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Multisystemic chronic sarcoidosis: unmasking of a true masquerader

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Abstract

Sarcoidosis is a diverse disorder that can potentially affect almost every organ system, and mimics a wide-range of diseases. Here, we present a case of multisystemic chronic sarcoidosis affecting lung parenchyma, intrathoracic and extrathoracic lymph nodes and skin. The organ specific clinical manifestations developed over a course of time that did imitate different diseases at different times. Only after the full-blown disease, symptoms and investigations could be placed altogether as sarcoidosis.

Key words: Sarcoidosis, multisystem, cutaneous sarcoid, lupus pernio, hypovitaminosis D, tuberculosis

Introduction

In 1877, sarcoidosis was first reported by Jonathan Hutchinson in London but Caesar Boeck is credited as being the first to use the term sarkoid (sarcoid).(1) Sarcoidosis could affect all ages, with a peak incidence among those between the ages of 20 to 39 years, and nearly two-third of cases are in women. Also, it is more common in non-smokers and rural inhabitants.(1,2) According to studies, a complex interaction of host immunologic, genetics and environmental variables is responsible for the pathogenesis of sarcoidosis.(3)

More than 90% of patients manifest pulmonary and intra-thoracic lymph node involvement. In extra-pulmonary cases, the most involved organ is skin (49.3%) followed by eyes (23.6%), liver (20.7%), extra-thoracic lymph-nodes (13.7%), parotid/salivary glands (5.7%) and bone/joints (1.4%) .(4) Three main criteria need to be fulfilled for the diagnosis of sarcoidosis : a consistent clinical picture; the presence of non-caseating granuloma in more than one organ, and the elimination of other possible causes of granulomatous illness.(5) If symptoms involve at least two organ systems it is termed as systemic sarcoidosis.(4) The diagnosis of sarcoidosis essentially depends on the clinician's assessment. The differentials are crucial to rule-out, as misdiagnosis and inappropriate treatment may cause deleterious health effects.

Case presentation

A 35-year-old woman initially presented with the complaints of chest discomfort, shortness of breath, occasional productive cough and generalized weakness, not associated with any fever or weight loss. On examination her vitals were stable with saturation of peripheral oxygen (SpO2) 99% in room air. Bilateral axillary and epitrochlear lymphadenopathy were noted. Investigations showed full blood count within normal limits, erythrocyte sedimentation rate (ESR) 27mm per first hour. Chest radiography revealed bilateral hilar and right paratracheal lymphadenopathy [Figure-1A]. High resolution computed tomography (HRCT) of the chest revealed extensive mediastinal and axillary lymphadenopathy and reticulonodular shadows affecting the whole of both lung fields [Figure-1B].

Electrocardiography, echocardiography,

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ultrasonography of the whole abdomen, serum lactate dehydrogenase, liver and renal function tests and other routine blood tests were within normal limits. Mantoux test was 3 mm in 72 hours. Three samples of sputum for acid-fast bacilli were negative. Sputum for Gene-Xpert didn't detect any Mycobacterium tuberculosis. Fine needle aspiration from the right epitrochlear lymph node was done initially, and cytology was suggestive of granulomatous inflammation (small clusters of epithelioid cells on the background of lymphocytes, fatty tissue fragments, necrotic material and blood). She had been started on a therapeutic trial of anti-tubercular therapy (ATT) due to the endemicity of tuberculosis in Bangladesh.

She didn't have any symptomatic benefit or radiological improvement on her regular follow up visits. Moreover in the 5th month of her illness while on ATT, she developed multiple itchy erythematous papules and plaques involving her back and upper limbs, sparing the palm and sole. Over her left ala of nose there was another single erythematous infiltrative shiny papule with telangiectasia, suggestive of lupus pernio [Figure-2]. She also complained of generalized myalgia, but no specific joint pain.

Repeat HRCT chest was consistent with the previous report but with more progressive features [Figure-3].

She manifested restrictive lung function on spirometry. [Figure-4].

Biopsy from the skin lesion unveiled multiple small discrete non-caseating granulomas made of epithelioid cells over the dermis, consistent with the histopathologic picture of sarcoidosis.
She was eventually diagnosed to have "**Multisystemic Chronic Sarcoidosis (Pulmonary Stage II, Lymph nodes and Skin) with Severe Hypovitaminosis D**". We had stopped her ATT, and started her on oral prednisolone at a dose of 1mg/kg/day with oral Vitamin D supplement. She showed impressive recovery over next 4 months in terms of symptomatic wellbeing, reduced serum ACE (Angiotensin converting enzyme) level (48 U/L) indicating reduced granuloma burden, healed cutaneous lesions [Figure-5] and resolving radiological shadows [Figure-6].

