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Coexistence of Sarcoidosis and Tuberculosis Presenting with Severe Pulmonary Artery Hypertension: A Clinical Dilemma

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors BB and VT designed the study, wrote the protocol, the first draft of the manuscript and managed the literature searches. Both authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Background: Chronic granulomatous conditions affecting the respiratory system such as tuberculosis and sarcoidosis have similar case presentations suggesting them to be polar ends of the same disease spectrum thus putting physicians into a clinical dilemma. This case report highlights one such unique presentation.

Case Presentation: A young female, presented with respiratory distress and significant weight loss. Investigations showed severe pulmonary artery hypertension (PAH), renal failure and generalized lymphadenopathy suggesting multisystem involvement. The initial diagnosis was sarcoidosis warranting corticosteroids but since Mantoux test suggested tuberculosis we were in a dilemma regarding therapeutic options.

Conclusion: This case highlights a rare presentation of sarcoid tuberculous with severe PAH urging physicians to consider this chronic granulomatous disease spectrum during work up of their

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patients. The authors would also like to emphasize the importance of starting combined therapy on early recognition to combat a possible disease entity like tuberculous sarcoid patients. These predictors, however, need further work to validate reliability.

Keywords: Heart blocks; pulmonary artery hypertension; sarcoidosis; sarcoid tuberculous; tuberculosis.

ABBREVIATIONS

NYHA : New York Heart Association
JVP : Jugular Venous Pressure
HB : Haemoglobin
TLC : Total Leucocyte Count
ESR : Erythrocyte Sedimentation Rate
AST : Aspartate Transaminase
ALT : Alanine Transaminase
ECG : Electrocardiogram
ECHO : Echocardiogram
PASP : Pulmonary Artery Systolic Pressure
LVEF : Left Ventricular Ejection Fraction
HRCT : High Resolution Computerised Tomography
ANA : Anti-Nuclear Antibodies
FNAC : Fine Needle Aspiration Cytology
ACE : Angiotensin Converting Enzyme
RNTCP : Revised National Tuberculosis Control Programme
CRCL : Creatinine Clearance
AKI : Acute Kidney Injury
PCR : Polymerised Chain Reaction
IGRA : Interferon Gamma Release Assay

1. INTRODUCTION

India has the highest burden of tuberculosis (TB), with an incidence of 2.8 million [1]. Sarcoidosis is another condition, mimicking tuberculosis, with non-caseating granulomas when compared to caseating ones in TB. Due to a clinico-radiological resemblance, either condition can be misdiagnosed, with physicians favouring a diagnosis of TB considering its high prevalence in India [2]. Rarely, both entities may co-exist, challenging physicians resulting in a dilemma during the course of treatment [3-5].

The term tuberculous sarcoidosis was first used to categorize patients with indistinguishable clinical features [5]. This disease spectrum includes patients with (a) prior TB who developed sarcoidosis (b) concomitant TB and sarcoidosis and (c) prior sarcoidosis who developed tuberculosis [3]. A sub-classification has been proposed wherein Sarcoidosis (S) and Tuberculosis (TB) are the opposite ends of the spectrum with Sarcoid tuberculous (ST) and Tuberculous Sarcoid (TS), ST being predominantly sarcoid with tuberculous features and vice versa in TS [6].

Treatment for both entities differ and the lack of an accurate diagnosis could be detrimental. Corticosteroids are indicated in sarcoidosis whereas a quadruple antibiotic regimen is recommended for tuberculosis. A corticosteroid monotherapy in a patient with tuberculosis would result in a flare-up of the infection while an antibiotic regimen in sarcoidosis would result in no obvious clinical improvement. The following case report highlights the difficulties and importance in primary diagnosis and challenges in the management of tuberculous sarcoidosis.

2. CASE PRESENTATION

A 35-year-old female, known case of hypothyroidism and no other co morbidities, presented with 15 days history of breathlessness, easy fatigability, cough and pedal oedema. She felt fatigued hampering her daily routine and her breathlessness had progressively worsened (New York Heart Association (NYHA) grade 2 to grade 4). She had noticed an unintentional weight loss of 5 kg over 1 year. She had no other significant past or family history. No history of contact with pulmonary tuberculosis.

On general physical examination, she had tachycardia, tachypnoea, BP was 150/90mmHg and was hypoxic. Significant pallor and signs of heart failure such as raised jugular venous pressure (JVP), tender hepatomegaly and pedal oedema were noted. Another relevant systemic examination was unremarkable and there were no extrapulmonary manifestations of sarcoidosis noted on examination.

