Radiology Forum

A Case of Tuberculosis-Sarcoidosis in a Patient with Interstitial Lung Disease and Persistent Fever

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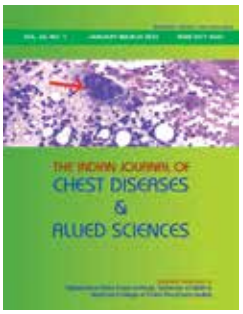

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ABBREVIATIONS USED IN THIS ARTICLE

TB = Tuberculosis

BMI = Body mass index

TU = Tuberculin

ANA = Anti-nuclear antibody

BAL = Bronchoalveolar lavage

TBLB = Transbronchial lung biopsy

CBNAAT = Cartridge-based nucleic acid amplification test

Clinical Summary

Tuberculosis (TB) and sarcoidosis are common chronic granulomatous diseases. Although being different clinical entities, the two diseases show similarity in their presentation. Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*; whereas sarcoidosis is a multi-systemic disease of unknown aetiology. A high index of suspicion is required to consider this dual presentation in the same patient. Conventional dictum in clinical medicine has always emphasised to explain the varied symptoms of a patient with a single diagnosis. Here, we highlight the dual entity of tuberculosis-sarcoidosis.

Investigations

A 65-year-old female, home-maker, presented with history of breathlessness on exertion, productive cough, low-grade fever with evening rise of temperature which was not relieved by several courses of antibiotics, fatigue and unquantified weight loss for two months. She denied history of anti-tuberculosis regimen in the past. She had never smoked or consumed alcohol. Her family history did not reveal any hereditary lung disease. She was a known case of hypothyroidism since 15 years and was on daily oral levothyroxine 100microgram.

On general physical examination, she had a body mass index (BMI) of 23.5Kg/m^2, pallor, grade-2 clubbing, bilateral pitting pedal oedema and hypoxaemia (digital pulse oximetry saturation of 90% while breathing room air), blood pressure of 140/90 mmHg. Physical examination was unremarkable for icterus, cyanosis or any joint abnormality.

Examination of the respiratory system revealed bilateral basal end-inspiratory crackles; typical velcro nature on auscultation. The findings of cardiovascular, gastrointestinal and neurological examinations were essentially normal.

Laboratory investigations revealed haemoglobin 11.7g/dL with normal blood counts and other biochemical parameters. Viral markers were negative. The induced sputum was negative for acid-fast bacilli on smear microscopy. Tuberculin test (10 TU) revealed an induration of 24mm with blister formation at 72 hours. The initial chest radiograph (postero-anterior

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view) revealed bilateral reticulonodular infiltrates predominantly at mid- and lower-zones (Figure 1A). She was initiated on first-line anti-tuberculosis therapy according to body weight but without any response. On analysis of serial chest radiographs taken within a gap of one month, there was worsening of pulmonary infiltrates (Figure 1B).

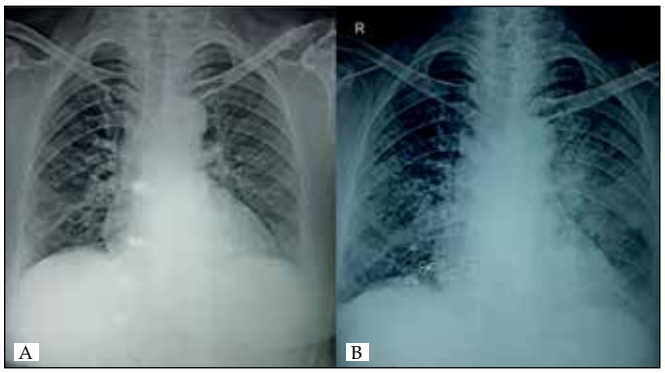

Figure 1. Chest radiograph (postereo-anterior view) showing (A) bilateral reticulonodular opacities (B) with progression on subsequent chest radiograph.

Spirometry revealed mixed pattern abnormality. Echocardiography was normal. On further evaluation, she had negative anti-nuclear antibody (ANA) and rheumatoid factor, normal calcium levels but raised serum angiotensin converting enzyme (119IU/mL) levels. High resolution computerised tomography of the chest revealed multiple small-size pulmonary nodules with central and peripheral distribution scattered along bilateral lung fields, patchy areas of ground-glass haziness with adjacent bronchiectasis and few enlarged right paratracheal, subcarinal and left hilar lymph nodes (largest measuring 12mmx10mm) with calcification (Figure 2).

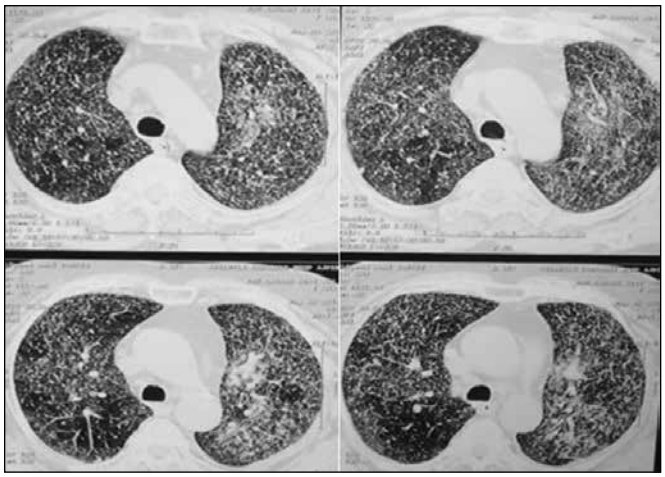

Figure 2. High resolution computed tomography of chest showing bilateral, multiple, small-size pulmonary opacities with central and peripheral distribution.