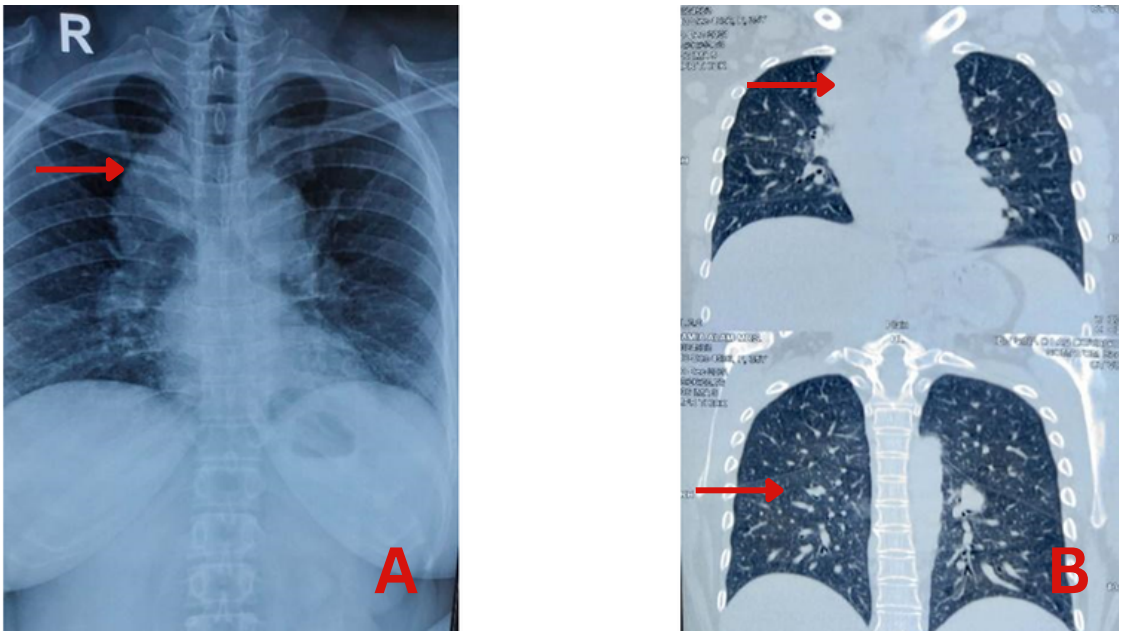

Figure 1 - Initial imaging:

A: Chest radiograph (P/A view): Bilateral hilar and right paratracheal lymphadenopathy.
B: HRCT chest: Extensive mediastinal (pre, para tracheal, aorto-pulmonary window, azygo-esophageal recess, pre and subcarinal regions) lymphadenopathy. Reticulonodular shadows affecting the whole of both lung fields.

