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Case Series

The hidden intruder pulmonary tuberculosis masquerading in interstitial lung disease: A case series

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Abstract

Parenchymal lung diseases, such as interstitial lung disease (ILD), may increase the risk of developing pulmonary tuberculosis (TB). Difficulty lies in detecting pulmonary tuberculosis in such patients due to the underlying fibrosis which mask the infection. Many individuals with undiagnosed active or latent do exist since approximately one-third of the world's population having been exposed to mycobacterium tuberculosis (MTB). We report case series of interstitial lung disease (ILD) with concomitant, microbiologically confirmed pulmonary tuberculosis. This highlights the importance of thorough history taking and clinical evaluation to avoid misdiagnosis and ensure appropriate management.

Keywords: Acid fast bacilli, Broncho alveolar lavage, Immunosuppressive, Interstitial lung disease, Mycobacterium tuberculosis, Pulmonary fibrosis

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1. Introduction

Individually well established as major drivers of global respiratory morbidity and death are tuberculosis (TB) and interstitial lung disorders (ILDs). Especially in endemic nations, TB, an infection caused by Mycobacterium tuberculosis (MTB), is a major cause of death globally. Commonly causing chronic irreversible respiratory dysfunction and lowered quality of life are ILDs, a complicated group of diseases defined by progressive fibrosis and inflammation of lung parenchyma.[1,2]

While both TB and ILDs have been widely investigated as separate diseases, their co-occurrence in that of TB superimposed on existing ILD-is a unique and challenging clinical scenario. Patients with ILDs especially those with idiopathic pulmonary fibrosis (IPF), in whose incidence rates have been demonstrated to be up to five times higher than in the general population have a much higher risk of TB. Structural damage to the lung, impaired mucociliary clearance, and extensive use of immunosuppressive medicine in ILD treatment all contribute to this increased vulnerability.[3] Given overlapping clinical and radiological characteristics, TB diagnosis in ILD is particularly difficult. Radiologically, TB can show in ILD patients in an unexpected way, such as with nodules, consolidations, or cavitations simulating disease progression or secondary consequences of disease such bacterial pneumonia.[4] Studies have shown, in fact, that many ILD patients are originally misdiagnosed as smear-negative TB, therefore postponing appropriate therapy.

In this scenario, TB is confirmed by strict bacteriological diagnosis commonly derived from sputum Acid Fast Bacilli (AFB) and cultures, GeneXpert assays, or bronchoalveolar lavage (BAL). The former may be difficult in ILD patients since they frequently have persistent dry cough and procedure induced hypoxemia can occur. Furthermore, confusing the diagnosis are histological alterations such granulomatous inflammation observed in TB as well as some ILDs.[5] Treatment management presents another challenge. Together with the increased risk of side effects in fibrotic

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lungs, interaction between immunosuppressive drugs and anti-TB therapy must be carefully considered under multidisciplinary supervision. The importance of individualizing therapy regimens is highlighted by the possibility of higher hepatotoxicity and the difficulty of sustaining successful treatment of TB while ongoing ILD treatment.[6]

The unique and clinical severity of coexistent TB and ILD makes this case series meant to draw attention to the diagnostic challenges, treatment subtleties, and outcomes involved in this overlap especially relevant. By means of this instance, we highlight the requirement of higher clinical suspicion, the need of multidisciplinary cooperation, and the value of tailored management approaches in maximizing results for a population of high risk.

Although TB and ILDs are thoroughly characterized individually, their relationship especially TB superposed atop ILD is rare and diagnostically difficult. Particularly in cases of significant clinical suspicion, TB must be bacteriologically proven under these conditions commonly by sputum culture, GeneXpert, or bronchalveolar lavage.[7] Presenting series of cases outlining this interaction, including challenges in diagnosis, therapeutic options, and result given the clinical uniqueness and rarity of TB and ILD coexisting together.

