Chronic Cavitary Pulmonary Aspergillosis: Complication of Pulmonary Tuberculosis

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ABSTRACT

Pulmonary Aspergillosis is a fungal infection of the lungs that can lead to invasive disease and the formation of cavities, especially in the immunocompromised population. The most common clinical features are no symptoms at all to fever, cough, nondescript chest discomfort, trivial hemoptysis, and shortness of breath. Most patients respond well to Itraconazole therapy. Pulmonary Tuberculosis is one of the conditions that can lead to Aspergillosis, especially in cavities that are formed by Mycobacteria; both often manifest with similar clinical features and lead to diagnostic error. We present a case of a 28-year-old male diagnosed with pulmonary tuberculosis who developed symptoms of persistent cough, hemoptysis, increasing fatigue, and weight loss despite compliance with antitubercular therapy. Ultimately diagnosis of Cavitary pulmonary aspergillosis was made on clinical, laboratory, and radiological grounds. In a patient presenting with worsening symptoms of tuberculosis, there should be a suspicion of aspergillosis, necessitating the performance of standard fungal infection investigations.

Keywords: Immunocompromise iosts; lung cavity; pulmonary aspergillosis; tuberculosis.

INTRODUCTION

Aspergillus is a ubiquitous fungus, and causes an illness called "aspergillosis' usually via inhalation of infectious conidia. Aspergillosis may include allergy, pulmonary invasion, cutaneous infection, or extrapulmonary dissemination. The spectrum of pulmonary aspergillosis ranges from allergic to chronic and acute invasive pulmonary aspergillosis. Chronic aspergillosis further encompasses simple aspergilloma, chronic cavitary pulmonary aspergillosis, chronic fibrosing pulmonary aspergillosis, aspergillus nodules, and semi-invasive aspergillosis.2

Chronic Pulmonary Aspergillosis can be considered an underlying factor in smear-negative tuberculosis and a potential contributor to tuberculosis treatment failure.3 It may also mimic pulmonary tuberculosis itself as smear-negative or "clinically diagnosed" tuberculosis.4

Diagnosis rests on a combination of radiological examination, histopathology, and detection Aspergillus IgG in serum and isolation of the fungus from the respiratory tract. 5 We report a case of chronic cavitary pulmonary aspergillosis seen as a complication of pulmonary tuberculosis in a patient receiving treatment for the underlying tuberculosis.

CASE REPORT

A 28-year-old male from rural Nepal was diagnosed with pulmonary tuberculosis four months back when he presented to a local health center in Myagdi district with one month of low-grade fever, cough, and weight loss. He had GeneXpert positive for tuberculosis in sputum with rifampicin sensitivity. The intensive phase of antitubercular therapy was started as per national protocol which included three tablets of HRZE daily with each tablet comprising isoniazid 75 mg, rifampicin 150 mg, pyrazinamide 400 mg, and ethambutol 275 mg. In one month's follow-up, he was afebrile, had decreased cough, and had gained weight. In two months follow-up, he reported an increase in his cough with productive sputum in the last month. However he had acid-fast negative sputum smear microscopy and negative sputum GeneXpert, hence treatment was changed to the consolidation phase (three tablets of HR daily to be given for four months).

There was no history of shortness of breath, fever, chest pain, swelling of limbs, paroxysmal nocturnal dyspnea,

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or orthopnea. He smoked one pack of cigarettes daily for nine years but did not consume alcohol. General and systemic examinations revealed no significant abnormality

Laboratory investigation findings have been shown in Table 1 below with a normal reference range.

Tale 1. Laboratory investigation findings.		
Laboratory Parameters	Patients laboratory value	Reference range
Haemoglobin	11.6gm/dl	13.5 - 17.5 gm/ dl
Total WBC Count	7,600 cells/mm3	4500-11000 cells/mm3
Neutrophils	63%	54- 62%
Lymphocytes	24%	25- 33%
Eosinophils	06%	1-3%
Monocytes	07%	3-7%
Basophils	0%	0-0.75%
Random Blood Glucose	88mg/dl	<140 mg/dl

Urine R/E: Within normal limits

Sputum for Acid Fast Bacilli: Negative on two early morning samples taken 24 hours apart.