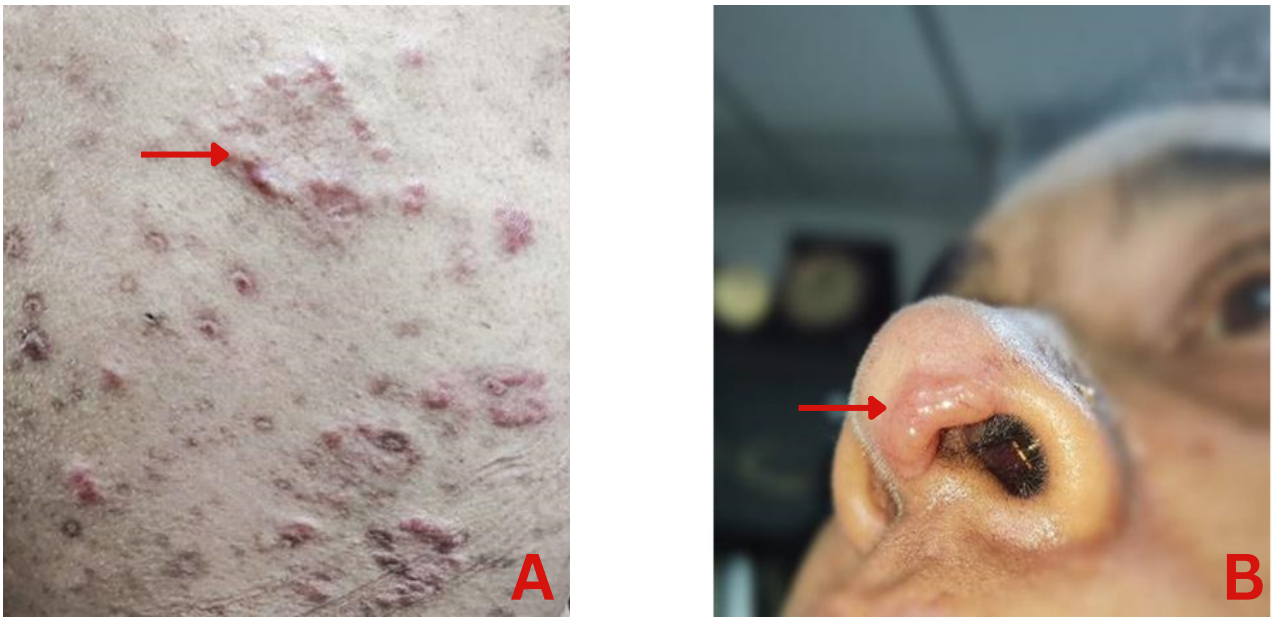

Figure 2

A: Erythematous and infiltrative papules along with annulare plaques having infiltrative elevated border and central clearing involving the back.
B: Lupus pernio.

Table 1 - Repeat investigations

Investigation	Result	Reference range
Hemoglobin	10.3 g/dL	12-16
Total white blood cell count	2,920×10^9/L	4,500-11,000
Neutrophil	51%	
Lymphocyte	35%	
Platelet count	123,000×10^9/L	150,000 - 450,000
ESR	53 mm in 1st hour	0-20
Serum calcium level	9.28 mg/dL	8.5-10.3
Serum angiotensin converting enzyme (ACE) level	199 U/L	20-70
Serum Vitamin D (25-OH) level	10.40 ng/mL	30-100
serum lactate dehydrogenase	166 U/L	100-190

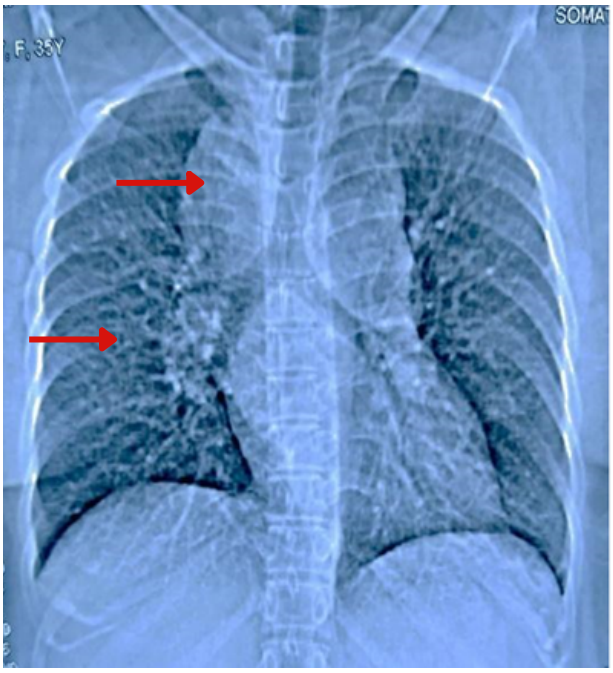

Figure 3 -Repeat HRCT chest:
Extensive mediastinal lymphadenopathy with bilateral pulmonary reticulonodular shadowing. [Bilateral axillary and upper abdominal lymphadenopathy were also reported, not shown on this image].