2. Case Series

2.1. Case 1

60 year old male known smoker Rheumatoid arthritis – Interstitial Lung disease (RA-ILD), Systemic Hypertension, Type 2 Diabetes Mellitus (DM) & Coronary artery disease (CAD) on medications came to respiratory medicine OPD with complaints of shortness of breath since 2 weeks, Modified Medical Research Council (MMRC), grade II-III, orthopnea present, no paroxysmal nocturnal dyspnea; cough with expectoration for 3 months, mucoid non foul smelling, non-blood stained; History of fever for 2 weeks on and off; complaints of bilateral swelling of legs for 3 months; history of loss of weight present.

On examination, patient was moderately built. No icterus, clubbing, lymphadenopathy and bilateral pitting pedal edema present. Vitals were stable. Respiratory examination revealed bilateral fine infrascapular crepitations.

Total leucocyte count was 11,100/cu mm with polymorphs 67.3% Lymphocytes 19.6%, monocytes 7.9%, Eosinophils 4.6%, Hemoglobin 10.2gm% and Platelet 358 *10^3/cu mm. Renal and liver functions were within normal limits. HIV serology was non-reactive. Sputum smear examination was positive for AFB. 2DEcho showed ejection fraction (EF) 68% No regional wall abnormality, Mitral regurgitation (MR) (trivial), Tricupsid regurgitation (TR) (trivial), no pulmonary artery hypertension (PAH). Ultrasound abdomen showed fatty liver (grade-1) and lymph nodes – few matted lymph nodes noted around the umbilical region, largest measuring -1.1 *1.0cm, another lymph node with preserved fatty hilum noted at left iliac region -1.8*1.5cm in right upper quadrant of the abdomen. Few subcentrimetric lymph nodes with preserved fatty hilum noted at the left iliac region measuring -0.5 cm in its short axis.

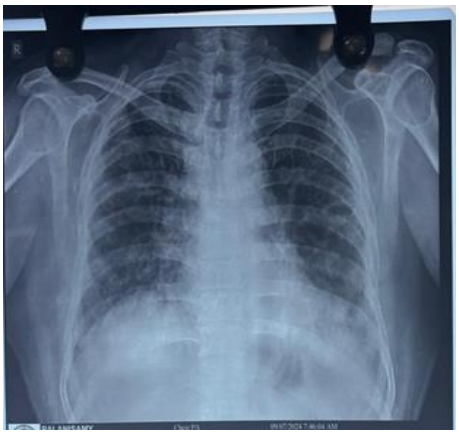

Figure 1: Chest x-ray: Cavity with air fluid noted in left midzone with bilateral patchy opacities in lower lobe

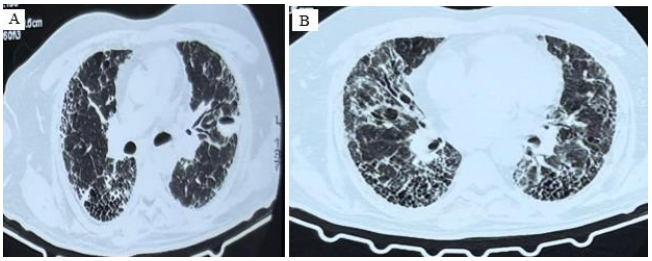

Figure 2: A,B: CT Chest: Bilateral honeycombing with traction bronchiectasis noted in both lung fields. Evidence of left thick walled cavity in upper lobe

2.2. Case 2

A 48-year-old female, known case of interstitial lung disease (ILD), presented with complaints of cough with expectoration for the past 3 months. The sputum was mucopurulent in nature, non-foul smelling, and not blood-stained. She also reported progressive shortness of breath for the past 6 months, currently graded as MMRC Grade III. Additionally, she had a history of fever for the past 1 week, which was predominantly an evening rise in temperature. She also complained of loss of appetite and unintentional weight loss for the past 1 month.

On general physical examination, the patient was moderately built and ill-nourished. Pallor was present, and she had digital clubbing. No lymphadenopathy was noted. Bilateral pitting pedal edema was present. Her vital signs were stable at the time of examination.

