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Common Misleading Presentation with an Uncommon Cause Cryptococcal Pneumonia

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Abstract:
A 52-year-old male patient presented with chronic cough, expectoration, fever and loss of appetite of 6 months duration. Radiological diagnosis of right lower lobe pneumonia was made based on chest x ray. On investigating, the gram stain and sputum culture were negative for pathogenic organism. Sputum AFB and CBNAAT were also negative. His immune status was normal. Bronchoscopy was done and revealed narrowing of right upper lobe bronchus. CECT chest showed soft tissue lesion with solid and cystic attenuation in right lower lobe. CT GUIDED FNAC was done and showed macrophages with epithelioid cells and ill formed granulomas. He was then started on trial of CAT 1 ATT based on presumptive pulmonary TB diagnosis. After one month patient came back with worsening of symptoms. There was increased opacity radiologically and later CT guided biopsy was done, suggestive of cryptococcal species. ATT was stopped and patient started on oral fluconazole 4oomg once daily for 4 months and reviewed.
Observation - There was both radiological and clinical improvement in the patient's condition.
Keywords: Cryptococcus, immunocompetent, fluconazole, FNAC.

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I. Introduction:

Cryptococcosis is an invasive fungal disease that occurs throughout the world. Immunocompromised patients are at increased risk of severe and or disseminated pulmonary infection, but it is rare to occur in immunocompetent host.

There are no sufficient & accurate data regarding management of pulmonary cryptococcosis in immunocompetent patients. Available articles recommend oral fluconazole for patients with mild to moderate symptoms and amphotericin B + flucytosine followed by fluconazole for disseminated and severe disease. It is not clear if patients who have histological evidence of Cryptococcus neoformans, cultures negative will respond to drug treatment. We evaluated and managed a patient whose presentation and course raised important questions regarding atypical presentation, antifungal choices, duration of therapy and resolution of clinical, serologic and radiographic findings.

CASE PRESENTATION:
A 52-year-old patient from Kamhili (Andhra Pradesh) who works near coconut trees came with chief complaints of cough for 1 year, fever for 8 months and loss of appetite and weight (10 kg) for 8 months.

History: His symptoms initially started as dry cough, later associated with expectoration which is white, mucoid, non-foul smelling. There are no postural or diurnal variations. He had low grade fever intermittent, associated only with chills; no rigors, not associated with sweating. He lost almost 12 kg in 1 year.

Initially he was treated for pneumonia by a local RMP. His symptoms didn't subside and he went to a private hospital in Visakhapatnam where it was diagnosed as right upper lobe pneumonia and was treated with antibiotics. (Inj. CEFOPERAZONE 1 g i.v.BD). His symptoms didn't relieve and was referred to GHCCD, Visakhapatnam.

This case was treated as right upper lobe unresolving pneumonia. His routine lab investigations were normal. HIV testing was negative. No other co morbid conditions were present. PTB was ruled out by performing sputum AFB, 24-hour sputum and sputum CBNAAT.

Hemoglobin	11.1g/dl
Wbc	17340cells/cu mm
Smear for malaria parasites	negative
Serum electrolytes	Na+ 134meq, K+ 4meq
platelets	2.4 lakhs /cu mm
LFT	SGPT-18U, SGOT-24U, ALKP-19U
HBSAG, HIV, HCV	NON-REACTIVE
RFT	S. CREATININE - 0.9 B. UREA-24mg/dl
RBS	124mg/dl

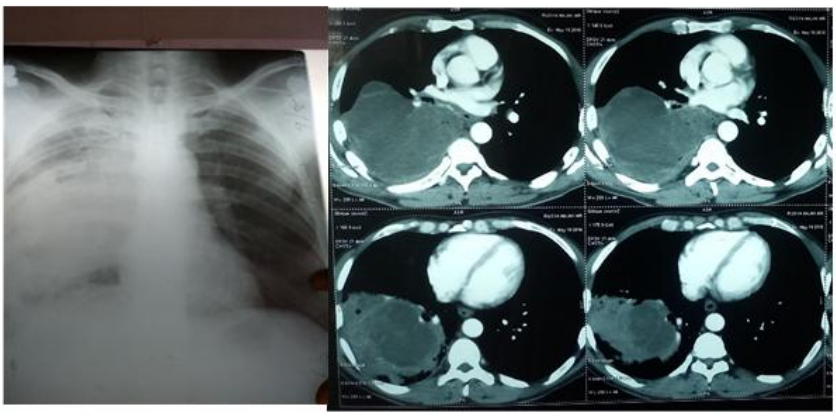
INTERVENTION:

Bronchoscopy showed normal study and BAL CBNAAT was negative. BAL culture was consolidation. His CECT chest showed a large 8.6 x 6.4 cm lesion with heterogeneous enhancement with cavities in superior segment of right lower lobe (FIG 1). Multiple tree in bud appearances in right upper lobe and superior segment s/o endobronchial infection.

CT guided TTLB was performed from the lesion site and was sent for HPE. It showed chronic inflammatory cells comprising of macrophages and lymphocytes. No evidence of malignancy was noted. He was then started on trial of ATT in view of pulmonary TB (radiological evidence) and was discharged.

