

*Case Report*

A Rare Triad of Aspergilloma, Allergic Bronchopulmonary Aspergillosis & Chronic Pulmonary Aspergillosis by Aspergillus Niger in an Immunocompetent Host

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ABSTRACT

Co-existence of Allergic Bronchopulmonary Aspergillosis, Aspergilloma and Chronic Pulmonary Aspergillosis is a rare presentation. We present a case of 26 yr old female patient from India who presented with worsening control of asthma for the past two years coupled with fever, cough and weight loss, all of 2 months duration. On evaluation she was found to have a rare triad of Allergic bronchopulmonary aspergillosis, Aspergilloma and Chronic Pulmonary Aspergillosis. She was put on oral prednisolone and oral voriconazole. On follow-up visits she showed considerable improvement. Co-existence of ABPA with Aspergilloma has been noted in the literature but a triad involving Chronic Pulmonary Aspergillosis should also be kept in mind while treating patients.

Key Words: Aspergillus niger, Allergic bronchopulmonary aspergillosis, Invasive Pulmonary Aspergillosis

INTRODUCTION

Aspergillus is a fungus with ubiquitous presence in the environment. It frequently produces respiratory diseases which vary in the pathogenesis and clinical manifestations. It is known to manifest in various forms, from simple colonization of the airways to Allergic bronchopulmonary Aspergillosis (ABPA) to life threatening invasive disease. ABPA is characterized by hypersensitivity reaction (Type 1 and Type 3) to aspergillus antigens whereas aspergilloma represents saprophytic growth of aspergillus in pulmonary cavities growing

as a ball of fungus admixed with fibrin, mucus, inflammatory cells, degenerating blood and epithelial cells.

Continuum between colonization and tissue invasion with aspergillus species is known and the degree of invasion, in fact, depends on the type and severity of immunosuppression. The various forms of invasive aspergillosis may be Invasive Bronchial Aspergillosis (IBA), Chronic Invasive Pulmonary Aspergillosis (CPA) and Invasive Pulmonary Aspergillosis (IPA).

Although individual forms of these named aspergillus manifestations may be seen with varying frequencies, we report a rare combination of CPA in a known asthmatic with ABPA and fungal ball in a relatively immunocompetent patient, that too associated with less common *Aspergillus niger* species.

CASE REPORT

A 25 yr old female patient, a known asthmatic for the past 10 yrs, presented to the hospital with worsening control of asthma for the past two years coupled with fever, cough and weight loss, all of 2 months duration. She gave a history of right-sided pneumothorax 6 yrs back on a hiking trip. She used Metered Dose inhaler (formoterol + budesonide) for her asthma with salbutamol inhaler as rescue medication.

Prior to her admission in this hospital, she gave a history of low grade fever, present daily for the past 2 months, not associated with chills and rigors. She complained of cough of 2 months duration associated with yellowish expectoration of around 50-70 ml daily which was foul-smelling and occasionally blood-stained. She gave history of expectoration of golden-brown mucus plugs, occasionally. She also complained of weight loss of 7 kgs in this 2 months period from 52 kgs to 45 kgs (13.5% loss).

She gave no history of anti-tuberculosis drugs in the past. She is not a diabetic or a hypertensive. There is no history of drug abuse or documented steroid intake except for her asthma medication.

In the days prior to her admission in our hospital she was investigated in other centres. Her sputum cultures yielded *Pseudomonas aeruginosa* on one occasion and *Streptococcus* on another and she received antibiotics based on sensitivity pattern but had no relief in her symptoms. Chest radiograph, done two months later,

showed development of a new cavity with air-fluid level in right upper zone. Sputum examinations for acid-fast bacilli were consistently negative.

On admission at our hospital, she was febrile and tachypnic. General physical examination revealed pallor. No lymphadenopathy or clubbing was present. On auscultation bronchial breath sounds were noticed in right upper lung fields with bilateral rhonchi.

