



# Evolution of Diagnosis from Tuberculosis to Dual Fungal Infection

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## Abstract

Invasive mold infections are not only seen in immunocompromised but also common in immunocompetent individual. The rate of fungal infections is rising because of wide spread use of antibiotics, immunosuppressant and certain environmental factors. The availability of fungal biomarkers like galactomannan, beta D glucan has helped in the early diagnosis of fungal infections. Early clinical suspicion and appropriate use of biomarkers with tissue diagnosis allow us to select appropriate antifungal therapy. We present a case of young individual from India presented with pneumonia which initially thought to have tuberculosis later diagnosed with dual fungal infection.

## Case Presentation

A 35-year male patient, who was a known case of non-cirrhotic portal fibrosis, had chronic diarrhea since 2006. He underwent colonoscopy in 2013 which showed ulcerative colitis and steroids were started for the same. He was admitted elsewhere with continuous fever, weight loss of 15 kg over one month and recent onset of hemoptysis. Sputum culture grew ESBL *E. coli*. CECT chest revealed left lower lobe consolidation with ground glass appearance and moderate right side pleural effusion (Figure 1). Bronchoscopy and BAL (Bronchoalveolar Lavage) fluid was taken. BAL fluid bacterial and fungal culture was negative. GeneXpert MTB/Rif and TB MGIT culture were also negative. However, BAL Galactomannan (GM) was 3.9 Optical Density (OD). IV meropenem and

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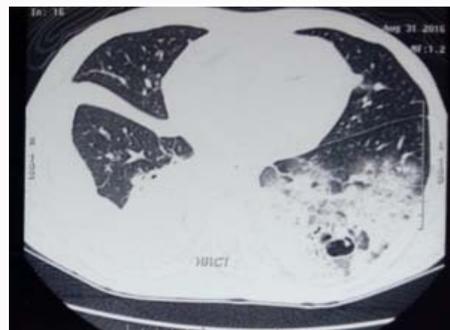


Figure 1: Pleural effusion.

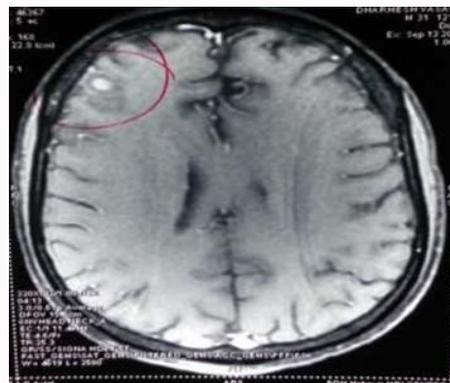
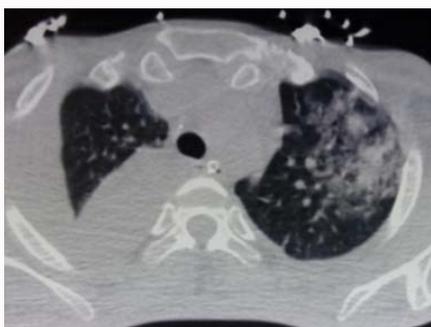


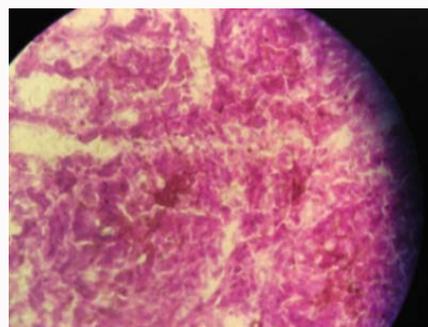
Figure 2: Anterior frontal cortex.

**Table 1:** Modified ATT.

Differential diagnosis	Points in favor	Points against
Pulmonary TB (Susceptible)	Continuous fever, weight loss, hemoptysis	Sputum GeneXpert negative BAL GeneXpert negative although there were gross radiological findings
MDR (Multi-Drug Resistant) TB	Disease progression while on 1st line ATT	GeneXpert and MGIT culture both were negative for TB.
Pneumonia due to <i>E. coli</i>	Sputum positive for <i>E. coli</i>	Sub-acute presentation unlikely Ground glass appearance is less likely <i>E. coli</i> is a very rare cause of pneumonia
Probable Invasive Pulmonary Aspergillosis (IPA) (EORTC/MSG criteria)	Host factor—Chronic liver disease, critically ill, prolonged steroids Positive BAL GM	Classical radiological features are not present (halo sign, dense nodule, and cavitation). However, this is well described only in neutropenic host