At follow up after 2 months, patient was admitted in hospital with increasing symptoms. Chest X ray showed increase in opacity involving right upper and mid zones. CECT chest was done again and it showed a moderately large soft tissue lesions with solid and cystic attenuation with septations in right lower lobe extending into right upper lobe, GGOs in right lower lobe. There was moderate narrowing of right upper lobe and lower lobe bronchus with calcified mediastinal lymphadenopathy. Lesions increased in size when compared to previous CT.

FIG 1: RADIOLOGY –(A) CHEST X RAY PA VIEW showing right lower lobe heterogenous opacity, (B) CECT chest showing 8.6 x 6.4 cm lesion with heterogeneous enhancement with cavities in superior segment of right lower lobe



(A) (B)

FIG 2: Histopathological examination of lung biopsy showing local collection of foamy macrophages with round bodies and double layer formed of hyaline membrane and basophilic cell wall s/o fungal aetiology – cryptococcal species: H&E stain

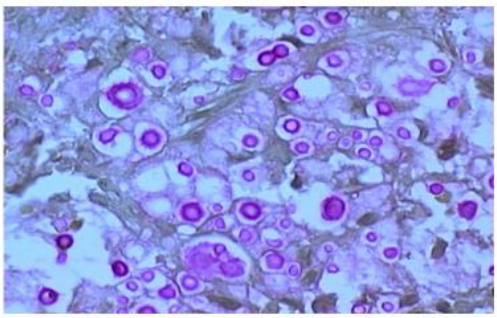
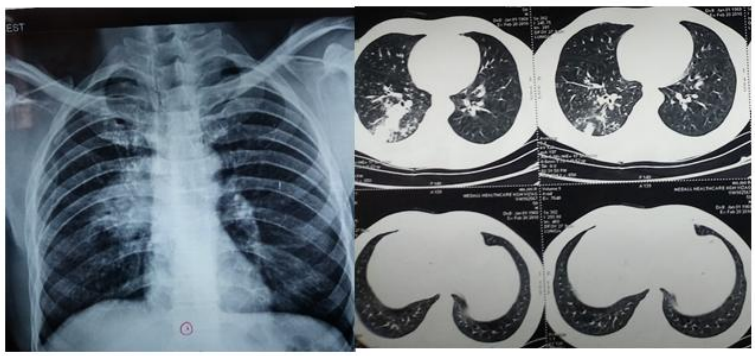


FIG 3: RADIOLOGY- (A) CHEST X-RAY PA VIEW, (B) CT CHEST LUNG WINDOW Showing resolution after 4 months of oral fluconazole therapy.



(A) (B)

CT guided TTLB was performed again and was sent for HPE. It showed foamy macrophages with plasma cells, lymphocytes and few eosinophils with ill formed granulomas. ZN staining did not show any AFB.IHC for cytokeratin, TTF-1 was negative.

Finally, biopsy was repeated using USG and the tissue was sent for HPE. It showed a local collection of foamy macrophages with round bodies and double layer formed of hyaline membrane and basophilic cell wall s/o fungal etiology – cryptococcal species (FIG 2).

Patient was started on fluconazole 400 mg OD for 6 months on 20 july,2018.
After starting fluconazole, the symptoms improved and CXR and CT chest showed resolution of the lesion (fig 3).

II. Discussion

Though lung is the most common portal of entry for cryptococcal infections, cryptococcal pneumonia is an uncommonly diagnosed disorder. In one study of 1491 patients diagnosed with cryptococcosis, a total of 58 (4%) presented with pulmonary disease and only 12 (0.8%) were not HIV-infected [i]. Also, among non-immunocompromised subjects, Nadrous et al [ii] reported that 36 (86%) of 42 patients with cryptococcal infection, in contrast, had isolated pulmonary involvement. Approximately 30% of the patients with pulmonary cryptococcosis are asymptomatic. Of the remainder, one-half have cough or chest pain, 32% have sputum production that is bloody 18% of the time. There are no updated or recently obtained guidelines for the management of pulmonary cryptococcosis in either the immunocompromised or immunocompetent patient. On the evidence of available retrospective series and previous case reports, guidelines have been published that recommend to use oral fluconazole for 6 to 12 months for patients with mild to moderate symptoms and amphotericin B plus flucytosine for minimum 4 weeks followed by an 8-week consolidation course of fluconazole for CNS manifestation and disseminated form [iii].

III. Conclusion:

In conclusion, we believe that patients with proven or probable cryptococcal pneumonia, whether symptomatic or not, should at least receive a single course of antifungal therapy. The guidelines of the IDSA for the treatment of pulmonary cryptococcosis in immunocompetent patients along with the evidence from previous literature [iv] can be summarized as follows:

Oral fluconazole 400 mg/day for 6–12 months for mild/moderate illness. Severe disease - cryptococcal meningitis (i.e., amphotericin B deoxycholate, 0.7–1.0 mg/kg IV + flucytosine 100 mg/kg per day in four divided doses over four weeks; followed by fluconazole 800 mg daily for eight weeks; then fluconazole 200 mg daily for six to twelve months). Itraconazole or voriconazole 200 mg twice daily might be given if fluconazole is contraindicated or resistance has developed.

Orally, take 400 mg posaconazole twice a day. For persistent radiographic abnormalities and symptoms that do not respond to antifungal medication, surgery is a rare alternative.

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