Mantoux test: Wheal size <5mm

GeneXpert MTB assay test: Negative

Serum IgG for Aspergillosis: Positive

His chest x-ray showed bilateral cavitary lesions (figure 1). A chest CT scan (figure 2) was then performed which showed bilateral cavitary lung lesions with endobronchial spread of infection with right middle lobe consolidation and left lung cystic bronchiectatic changes.

The diagnosis of chronic cavitary pulmonary aspergillosis complicating pulmonary tuberculosis was made and the patient was started on itraconazole 200 mg twice daily in addition to ongoing antitubercular therapy. His symptoms improved over one month. He reported a marked reduction in fatigue, a gain in appetite and weight, and a decrease in cough. Three months later, he was asymptomatic; a repeat chest x-ray showed a marked reduction in the cavity size, and antitubercular therapy and itraconazole were stopped.



Figure 1. Chest x ray findings showing bilateral cavitary lung lesion suggestive of cavitary aspergillosis.

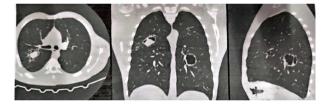


Figure 2. CT Chest showing Bilateral Cavitary Lung Lesions suggestive of Aspergilloma with endobronchial spread of infection with Right Middle Lobe Consolidation and Left Lung Cystic Brochiectetic changes.

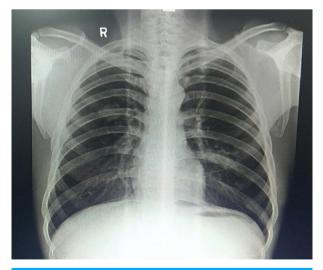


Figure 3. Chest x ray on follow up visit showing marked reduction in cavity size.

DISCUSSION

Our report describes a person with pulmonary tuberculosis who developed cavitary pulmonary aspergillosis as a complication along the course of illness. Pulmonary aspergillosis can mimic pulmonary tuberculosis and thus can be misinterpreted .4 In both of them, patients may be asymptomatic or may present with fever, cough, nonspecific chest discomfort, hemoptysis, and shortness of breath. A study done in India reported 30.7% of aspergillus species among fungal isolates obtained from the sputum of pulmonary tuberculosis patients and showed the need for clinicians to suspect aspergillus fungal infection in patients with pulmonary tuberculosis undergoing treatment.6

More than 80% of cases of invasive aspergillosis involve the lungs. 1 Both the frequency of invasive disease and the pace of its progression increase with greater degrees of immunocompromise.7 The hallmark of chronic cavitary pulmonary aspergillosis is one or more pulmonary cavities expanding over a period of months or years in association with pulmonary symptoms and systemic manifestations such as fatigue and weight loss as seen in our patient.8

A positive culture supports the diagnosis but only 10-30% of patients with invasive aspergillosis have a positive culture. 5 Definitive confirmation of diagnosis of chronic cavitary pulmonary aspergillosis requires; 1) one large cavity or two or more cavities on chest imaging with or without a fungal ball in one or more of the cavities; 2) at least one of the following symptoms for at least three months: fever, weight loss, fatigue, cough, sputum production, hemoptysis, or shortness of breath; and 3) a positive aspergillus IgG with or without culture of aspergillus species from the lungs.9 Characteristic radiologic features of chronic cavitary pulmonary aspergillosis include ill-defined consolidation progressing to well-defined cavities that are thin-walled and lack associated pleural thickening. Multiple cavities of different sizes may contain fungal balls, debris, or fluid. 9 The detection of Aspergillus precipitins (IgG) in the blood along with radiological features suggests chronic pulmonary aspergillosis. We reached the diagnosis on clinical, radiological, and laboratory grounds. Detailed and sequential radiographic data to observe the slow progression of the disease could not be obtained due to financial constraints. Similarly; directed lung biopsies for histopathological examination could not be obtained due to the resource-limited setting.

