

Case Report

BRONCHOSCOPY AIDED ENDO-BRONCHIAL INSTILLATION OF ITRACONAZOLE FOR THE TREATMENT OF ASPERGILLOMA

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INTRODUCTION

Different species of *Aspergillus* cause a broad spectrum of disease in the human host. It is found in domestic, peri-domestic and outdoor environments. Many of us breathe the spores of this fungus everyday without being affected. Aspergillosis- a disease caused by this fungus usually affects the people with lung disease or weakened immune system (www.cdc.gov/fungal/aspergillosis). The spectrum of illness includes allergic reactions, lung infections, and infections in other organs, ranging from hypersensitivity reactions to direct angioinvasion. *Aspergillus* primarily affects the lungs, causing 4 main syndromes, including allergic bronchopulmonary aspergillosis (ABPA), chronic necrotizing *Aspergillus* pneumonia, aspergilloma, and invasive aspergillosis (Barnes and Marr, 2006). However, in immune-compromised patients, the fungus may hematogenously disseminate beyond the lung, potentially causing endophthalmitis, endocarditis, and abscesses in the myocardium, kidney, liver, spleen, soft tissue, and bone (Denning, 1998). Aspergilloma may mimic a lung cancer in healthy people with an intact immune response (Yasuda *et al.*, 2013). Invasive Aspergillosis is associated with significant mortality, with a rate of 30-95% (www.jcvi.org). Chronic necrotizing *Aspergillus* pneumonia has a reported mortality rate of 10-40%, but rates as high as 100% have been noted because it often remains unrecognized for prolonged periods (www.mpoullis.com). Aspergilloma is associated with hemoptysis, which may be severe and life threatening. ABPA may cause problems with asthma control. Repeated episodes of ABPA may cause widespread bronchiectasis and resultant chronic fibrotic lung disease. Presenting symptoms is usually cough, haemoptysis that may be life threatening. The radiological findings are that of a ball like structure within pre-existing lung cavity on plain radiography and computerized tomography of the chest.

CASES

We report a case of a 63 yrs old male - farmer who was admitted in Pulmonary Medicine Department, SMKVMCH, Madagadipet, and Puducherry-105. He was presented with the complaints of breathlessness for the past 5 yrs, cough with expectoration for 5 yrs. The cough was productive and copious. There was no change with posture in sputum production. Sputum was blood stained on/ off for past 3 months (hemoptysis) otherwise mucoid in nature with no offensive odour. The patient had hemoptysis on and off for 3 months and 50 ml per episode for the past 3 days. He had also the complaint of dyspnoea for 5 yrs, Grade 2 (MRCC). He had lost weight, 5 kg in one yr. However, he did not have chest pain and fever. He was not suffering from hypertension, diabetic mellitus, and bronchial asthma but on query, he told that he had been suffering from Pulmonary TB and got treatment 2 yrs back. The patient was a known cigarette smoker for the past 10yrs, 11 cigarettes per day, Smoking index- 110, known alcoholic for the past 10 yrs. He had normal bladder and bowel habits with normal sleep patterns. General examination revealed that he was moderately built and moderately nourished with dyspnoic (grade 2), anaemic, with no cyanosis, no lymphadenopathy, no engorged veins over chest wall, no external markers of T.B, *Corpulmonale* but clubbing present (grade 2).

Examination of Respiratory System

We found the oral cavity was normal, nose-no dns, no septal hypertrophy. But we found that anterior pillar of the pharynx was congested. Trachea was shifted to left side; apical impulse was confirmed at 5th intercostal line, 2cm lateral to midclavicular line. Chest wall was symmetrical with no engorged veins and discharging sinus, etc. No spinal deformity was noticed. Chest movement rate was 16/min, thoraco-

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abdominal rhythm and pattern were normal. Chest expansion was 2cm. Anterior thoracic movements showed that left side of chest moves less than right side and the posterior thoracic movements showed that left side of chest moves less than right side. There was no tenderness over chest wall. Vocal fremitus increased in left side infra mammary, infra anterior axillary area. There were dull percussion notes over I.M.A I.A.A I.S.A. Vesicular breath sounds were normal. Bronchial breathing was tubular, decreased in left side, infra mammary, infra anterior axillary, infra scapular areas, Crepts heard over, left supra mammary, infra anterior axillary, infra scapular areas

Differential Diagnosis

There was left lingular and lower lobe consolidation suggestive of either reactivation of PTB Or Obstructive Lung Disease (OLD) or both.