On investigations, there was anaemia (Haemoglobin (Hb) – 6.3 g/dl {Normal – 12-15 mg/dl}) which was later attributed to iron deficiency, leucocytosis (Total leucocyte count (TLC) – 20,000 cells/cumm {Normal – 4000 – 11000 cells/cumm}, Neutrophils – 86% {Normal 40-80%}, with absolute neutrophil count (ANC) of 17,200/mm^3 {Normal – 1500-8000/mm^3}) with Erythrocyte sedimentation rate (ESR) of

91mm/hr {Normal – 0-20 mm/hr}. There was significant proteinuria (2+) via routine dipstick method and renal failure (Serum creatinine - 2.03 mg/dl {Normal – 0.6-1.2 mg/dl}). A 24-hour urine protein was done to quantify the proteinuria which was 107.32 mg/day. Liver function test revealed hypoalbuminemia (2.9 g/dl {Normal 3.5-5.2 g/dl}) with mild transaminitis (Aspartate transaminase (AST) – 59U/L {Normal – 0-31U/L}, Alanine transaminase (ALT) – 95U/l {Normal – 0 -33U/l}).

Chest X-ray was suggestive of pulmonary oedema (Fig. 1).

X-ray film showing mediastinal widening (green arrows), cardiomegaly (blue line) and increased bronchovascular markings (red arrows).

ECG revealed features suggestive of Right Bundle Branch Block (LBBB) and Left Anterior Fascicular Block(LAFB). 2D-ECHO showed severe Pulmonary Artery Hypertension (PAH) with Pulmonary artery systolic pressure (PASP) of 70mmHg, Left ventricular ejection fraction (LVEF) of 50% and mild pericardial effusion. Ultrasound abdomen and pelvis revealed no sonological abnormality.

Severe PAH led us to investigate for its aetiology. The sleep study revealed mild obstructive sleep apnoea. Collagen vascular disease was also considered due to multisystem involvement. Antinuclear antibody (ANA) profile was sent which was negative. High-resolution CT (HRCT) was done to look for evidence of interstitial lung disease, which showed axillary, mediastinal and retroperitoneal lymphadenopathy and left lingular consolidation (Fig. 2).