Itraconazole at a dose of 200mg twice daily is currently the preferred oral agent for chronic and allergic forms of aspergillosis. Voriconazole or posaconazole can be substituted when failure, emergence of resistance, or adverse events occur.¹⁰ The patient was started on itraconazole with sequential symptomatic improvements seen during one and three months follow-ups. Also, the repeat chest x-ray at three months showed resolved cavitary lesions.

Chronic cavitary pulmonary aspergillosis may remain undiagnosed in many patients with pulmonary tuberculosis, especially in developing countries where its prevalence is particularly high.6 Fungal infection must be suspected in all sputum-positive patients and therefore routine examinations to diagnose fungal infections must be made in all pulmonary tuberculosis patients to start antifungal therapy at the right time. 10

CONCLUSIONS

In conclusion, our case report underscores the importance of considering chronic cavitary pulmonary aspergillosis as a potential complication in patients diagnosed with pulmonary tuberculosis. The overlap in clinical symptoms between the two conditions, coupled with the possibility of concurrent infections, highlights the need for a high index of suspicion and comprehensive diagnostic investigations. Further research and awareness efforts are warranted to enhance the recognition of chronic cavitary pulmonary aspergillosis in the context of tuberculosis, ultimately improving the management and outcomes for these patients.

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CONFLICT OF INTEREST

None

REFERENCES

- Dagenais TR, Keller NP. Pathogenesis of Aspergillus fumigatus in Invasive Aspergillosis. Clinical microbiology reviews. 2009;22(3):447-65.[PubMed]
- Park HS, Jun SC, Han KH, Hong SB, Yu JH. Diversity, Application, and Synthetic Biology of Industrially Important Aspergillus Fungi. Advances in applied

- microbiology. 2017;100:161-202.[PubMed]
- 3. Oladele RO, Irurhe NK, Foden P, Akanmu AS, Gbaja-Biamila T, Nwosu A, et al. Chronic pulmonary aspergillosis as a cause of smear-negative TB and/or TB treatment failure in Nigerians. The International Journal of tuberculosis and lung disease: the official journal of the International Union against Tuberculosis and Lung Disease. 2017;21(9):1056-61.[PubMed]
- 4. Kim SH, Kim MY, Hong SI, Jung J, Lee HJ, Yun SC, et al. Invasive Pulmonary Aspergillosis-mimicking Tuberculosis. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2015;61(1):9-17.[PubMed]
- Denning DW, Cadranel J, Beigelman-Aubry C, Ader F, Chakrabarti A, Blot S, et al. Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management. The European Respiratory Journal. 2016;47(1):45-68.[PubMed]
- 6. Sivasankari S, Senthamarai S, Anitha C, Sastry AS, Bhatt S, Kumudhavathi MS, et al. Prevalence of invasive aspergillosis among (PTB) patients in Kanchipuram, India. Journal of Clinical and Diagnostic Research: JCDR. 2014 Mar;8(3):22. [PMC4003648]

- Herbrecht R, Natarajan-Amé S, Letscher-Bru 7. V, Canuet M. Invasive pulmonary aspergillosis. Seminars in respiratory and critical care medicine. 2004;25(2):191-202.[PubMed]
- Pueringer J, Stephens P, Pandya NK, Zaidi S. A Case of Invasive Pulmonary Aspergillosis vs. Pulmonary Aspergilloma in Immunocompromised Patient With Preexisting Lung Cavity. Cureus. 2022;14(8):e28073. [PubMed]
- Cadena J, Thompson GR, 3rd, Patterson TF. Invasive Aspergillosis: Current Strategies for Diagnosis and Management. Infectious disease clinics of North America. 2016;30(1):125-42.[PubMed]
- 10. Maturu VN, Agarwal R. Itraconazole in chronic pulmonary aspergillosis: In whom, for how long, and at what dose? Lung India: official organ of Indian Chest Society. 2015;32(4):309-12. [PubMed]