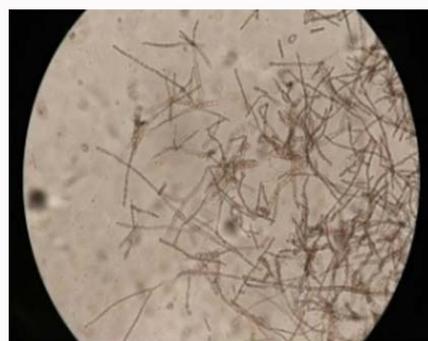
**Figure 3:** Right side pleural effusion.



**Figure 5:** Thin septate fungal.



**Figure 4:** Midline shift.



**Figure 6:** Dematiaceous fungus.

standard weight-based 1<sup>st</sup> line Anti-Tubercular Treatment (ATT) was started. After 3 days of starting ATT, he developed headache followed by convulsion. Initial CT brain imaging was unremarkable. Later MRI brain was done which showed a small disc enhancing lesion in anterior frontal cortex (Figure 2). At this time ATT was modified to moxifloxacin, ethambutol, ethionamide, PAS and amikacin. No improvement occurred on modified ATT and the patient was shifted to our institute for further management (Table 1).

CT scan chest was performed which showed left upper lobe consolidation, resolution of left lower lobe consolidation and moderate right-sided pleural effusion (Figure 3). BAL was repeated. BAL fluid bacterial and fungal culture was negative. GeneXpert was also negative for TB. BAL GM index was 3.9 OD. Probable IPA (Invasive Pulmonary Aspergillosis) was diagnosed as per EORTC/MSG criteria (susceptible host, compatible clinico-radiologic syndrome and positive biomarker test). ATT and steroids were stopped and L-AMB (Liposomal Amphotericin B) and liquid

Posaconazole were started. Voriconazole was avoided in a view of liver dysfunction (child Pugh-C). After 3 days of starting treatment patient developed headache and became irritable. MRI brain revealed large lobulated, mixed intensity lesion in right frontal lobe with significant edema and midline shift, few surrounding satellite lesions were also seen (Figure 4). MR spectroscopy showed marked elevated lipid lactate peak. Decompressive craniotomy and evacuation of the abscess was done. Histopathology of intra operative specimen showed thin septate fungal hyphae with brown pigment (Figure 5) and fungal culture grew *Cladophialophora bantiana* which is a dematiaceous fungus (Figure 6). The diagnosis of IPA was reviewed to consider whether *Cladophialophora bantiana* could be the etiological agent of the lung lesion which has been rarely reported in literature. Although GM crosses positivity has been seen with dematiaceous fungi like *Exserohilum rostratum*, it is not known to occur with *C. bantiana*. Based on this we conferred that GM positivity in this patient was due to IPA. Dematiaceous fungal brain abscess ideally needs triple therapy with amphotericin-B, voriconazole, 5FC or alternatively amphotericin-B, Posaconazole, 5FC. However, the patient developed diarrhea with 5FC and serum Posaconazole level was sub therapeutic

probably due to poor absorption. 5FC and Posaconazole were stopped and voriconazole was started. Despite aggressive management the patient died due to gram negative sepsis.

## Discussion

COPD, liver cirrhosis, critical illness, mechanical ventilation are emerging risk factors for IPA [1]. Classical radiological features are well described in neutropenic, however radiological picture of aspergillosis in the non-neutropenic host is variable and may resemble pulmonary TB leading to diagnostic confusion and empiric Anti-Tubercular Treatment (ATT) [2]. However, a negative GeneXpert negative in the patient with gross radiological finding goes against TB. Availability of galactomannan has greatly revolutionized the diagnosis of IPA. The cutoff for BAL GM is still debated, but an Optical Density (OD) of less than 0.5 virtually rules out the diagnosis of IPA, while a value of more than 3 has near 100% specificity [3]. Positive GM in patients with dematiaceous fungal infection like should raise the possibility of concomitant invasive aspergillosis [4]. In immunocompromised patient simultaneous dual infection can occur. In this type of patient, tissue diagnosis is very useful [5].

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