Her chest radiographs were suggestive of right upper zone consolidation with prominent bronchial markings with volume loss on the right side with hyperinflation on the left. (figure 1). Computed tomography(CT) of the chest revealed a fungus ball in a cavity giving a typical air crescent sign with surrounding consolidation in the right upper lobe with pleural thickening.(figure 2). Presence of bilateral high attenuation mucus-filled bronchi with central bronchiectasis supported the diagnosis of ABPA. (figure 3). CT-guided fine needle aspiration yielded fungal mycelial elements with spores. (figure 4). Sputum culture yielded *Aspergillus niger*. (figure 5)

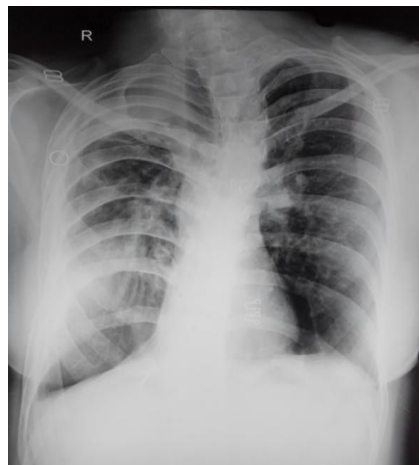


Figure 1- chest radiograph suggestive of right upper zone consolidation with prominent bronchial markings with volume loss on the right side

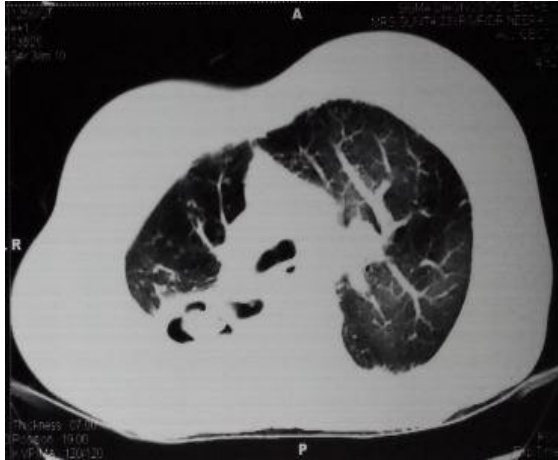


Figure 2- Computed tomography(CT) of the chest revealed a fungus ball in a cavity giving a typical air crescent sign with surrounding consolidation in the right upper lobe.



Figure 3- Computed tomography(CT) of the chest also revealed the presence of bilateral high attenuation mucus-filled bronchi with central bronchiectasis



Figure 4- Microscopic picture of Lactophenol cotton blue (LCB) mount of the isolate at 40X magnification showing the black conidial head typical of *Aspergillus niger* species



Figure 5- Colony of *Aspergillus niger* growing on Sabouraud dextrose agar showing both the white filamentous growth covered with numerous black spores

Blood investigations were significant for anemia (Hb-10.3 g/dl), eosinophilia (1200/cumm), ESR-85 mm/hr. Serum IgE levels were significantly raised (1550 IU/ml). Specific IgG against *Aspergillus fumigatus* was within normal range (12 IU/ml) probably because our patient had manifestation because of *Aspergillus niger*. Renal and liver function tests were within normal range.

Immediate cutaneous reactivity to *Aspergillus niger* was present on skin prick test. Spirometry results have revealed reversible airway obstruction on more than one occasion in the past. Fibre-optic bronchoscopy did not reveal any endobronchial lesion except congested areas of mucosa in right tracheo-bronchial tree with presence of thick secretions, which on microscopy revealed acute and chronic inflammatory cells but no organisms. She was started on oral prednisolone 40 mg per day and oral voriconazole 200 mg OD. She was asked to continue her inhalers.