Investigations

BLOOD ROUTINS

RBS- 136mg/dl

UREA- 20mg/dl

H.B- 8.0gm%

T.L.C- 7,600 cells

DIFFERENTIAL

CREATININE- 1.2mg/dl

E.S.R- ½ HALF HOUR- 70mm

HOUR- 110mm

POLY-80

LYMPHO-11

EOSINO- 09

Chest x ray showed that mid and lower zone consolidation in the left lung. Sputum investigation revealed negative for A.F.B staining for 3 consecutive days. On gram staining, plenty of inflammatory cells with gram negative bacilli were seen. In Pulmonary Function Test, both pre and post tests showed FEV1/FVC > 99 with mild air way obstruction.

The patient was provisionally diagnosed with left lower lobe consolidation with hemoptysis for evaluation. He underwent appropriate treatment as follows:

Inj. Ampicillin 500mg i.v qid

Inj. Gentamycin 60mg i.v qid

Inj. Metrogyl 500mg i.v qid

Tab. Tropic E tds

Syp. Acelast 10ml tds

Tab. Famo 20mg b.d

Tab. Calcium 500mg b.d

After a month of treatment, the patient was examined and crepts were heard over infra mammary, infra axillary and infra scapular areas in left side. Chest X ray and CT scan were taken and they revealed an intra cavity lesion, suggesting a fungal ball with consolidation on of left lower lobe, fibrotic strands in left upper and lower lobe, mild left pleural thickening and pre cranial, pre tracheal lymphadenopathy

When bronchoscopy was performed, lateral basal segment of left lobe appeared narrow, congested with profuse muco-purulent secretions in anterior, posterior, and lateral basal segments. Specimens were collected from left lower lobe, samples sent for A.F.B, gram staining, fungal.

Interventional Bronchoscopy

An appropriate and innovative treatment of bronchoscopic aided endo-bronchial instillation of itraconazole, the patient recovered well and discharged with an advice of continuing oral itraconazole for three months.

DISCUSSION

Aspergilloma, commonly referred to as “fungus ball,” occurs in pre-existing pulmonary cavities that were caused by tuberculosis, sarcoidosis, or other bullous lung disorders and in chronically obstructed paranasal sinuses. The diagnosis of aspergilloma usually requires clinical, radiological, and serological evidence. Pulmonary aspergilloma frequently complicates an existing cavity that was due to tuberculosis in most of the cases. Most patients of pulmonary aspergilloma are asymptomatic. Hemoptysis and dyspnoea with or

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without cough and fever (50-80%) were the usual and major symptoms in our case similar to other reports (Baradkar *et al.*, 2009). Most frequently, internal bleeding occurs, but hemoptysis may be massive and even fatal. Malaise and weight loss are additional symptoms. Aspergillomas are not static lesions. They may decrease, increase or remain stable in size and only <10% of cases may lyse.