Fiberoptic bronchoscopy did not reveal any endobronchial abnormality. Bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) were performed. BAL smear showed mixed inflammatory cells with no acid-fast bacilli. However, TBLB showed multiple granuloma formation with epitheliod histiocytes, occasional giant cells and lymphocytes; but without any caseaous necrosis suggestive of chronic granulomatous inflammatory disease (Figure 3 A and B). The transbronchial lung biopsy tissue on Gene-Xpert, a cartridge-based nucleic acid amplification test (CBNAAT) confirmed *Mycobacterium tuberculosis*.

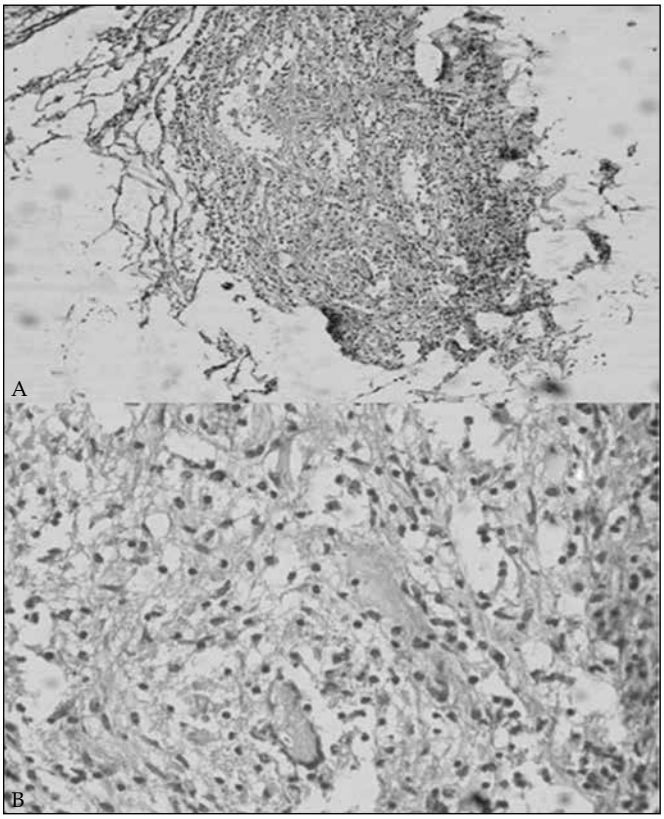

Figure 3. Transbronchial lung biopsy showing epitheliod cells, lymphocytes, multinucleated giant cells forming granulomas without any caseous necrosis. (Haematoxylin and Eosin (A) X 10 and (B) X 40).

The patient was continued on anti-tuberculosis therapy along with oral prednisolone that resulted in decline in fever and marked symptomatic improvement in breathlessness after two weeks.

Discussion

Tuberculosis and sarcoidosis are chronic granulomatous diseases. Although being different clinical entities, both show similarity in many aspects. Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*; while sarcoidosis is a systemic disease of unknown aetiology. The histological similarity of epithelioid

granuloma in both TB and sarcoidosis has resulted in robust studies to study an association between these two conditions.[1] Concomitant occurrence of these two conditions is very uncommon and less commonly TB develops as an opportunistic infection in sarcoidosis patients after systemic corticosteroid therapy.[2]

Tuberculous-sarcoidosis as a separate clinical entity has also been described with evidence to postulate that altered mycobacterial infection or its biodegraded products could be the underlying aetiological factors responsible for the emerging entity of tuberculosis-sarcoidosis as a distinct diagnosis.[3,4]

Tuberculosis-sarcoidosis term was coined for the patients showing overlap of presentation fulfilling diagnostic criteria of both TB and sarcoidosis. There may be three varied presentations of tuberculous-sarcoidosis[3]: (a) patients who had TB and later develop sarcoidosis; (b) patients who present with co-existent sarcoidosis and TB and (C) patients of chronic sarcoidosis who develop overt TB after corticosteroid therapy.

The other school of thought postulated that although diagnostic criteria for tuberculosis-sarcoidosis have been described; however this entity is still under lot of scrutiny by various authrs.[5,6] Sarcoidosis has been reported to precede, follow or present with TB, therefore typical and atypical presentation of sarcoidosis should also be considered in clinical setttings.[7] Further, some authors have hypothesised that the two entities are not mutually exclusive, but rather represent polar forms of the same disease spectrum based on the host immune response.[8]

In developing countries, like ours where TB burden is very high, the differentiation of TB and sarcoidosis is at time challenging in view of similar clinical and histological features. This is quite significant as the treatment of these two conditions is totally different. Therefore, every attempt should be made to improve diagnostic certainty for making optimal therapeutic decisions. Last but not least, one should also keep possibility of rare simultaneous occurrence of these dual entities as observed in the present case. Prudent diagnosis of tuberculous-sarcoidosis need to be made in suspected cases after careful evaluation that should mandatorily include histopathology with correlation with other investigations.

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