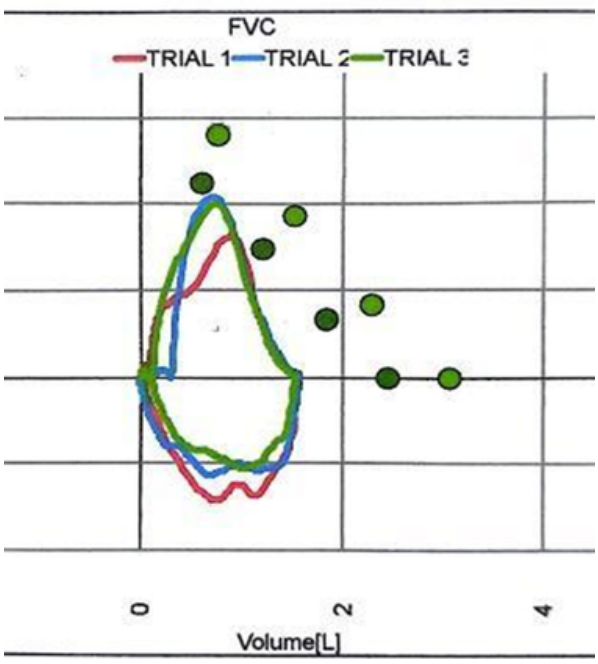

Figure 4 -Spirometry:
Moderate-severe restrictive picture

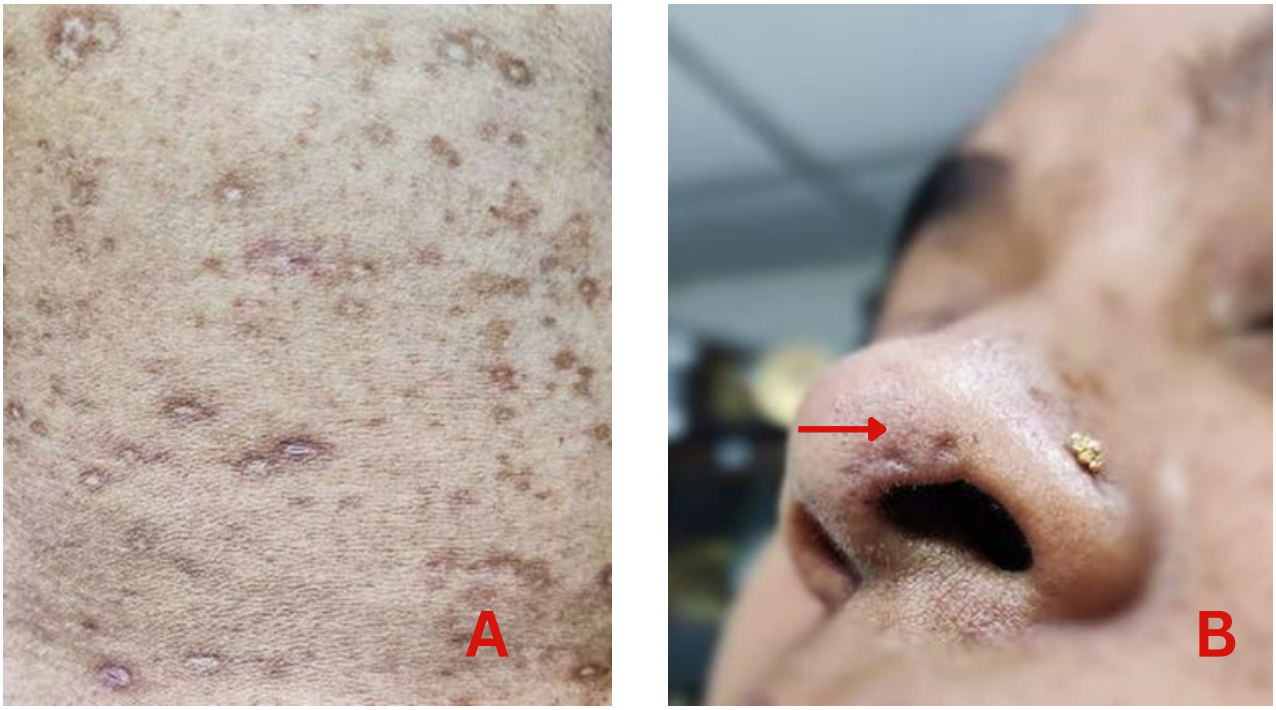

Figure 5 Follow-up visit on treatment:

A: Healed atrophic scars over back.
B: Healed scar of lupus pernio

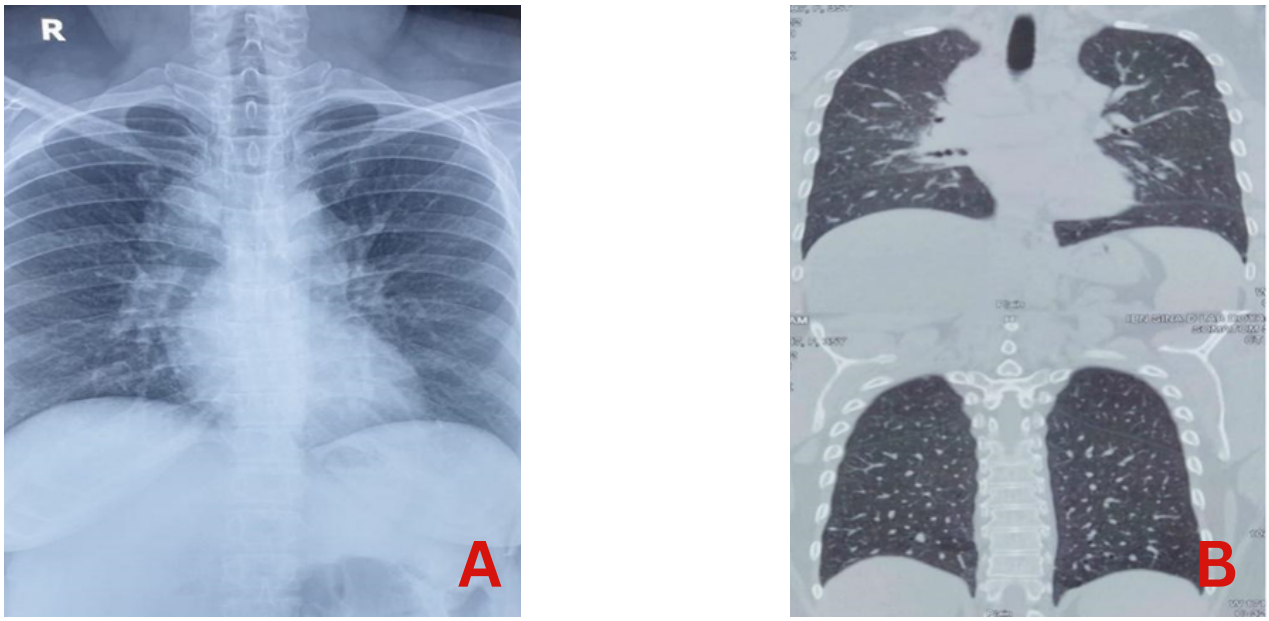

Figure 6 - Follow-up imaging:

A: Chest radiology (P/A view): Resolving shadows of mediastinal lymphadenopathy
B: HRCT chest: Reduced shadows of mediastinal lymphadenopathy with almost clear lung fields

Discussion

Sarcoidosis can involve any organ, clinical and radiological appearances are diverse in nature and the characteristic non-caseating granulomas can mimic tuberculosis, lymphoma, carcinoma, fungal disease, and berylliosis.(6) The case presented here was a tuberculosis (TB) mimic. All the symptoms of sarcoidosis were not present since the beginning of the illness. Her late presentation of cutaneous features made the diagnosis difficult. However, unresponsiveness to empirical ATT went in favor of sarcoidosis. Studies suggest, the lung parenchyma is almost always affected and enlarged bilateral hilar and right paratracheal lymph nodes are the most common radiological deviation; which was consistent with our finding. The granulomas resolve gradually or heal by fibrosis.(6) In almost two-third of cases it is self-limiting. Chronicity occurs in approximately 30% of cases and fatalities occur in 1 to 4%.(7) Respiratory failure is the most frequent cause of death associated with sarcoidosis.(8)

Micro-papules, papules, plaques, erythema nodosum, subcutaneous nodules, lupus pernio, ulcer, scar sarcoidosis, and alopecia are common cutaneous manifestations. Sarcoid papules can be a lichen planus mimic. Ernest Besnier in 1889, marked lupus pernio as an indicator of chronic sarcoidosis.(2) In our case we have got lupus pernio which established the chronicity of the disease. Mild anemia (hemolytic or non-hemolytic), leucopenia, neutropenia, monocytosis, eosinophilia and thrombocytopenia have been documented (9), as we have demonstrated in our case except monocytosis and eosinophilia. Serum ACE level represents the overall granuloma burden in sarcoidosis as it is produced by the epithelioid cells; but it does not have any prognostic value.(10)

Hypovitaminosis D has been proven to lead the pulmonary sarcoidosis from stage-2 towards stage-4, and has a strong positive association with disease hronicity.(11) Even so, it has no correlation with the lymph node involvement or the skin manifestations of sarcoidosis.(11) The role of vitamin-D therapy as treatment or prophylaxis of sarcoidosis can act as a double-edged sword. It might reduce the development and spread of granulomas, but in around 10% of cases it may cause asymptomatic hypercalcemia and hypercalciuria.(12) Under close monitoring, we treated her with vitamin-D supplements, and no adverse outcome was noted.

For sarcoidosis, we have treated our patient with corticosteroids which is the first line therapy and she responded well. Steroid-sparing therapy may be needed in uncontrolled diabetes and/or

hypertension, decompensated heart failure, glaucoma, severe obesity or as add-on therapy in neuro-sarcoidosis, severe infiltrative heart disease or ophthalmic injury. In the chronic disease course, the duration of therapy is generally considered to be approximately a year, as shorter courses have been reported with an increased risk of relapse.(12)

Conclusion

It is important to lower the threshold to consider sarcoidosis taking into account its deceptive nature which can easily lead to misdiagnosis and late diagnosis, especially in the TB endemic areas.

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