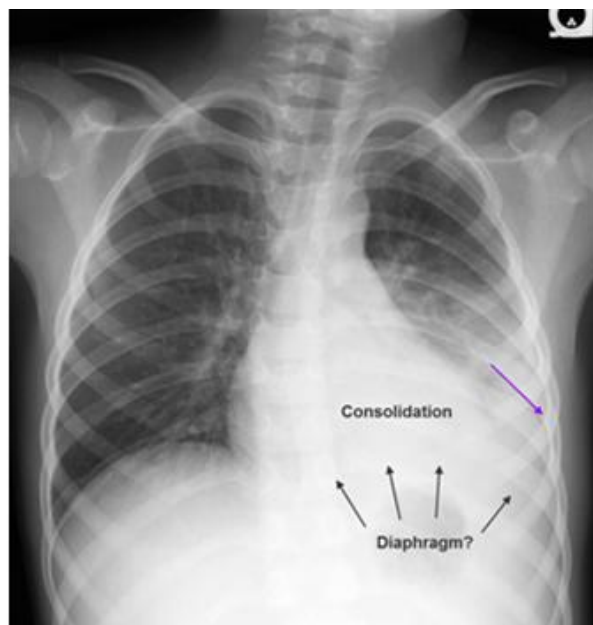


Figure 1: X –ray chest showing mid and lower zone consolidation in the left lung



Figure 2: X –ray chest showing the left lung after one month of treatment

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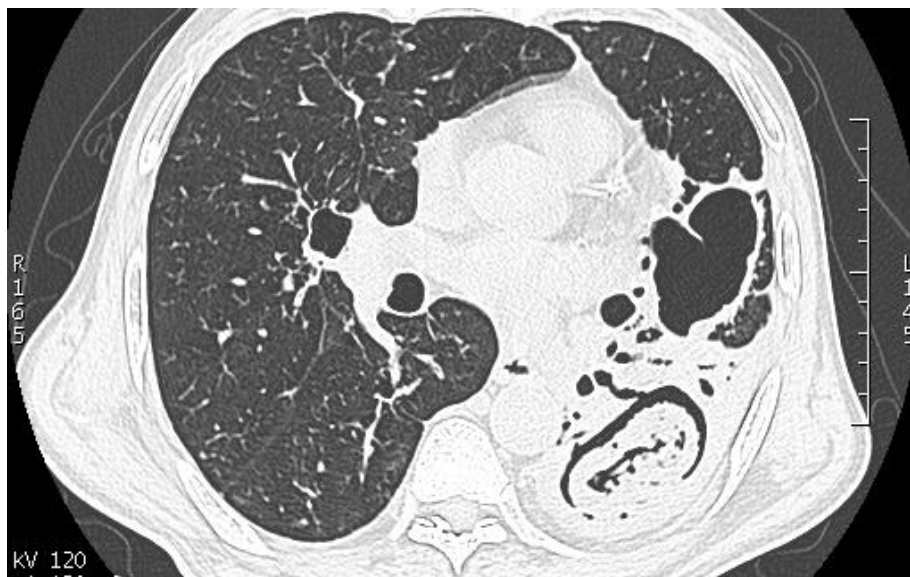


Figure 3: CT scan of the chest showing the cavitary lesion in the upper lobe of the left lung

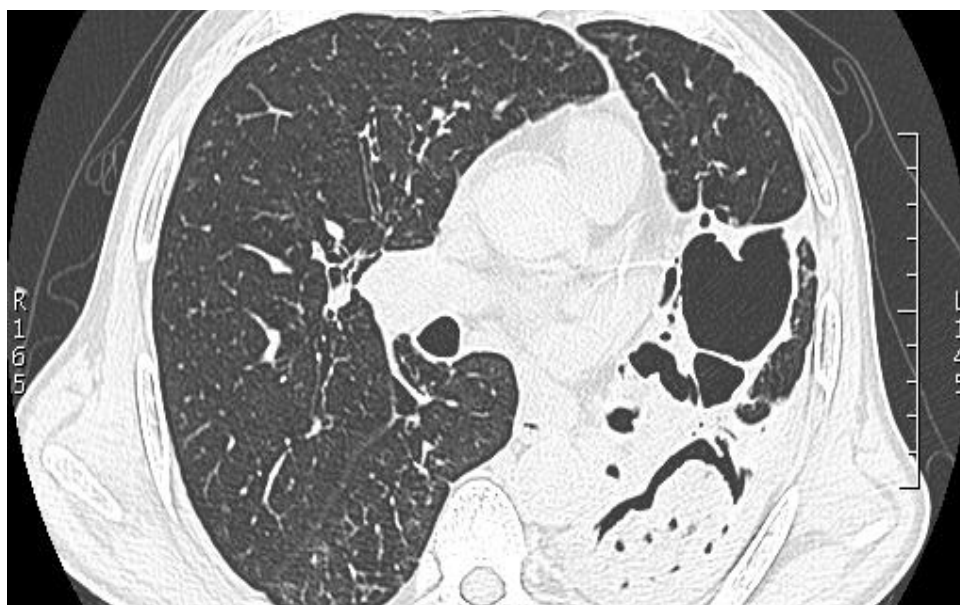


Figure 4: CT scan of the chest showing the cavitary lesion in the upper lobe of the left lung

Diagnosis is based on radiological findings, like radiological opacity with air crescent sign is of specific importance. Usually the size of the cavity is bigger than the ball which forms a rim of air around most of the part of the ball (Denning, 1998). CT scan is considered to be more accurate technique than conventional chest radiograph in defining fungus balls, particularly in fibrotic and distorted lung fields (Roberts *et al.*, 1987).

Definitive treatment of aspergilloma is surgical resection that frequently accounts for high morbidity and mortality. Further, the surgical treatment of pulmonary aspergilloma is challenging and controversial. Promising medical treatments are available with a lot of regimens and it includes amphotericin B; sodium or potassium iodide, itraconazole and fluconazole. Itraconazole is an orally active anti-fungal triazole. It is less toxic with higher tissue penetration and in vitro activity against *A.fumigatus* than amphotericin B. The

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antifungal triazoles target ergosterol biosynthesis by inhibiting the fungal cytochrome P450–dependent enzyme lanosterol 14- α -demethylase, resulting in altered cell membrane function and cell death or inhibition of cell growth and replication. The triazoles also inhibit cytochrome P450–dependent enzymes of the fungal respiration chain. Although some isolates of *A. fumigatus* have been found to be resistant to itraconazole, resistance to the anti-*Aspergillus* triazoles has been unusual thus far; however, recent studies suggest that the rate may be increasing (Walsh *et al.*, 2008). Though the success of trans-cavitary instillation of anti-fungal drugs may not be consistent in some cases (Kay, 1997), the bronchoscopy guided endobronchial instillation of itraconazole in our case tendered a successful recovery of the patient.

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