DISCUSSION

Some reports suggest the development of ABPA secondary to aspergilloma^[1] and other reports suggest the vice-versa.^[2,3] In 1973, Safirstein described

a case of aspergilloma secondary to ABPA. [2] In 1980, Israel et al. described a case with brief history of asthma followed by rapid development of aspergilloma. [3] In 1989, Shah et al reported 2 cases of ABPA developing aspergillomas. [4] In 1996, Anil et al described a case of ABPA with Aspergilloma. [5] From 1956 to 1980, Jewkes et al analysed 85 patients with aspergillomas but pre-existing ABPA was found only in 10 patients. [6] Although *A. Fumigatus* is the most common species, our patient's sputum culture yielded *A. Niger* species. Sputum examination is negative for aspergillus species in upto 50% of the cases. [7]

ABPA is predominantly present in asthmatics. Various reports indicate an incidence of ABPA in upto 11% of asthmatics. [8] Difficulties arise in its diagnosis owing to the lack of single criterion and availability of standardized tests. Patterson criteria [9] was used to diagnose ABPA-S (asthma, immediate cutaneous reactivity, elevated serum IgE, eosinophilia, fixed pulmonary infiltrates) in this patient although serum specific IgG were negative for *fumigatus* as the species in this case was *A. niger*. [10]

Aspergillomas usually form in the pre-existing pulmonary cavities formed secondary to tuberculosis, pneumatoceles, sarcoidosis, pneumonectomies, hydatid diseases, bronchiectasis or emphysematous bullae. Of these tuberculosis is the most commonly associated condition. [11] ABPA itself causes cavitation in 3-14% of the cases. [12,13] The time required for aspergilloma to form may vary from a few months to more than 10 yrs. [14] Since our patient had no history suggestive for pre-existing cavity or cystic lung disease for development of aspergilloma, we suggest that the possibility of ABPA leading to cavitation and development of aspergilloma exists and should be monitored for.

Additionally such type of dual presentation throws up new therapeutic dilemmas as corticosteroids though highly effective in ABPA can theoretically worsen the status of aspergillomas as was suggested by Sharma et al in 1998. [15]

Initially it was thought that the recent deterioration of symptoms and lack of asthma control in this patient was due to ABPA exacerbation but continuous low grade fever, persistent cough, breathlessness and weight-loss inspite of adequate bronchodilator therapy along with inhaled and systemic corticosteroids prompted us to further investigate this patient. We could find a bookish clinical and radiological manifestation of CPA in this patient. These were constitutional symptoms as described above along with typical radiological finding of cavities with aspergilloma, located in upper lobe, with pericavitary infiltrates along with pleural thickening. (Fig.1)

We could also observe new cavity formation and its expansion which is, again a characteristic of CPA. (fig 2)

These clinical features along with typical radiological findings in association with positive sputum smear and culture are probably enough to arrive at a diagnosis of CPA and lung biopsy is usually not required. We were, however, able to demonstrate fungal spores, mycelia in the percutaneous fine needle aspirate from the affected right upper lobe which was probably a sufficient enough evidence for tissue invasion.

Failure to respond to adequate antibiotics as per bacterial culture sensitivity results and, repeated negative smear and culture for mycobacteria ruled out the possibility of pyogenic or mycobacterial process which may closely mimic the clinico-radiological picture described above.

CPA is characterized by an indolent clinical course with symptoms ranging from months to years in individuals with immune

status ranging from normal to mild immunosuppression. Since both angio-invasion and dissemination are absent, it is also called semi-invasive or locally invasive aspergillosis. [16] The condition requires prolonged treatment with systemic anti-fungals including voriconazole which has shown promising results as demonstrated by an efficacy of 58% in patients of chronic pulmonary aspergillosis of which 46% were post itraconazole. [17]

A triad of CPA in a known bronchial asthma with ABPA with *Aspergillus Niger* fungal ball is probably a rarest of rare combination which compelled us to report this case. We also propose to keep this condition in mind while coming across a 'difficult to treat' asthmatic patient.

By now our patient has been on oral voriconazole for two weeks. The fever has subsided and cough, breathlessness markedly reduced in severity. The resolution of symptoms with anti-fungal therapy further substantiated the diagnosis of CPA in a known case of bronchial asthma with ABPA.

CONCLUSION

Co-existence of ABPA with Aspergilloma has been noted in the literature but a triad involving Chronic Pulmonary Aspergillosis should also be kept in mind while treating patients.

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