On respiratory system examination, the trachea was deviated to the left, and Trail's sign was positive. There was crowding of ribs on the left side and diminished chest movements on the same side. On percussion, an impaired

note was noted in the left interscapular and infrascapular areas. On auscultation, bilateral fine Velcro crackles were heard.

On investigation, total leucocyte count 12,000/cu mm with polymorphs 57.3% Lymphocytes 18.6%, monocytes 6%, Eosinophils 7.4%, Hemoglobin 10 gm% and Platelet 597 *10^3/cu mm. Renal and liver functions were within normal limits. HIV serology was non-reactive, HBsAg positive, HCV negative, Anti HBE 1.30. Sputum smear examination was positive for AFB (1+). 2DEcho showed EF 70% No regional wall abnormality, grade 1 left ventricular systolic dysfunction mild MR, mild TR moderate PAH (TRPG 45mm Hg). Ultrasound abdomen done no significant abnormality.

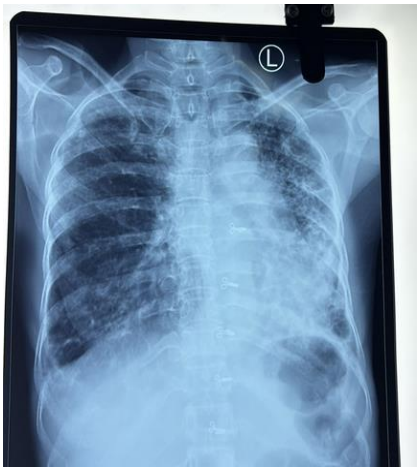

Figure 3: Chest x-ray evidence of parenchymal fibrosis with reticulonodular opacities in bilateral lung fields

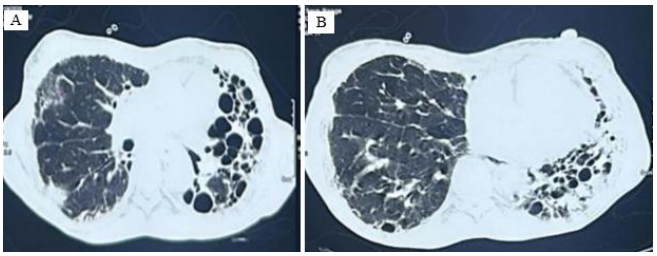

Figure 4: A,B: HRCT Chest :Chronic interstitial lung disease with interlobular and intralobular interstitial thickening, fibrosis, bronchiectatic changes, honeycombing, volume loss in the left lung involving upper lobe, lingula and lower lobe and interlobular and intralobular interstitial thickening, subpleural fibrosis with early honey combing noted subpleural aspect upper lobe right middle lobe and right lower lobe suggestive interstitial lung disease likely UIP pattern

2.3. Case 3

A 64-year-old male, known smoker and a diagnosed case of interstitial lung disease, presented with complaints of cough with expectoration for the past 2 weeks. The sputum was mucoid in nature, non-foul smelling, and not blood-stained. He also reported shortness of breath for the past 3 weeks, currently graded as MMRC Grade III. Additionally, he had intermittent fever for the past 2 weeks.

On general physical examination, the patient was moderately built and moderately nourished. There was no icterus, pallor, or lymphadenopathy. Bilateral pitting pedal edema was present. His vital signs were stable at the time of examination. On respiratory system examination, bilateral coarse crepitations were heard on auscultation.

On investigations, total leucocyte count 11,000 /cu mm with polymorphs 60% Lymphocytes 18.6%, monocytes 6%, Eosinophils 3%, Hemoglobin 14gm% and Platelet 420 *10^3/cu mm. Renal and liver functions were within normal limits. HIV serology was non-reactive. Bronchoscopy with BAL done and sent for analysis, bronchoalveolar lavage BAL AFB came positive. 2DEcho showed EF 60% No regional wall abnormality, grade 1 LV systolic dysfunction, no PAH. Ultrasound abdomen done no significant abnormality.