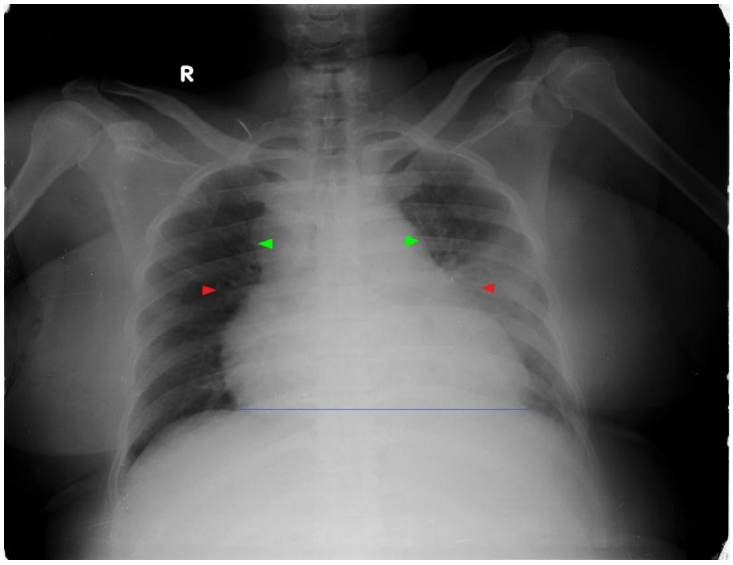

Fig. 1. Chest radiograph PA view

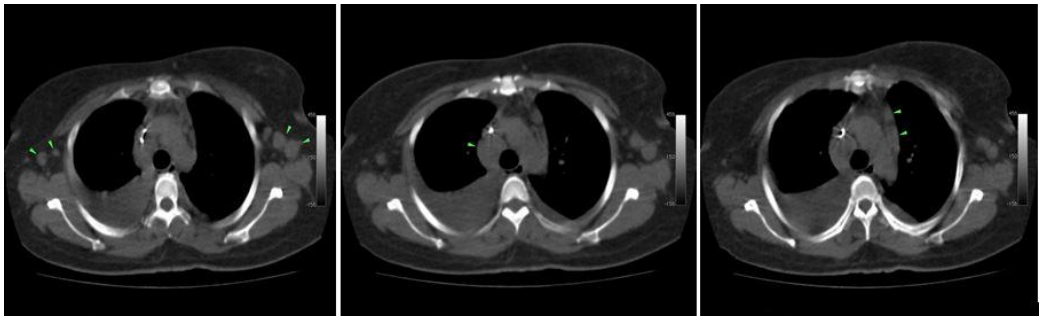

Fig. 2. High resolution computerised tomography (HRCT) - transverse plane

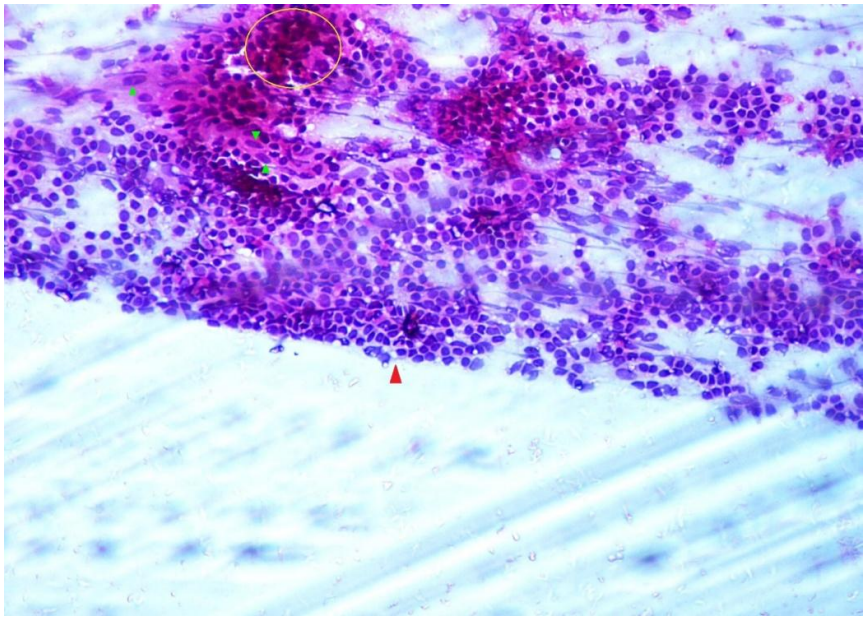

Fig. 3. Fine needle aspiration cytology from right axillary lymph node

HRCT showing axillary, hilar and mediastinal lymphadenopathy (from left to right) as shown by green arrows.

FNAC of the right axillary lymph node was performed that showed an eosinophilic amorphous necrotic background, with clusters of epithelioid cells amongst polymorphous lymphoid cells (Fig. 3).

A firm 1x1 cm firm swelling was noted in the right axillary region and aspiration of 0.2 ml of purulent material revealed: naked granuloma (early granuloma not surrounded by lymphocytes) and some mature granuloma with lymphocytes (yellow circle) and epithelioid cells (green arrow) suggestive of non-caseating granuloma along with lymphocytes in varying stages of maturation (red arrow).

Acid fast stain from both lymph node aspirate and sputum revealed no bacilli. The patient remained tachypnoeic and hypoxic and hence bronchoscopy was deferred.

In view of a granulomatous condition with multisystem involvement, a differential diagnosis of sarcoidosis was considered. Serum ACE and serum calcium levels were sent which were both normal. Subsequently, Mantoux test was done that was positive with 15 mm of induration. A clinical suspicion of coexisting TB was considered, especially due to a high prevalence of TB in India. Tuberculosis was suspected and treated on clinical and epidemiological background.

Patient was started on anti - heart failure medications, supplemental oxygen and anti-tubercular treatment, as per Revised National TB Control Programme (RNTCP) guidelines [1] along with steroids at 1 mg/kg body weight for sarcoidosis. Creatinine clearance (CrCl) was 47.32 ml/min and hence no dose adjustment was made. The recommended dosage reduction by 50% is indicated when CrCl is less than 10 ml/min [7]. The patient improved significantly over one month with evidence of symptomatic improvement. Eventually oxygen requirement was gradually reduced, the patient had gained weight and her general health was restored. Serum creatinine on discharge was 1.84 mg/dl and follow up levels after one month of treatment was 1.34 mg/dl.

