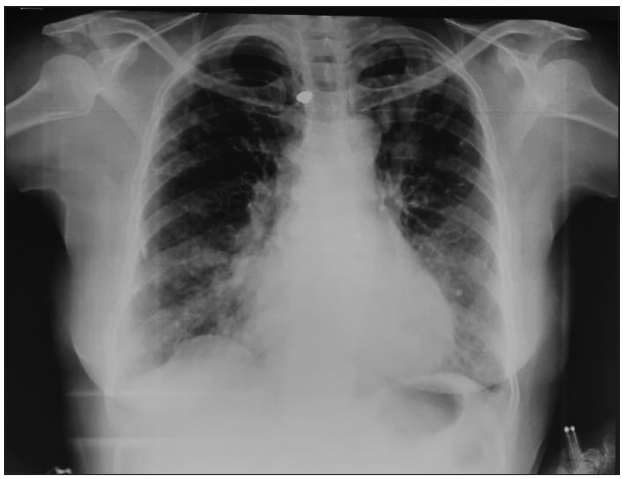

Figure 1: The patient's chest X-ray at presentation showed bilateral infiltrates predominantly in lower zones, finger in glove shadow in the left upper zone

During bronchoscopy, mucus plugs were observed in the right and left endobronchial trees. Bronchoalveolar (BAL) fluid was collected from multiple segments. On KOH examination, septate hyaline hyphae with acute angle branching were seen. The BAL fluid was inoculated on Sabouraud's Dextrose Agar and incubated at 25°C. After 4 days of incubation, greenish cottony growth was observed. Slide culture showed septate hyaline hyphae with conidia in chains and uniseriate vesicles [Figure 3]. The organism was able to grow at 44°C. Thus, *Aspergillus fumigatus* was identified based on growth characteristics, microscopy, and heat tolerance.

Based on a CT scan and KOH examination of BAL, a diagnosis of invasive pulmonary aspergillosis was made, and the patient was started on oral voriconazole (loading dose of 400 mg twice daily on day 1, followed by a maintenance dose of 200 mg twice daily). Before initiating the treatment, spirometry was performed. It revealed obstructive and restrictive defects in the respiratory cycle. After starting the treatment, lung function improved significantly [Table 1]. The patient experienced a significant decrease in dyspnea and an enhanced quality of life. Furthermore, there were no new acute exacerbations, particularly during winter.

Discussion

ABPA is caused by hypersensitivity to the *Aspergillus fumigatus* spores, and its recurrent episodes lead to bronchiectasis changes in the lung.[4] There is an estimated caseload of almost 1.4 million cases of ABPA in India, with a community prevalence of nearly 5%.[5,6] Many patients suffering from ABPA are diagnosed with pulmonary TB or have received antitubercular therapy before a diagnosis of ABPA. A prospective study observed that 46.8% of ABPA patients were initially misdiagnosed as pulmonary TB. In some instances, patients had received up to three courses of ATT.[7] Another retrospective study observed that 91% of patients with ABPA were initially diagnosed with pulmonary TB and were prescribed ATT.[8] In our case also, patient received ATT after a clinical diagnosis of pulmonary TB. However, there was no microbiological confirmation of TB before starting ATT.

Invasion of lung parenchyma is not frequently observed in ABPA. Dogra V *et al.* have reported a case in which a known

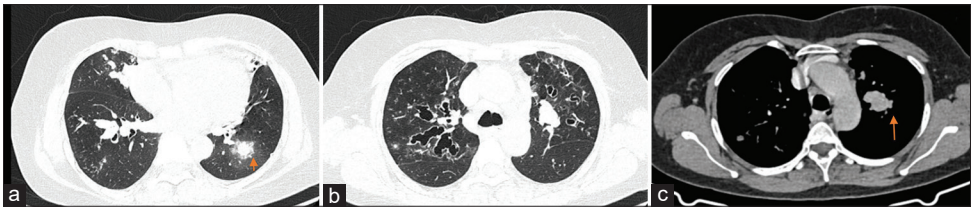

Figure 2: (a) CT thorax showing mucus-plugged bronchioles and halo sign (arrow) (b) CT thorax showing bilateral bronchiectasis and mucus plugging (c) CT thorax showing high attenuated mucus (arrow)

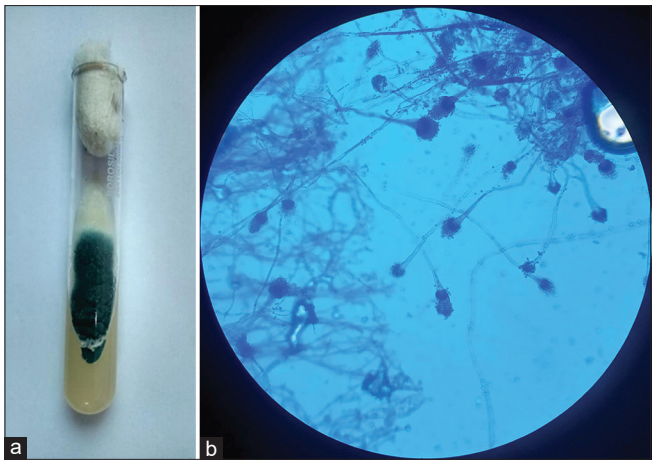

Figure 3: (a) Greenish cottony growth of fungi on SDA agar at 25° Celsius after 4 days of incubation (b) Lactophenol cotton blue mount showing septate hyaline hyphae. Conidia in chains are present on the upper one-third of the vesicle suggestive of *A fumigatus*

Table 1: Spirometry findings of the patient before and after the treatment

Parameter	Unit	Before treatment	After treatment	Change
FVC	L	1.48	2.59	1.11
FEV1	L	1.18	1.84	0.66
FEV1/FVC	%	79.73	71.04	-8.69
PEF	L/s	3.57	6.22	2.65
FEF 25	L/s	3.32	4.10	0.78
FEF50	L/s	1.37	1.77	0.4
FEF 75	L/s	0.38	0.34	-0.04

FVC, Forced vital capacity; FEV1, Forced expiratory volume in first sec; PEF, Peak expiratory flow rate

patient of APBA developed subacute invasive aspergillosis, which was treated by pneumectomy.[9] In another case, invasive aspergillosis developed in a patient who was taking oral methyl prednisolone and itraconazole for treatment of ABPA.[10] In our case, the patient's clinical course also suggests the typical natural history of ABPA, although the diagnosis was not made in the past. High attenuated mucus and bronchiectasis in the CT scan and hypereosinophilia and raised serum total IgE suggest that this patient was suffering from ABPA. The radiological finding of the halo sign and isolation of aspergillus from BAL fluid suggest subacute invasion in the lung parenchyma.

Invasive aspergillus diseases are generally more common in immunocompromised individuals, but no clear immunosuppression condition was observed in our case. Oral glucocorticoids are considered as preferred treatment in the management of ABPA. Azoles are indicated in case of exacerbation and glucocorticoid-dependent ABPA. High doses of inhaled steroids be avoided as single management.[2]

In conclusion, there is a need to look for evidence of subacute invasion in the cases of ABPA with recent exacerbation to initiate timely treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the state, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that their name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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