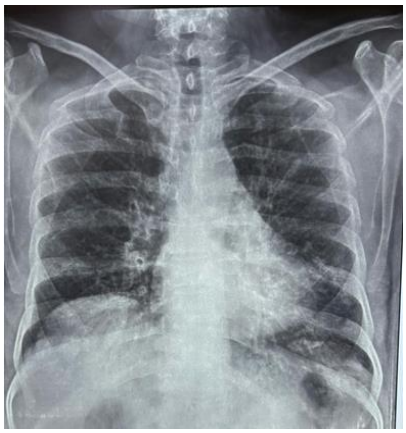

Figure 5: Chest x-ray: Cystic air space opacities noted in left lower lobe

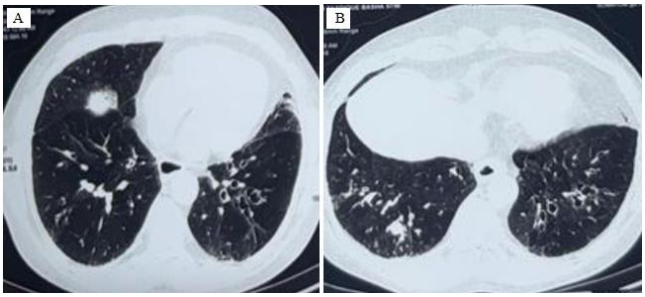

Figure 6: A,B: HRCT Chest: Reticulations predominantly subpleural lines diffusely more so in both lower lobes, honeycombing in anterior segment of left upper lobe and posterior segment of right upper lobe and posterior segment of left lower lobe, parenchymal bands with traction bronchiectasis in left lower lobe, few ground glass attenuating centrilobular nodules in both lung diffusely with foci of ground glass opacities suggestive interstitial lung disease likely UIP pattern with RB-ILD . Bronchioles with tree in bud appearance suggestive of infective Koch s tuberculosis

2.4. Case 4

A 66-year-old female, a known case of interstitial lung disease (ILD) and type 2 diabetes mellitus on regular medications, presented with complaints of cough with

expectoration for the past 1 week. The sputum was mucopurulent, non-foul smelling, and not blood-stained. She also reported breathing difficulty for the past 1 month, currently classified as MMRC Grade III to IV. There were no complaints of orthopnea or paroxysmal nocturnal dyspnea. She also had a history of fever for the past 3 days, characterized by an evening rise in temperature.

On general examination, the patient was ill-built and ill-nourished. Pallor was present, but there was no icterus or lymphadenopathy. Clubbing was noted. There was no bilateral pitting pedal edema.

Her vital signs were as follows: oxygen saturation was 80% on room air and improved to 95% with 4 liters of supplemental oxygen. Her blood pressure was 100/70 mmHg, and pulse rate was 78 beats per minute.

On respiratory system examination, coarse leathery crepitations were heard bilaterally in the infrascapular and interscapular areas.

On investigation, total leucocyte count 9,000/cu mm with polymorphs 63% Lymphocytes 20%, monocytes 5.6%, Eosinophils 6.3%, Hemoglobin 8.9 gm% and Platelet 347 *10^3/cu mm. Renal and liver functions were within normal limits. HIV serology was non-reactive, HBsAg positive, HCV negative. Sputum smear examination was positive for AFB (1+). 2DEcho showed EF 58% No regional wall abnormality, no LV systolic dysfunction mild severe PAH.

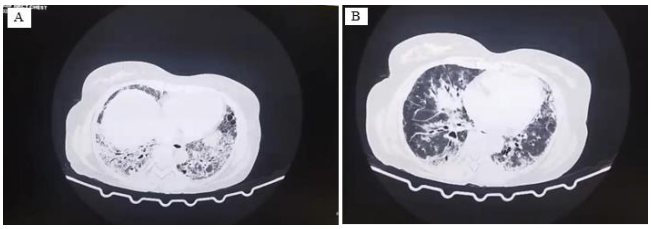

Figure 7: A,B: HRCT Chest: Evidence of extensive honeycombing with traction bronchiectasis with patchy areas of consolidation

2.5. Case 5

A 54-year-old female, a known case of old pulmonary tuberculosis, presented with complaints of breathlessness for the past 3 months, which has worsened over the past 1 week. Her dyspnea is currently graded as MMRC Grade II to III. She also reported cough with expectoration for the past 2 months. The sputum was scanty, yellowish-white, non-foul smelling, and not blood-stained. Additionally, she had fever for the past 2 days without associated chills or rigors.