3. DISCUSSION

TB and sarcoidosis are chronic granulomatous conditions with identical features however, a presentation with renal failure and heart failure with severe PAH is rare. A similar rare case of sarcoidosis with hypercalcemia, anaemia, acute kidney injury (AKI) and no respiratory complaints, had a PASP of 63 mmHg indicating severe PAH [8]. A cohort study wherein patients with sarcoidosis were screened for PAH reports that;

PAH is an indicator of advanced sarcoidosis, either due to direct myocardial or pulmonary involvement and is a predictor of poor outcome. In this cohort 62.6% of patients, all women, had PASP more than 40 mmHg warranting the need for early recognition, diagnosis and treatment [9].

Renal involvement in sarcoidosis, though unclear, is estimated to be about 35-50% [10]. Our patient had microalbuminuria. In a cohort study assessing the prevalence of proteinuria in sarcoidosis patients, it was observed that only 3% of the cohort had proteinuria in the absence of any other risk factors and 24-hour urinary protein excretion was moderate (mean 1.30, range 0.32-5.06 mg/dl). This paper concluded that proteinuria is rare in sarcoidosis and if present alternative causes should be ruled out [11].

In comparison to our report, a case of sarcoidosis with anaemia, attributed later to iron deficiency, renal failure and a heart block was reported suggesting similar manifestations. In about 5% of patients with sarcoidosis there is clinical evidence of myocardial involvement, ranging from arrhythmias to heart blocks, as was in our case [8].

Physicians might encounter difficulty while diagnosing tuberculosis in patients with sarcoidosis and vice versa. A case of pulmonary sarcoidosis was reported wherein the patient presented with symptoms of fever and dry cough, investigations showed anaemia and leucocytosis, started on anti- tubercular drugs but subsequently a diagnosis of pulmonary sarcoidosis was established due to worsening of symptoms on anti-tubercular therapy [12]. Another elderly woman was diagnosed to have sarcoidosis based on hilar lymphadenopathy and biopsy findings and started on corticosteroids. Later anti TB drugs were added as the patient had continuous fever spikes and a positive culture for TB [13]. Another case presented with erythema nodosum and dry cough, was diagnosed to have pulmonary and skin sarcoidosis based on CT and biopsy findings and was started on prednisolone, but subsequently culture grew Mycobacterium tuberculosis and patient was started on anti-TB drugs [14]. The converse has also been observed where a patient presented with features suggestive of military tuberculosis, started on anti – TB drugs but eventually returned with recurrence of symptoms warranting work up for similar granulomatous conditions suggesting a diagnosis of sarcoidosis [15]. In all of the above cases, a significant improvement was observed with combined antimicrobials and corticosteroids.

Sarcoidosis is diagnosed majorly by bilateral hilar lymphadenopathy on a chest radiograph along with a histopathological confirmation of a non-caseating granuloma and a Mantoux test anergy, which plays a clinically vital role for its diagnosis [16,17]. Apart from these simple diagnostic tools, advanced modalities such as polymerised chain reaction (PCR) for TB and interferon γ release assay (IGRA) have been proposed. However, it has been observed that a positive PCR may be seen in some biopsy samples of sarcoidosis and patients with a positive IGRA have been misdiagnosed as TB [17]. In our case, a significant weight loss, positive Mantoux test, high endemicity of TB and a noncaseating epithelioid granuloma suggested a coexistence of sarcoid tuberculous. A study explaining this co-existence suggested combined treatment with corticosteroids and antitubercular therapy [6].

4. CONCLUSION

This case report highlights the importance of considering coexistence of tuberculosis and sarcoidosis in patients with similar clinical presentations. Early recognition and diagnosis is worsening of overall outcome. In countries with high prevalence of tuberculosis the diagnosis of coexisting sarcoidosis may often be missed or not considered. Physicians must be aware of the possible entity called tuberculous sarcoid and overcome the dilemma in treatment. This case also emphasises on considering sarcoidosis as a differential diagnosis in patients with severe PAH and proteinuria, with or without other system involvement.

Tuberculosis and sarcoidosis are two similar chronic granulomatous respiratory conditions that can rarely coexist.

Sarcoidosis presenting with severe pulmonary artery hypertension and renal failure in the form of proteinuria along with heart blocks is quite rare.

This case highlights the importance of early diagnosis and treatment of tuberculous sarcoidosis, a rare clinical entity.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient (or other approved

parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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