On general physical examination, the patient was moderately built and moderately nourished. There was no icterus, cyanosis, clubbing, lymphadenopathy, or pitting pedal edema. Her vital signs were as follows: oxygen saturation was 89% on room air, blood pressure was 120/70 mmHg, and pulse rate was 85 beats per minute. On respiratory system examination, percussion revealed an impaired note over the left interscapular and left infrascapular areas. Bilateral coarse inspiratory crepitations were heard on auscultation.

Total leucocyte count was 10,100/cu mm with polymorphs 68 % Lymphocytes 16.5%, monocytes 6.9%, Eosinophils 3.5%, Hemoglobin 11.2gm% and Platelet 279 *10^3/cu mm. Renal and liver functions were within normal limits. HIV serology was non-reactive. Sputum smear examination was positive for AFB. 2DEcho showed ejection fracture 65% No regional wall abnormality, mild pulmonary artery hypertension.

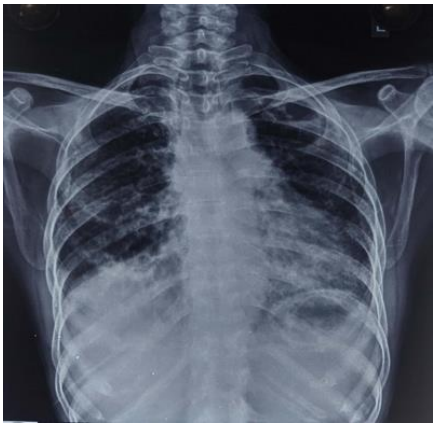

Figure 8: Chest X-ray: Left upper lobe thick wall cavity with reticulonodular opacities in bilateral lung fields

Table 1: Summary of case reports findings

Case	Age	Gender	Symptoms	Sputum AFB	BAL Findings
1	60	Male	SOB (MMRC II-III), cough with mucoid sputum, fever, weight loss	Positive	Not done
2	48	Female	SOB (MMRC III), mucopurulent sputum, fever, appetite & weight loss	Positive	Not done
3	64	Male	SOB (MMRC III), mucoid sputum, fever	Negative	BAL AFB positive
4	66	Female	SOB (MMRC III-IV), mucopurulent sputum, fever	Positive	Not done
5	54	Female	SOB (MMRC III-IV), scanty sputum, fever	Positive	Not done

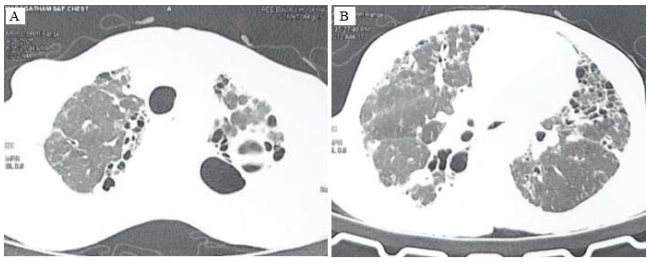

Figure 9: HRCT chest: cystic and varicoid bronchiectasis changes diffusely in bilateral lung parenchyma, few fibrocavitatory lesions in left apical lobe showing air fluid level, patchy areas of fibrosis in bilateral apical and posterior segments of right upper and lower lobe

3. Discussion

The coexistence of tuberculosis (TB) and interstitial lung diseases (ILDs) presents notable diagnostic challenges, especially in regions with a high burden of TB, where overlapping clinical and radiological characteristics frequently result in misdiagnosis. A meta-analysis conducted in 2024 indicated that tuberculosis (TB) is present in 26.3% of patients with interstitial lung disease (ILD) in high-burden countries, whereas the prevalence is 4.9% in low or intermediate-burden regions. This disparity highlights the difficulty in differentiating tuberculosis from interstitial lung disease progression or acute exacerbations, given that both conditions exhibit nonspecific symptoms, including cough and dyspnea, as well as radiological features such as ground-glass opacities and reticular patterns.

Delays negatively impact outcomes, as evidenced by studies in which tuberculosis was misidentified as exacerbations of idiopathic pulmonary fibrosis, resulting in deferred anti-tuberculosis treatment.

Radiological findings complicate differentiation, as TB-ILD cases frequently present with subpleural nodules (mean diameter 3.2 cm) and lobar consolidations, which differ from typical TB patterns. Silicosis-associated interstitial lung disease (ILD) exhibits a tuberculosis (TB) prevalence of 35.6%, underscoring the impact of underlying lung pathology on the heightened risk of infection. The diagnostic challenges highlight the necessity for thorough testing, including histopathological confirmation, in patients with interstitial lung disease experiencing deteriorating symptoms.[8-10] Due to the diagnostic difficulties arising from the overlapping characteristics of tuberculosis (TB) and interstitial lung diseases (ILDs), bacteriological confirmation of TB is crucial in suspected instances. Sputum culture is the definitive diagnostic method; however, its sensitivity is frequently limited in patients with fibrotic lung disease or those unable to produce sputum, which necessitates alternative diagnostic strategies. The GeneXpert MTB/RIF assay provides rapid and precise detection of Mycobacterium tuberculosis and rifampicin resistance, thereby enhancing diagnostic efficiency in these contexts. Bronchoalveolar lavage (BAL) is especially beneficial for patients presenting with non-productive cough or inconclusive imaging, as it enhances diagnostic yield and allows for concurrent evaluation of other infections or malignancies. The main diagnostic challenge in this case was distinguishing tuberculosis (TB) from the progression of interstitial lung disease (ILD) and promptly recognizing their coexistence. Empirical corticosteroids, frequently administered during exacerbations of interstitial lung disease (ILD), may unintentionally exacerbate undiagnosed tuberculosis (TB), thereby elevating the risk of disseminated disease. This underscores the necessity of conducting systematic screenings for latent or active tuberculosis prior to the commencement of immunosuppressive therapy, especially in endemic regions (Sharma et al., 2015).[11,12]

Treating tuberculosis in patients with underlying interstitial lung disease necessitates careful consideration from a therapeutic perspective. Upon confirmation of tuberculosis, anti-tubercular therapy should be initiated promptly; however, clinicians must be attentive to the risk of drug-induced pulmonary toxicity, given that individuals with interstitial lung disease are already susceptible to respiratory complications. The administration of corticosteroids must be meticulously customized, considering the advantages for interstitial lung disease management in relation to the potential risk of tuberculosis exacerbation. Patients with both tuberculosis and interstitial lung disease exhibit generally poorer clinical outcomes than those with tuberculosis alone. Kim et al. (2016) demonstrated that patients with concurrent idiopathic pulmonary fibrosis (IPF) and tuberculosis (TB) exhibited increased rates of respiratory failure and mortality, highlighting the need for timely, intensive, and multidisciplinary management in this complex patient group.[13,14]

4. Conclusion

The coexistence of tuberculosis and interstitial lung disease is uncommon yet clinically important, as symptoms and radiological findings frequently resemble exacerbation or progression of interstitial lung disease, resulting in diagnostic delays. Comprehensive and prompt assessment, including microbiological testing (BAL/sputum AFB), is essential for patients with ILD who experience deterioration or systemic symptoms, particularly in regions where tuberculosis is prevalent. These cases highlight the necessity of a heightened awareness for tuberculosis in interstitial lung disease patients presenting with new or exacerbating symptoms, facilitating prompt and suitable intervention.

5. Conflict of Interest

The authors hereby declare that there is no conflict of interest in this study.

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