Rom J Rheumatol 2025, 34(1):190-194 ISSN (print) 1843–0791, ISSN (online) 2069–6086

Revista Română de Reumatologie
Romanian Journal of Rheumatology

CASE REPORT

When The Skin Speaks For The Lungs: A Case Of Sarcoidosis With Erythema Nodosum

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Abstract

Erythema nodosum (EN) is a common but nonspecific form of panniculitis that may serve as an early cutaneous marker for systemic disease, including sarcoidosis. We report the case of a 32-year-old male who presented with painful erythematous nodules on both lower legs, bilateral ankle arthritis, and systemic inflammatory symptoms. Chest imaging revealed bilateral hilar lymphadenopathy and diffuse pulmonary micronodules. Laboratory investigations showed marked inflammatory markers and autoimmune thyroiditis. The constellation of findings was consistent with Löfgren syndrome - a well-defined acute presentation of sarcoidosis characterized by EN, arthritis, and bilateral hilar adenopathy. The patient responded favorably to corticosteroid therapy. This case underscores the diagnostic value of erythema nodosum as a clinical clue to underlying sarcoidosis and highlights the need for thorough systemic evaluation when EN is present.

Keywords: sarcoidosis, Löfgren syndrome, erythema nodosum, arthritis, autoimmune thyroiditis.

Introduction

Sarcoidosis is a multisystem inflammatory disorder marked by the presence of noncaseating granulomas in affected tissues. Although the lungs and intrathoracic lymph nodes are the most commonly affected sites -seen in over 90% of cases- sarcoidosis can involve virtually any organ. Granulomas in sarcoidosis are formed as a result of abnormal activation and accumulation of CD4+ T lymphocytes and macrophages in affected tissues. These immune cells produce a range of proinflammatory cytokines that drive the clinical manifestations and contribute to disease progression and complications[1,2].

Sarcoidosis usually affects individuals between 20 and 60 years of age. Although it was first recognized in younger adults, recent clinical observations indicate that the majority of diagnoses now occur after the age of 40 particularly in females, suggesting a shift in the demographic pattern of the disease [3]. The increased incidence in specific ethnicities and age brackets suggests a multifactorial etiology involving genetic susceptibility and environmental triggers [4].

Clinical manifestations can be highly variable, ranging from asymptomatic cases (10–15%), often discovered incidentally through imaging studies, to presentations involving organ failure [1]. Therefore, the diagnosis can be challenging and relies on the histopathological identification of non-caseating granulomas, characteristic clinical and imaging features, and, importantly, the exclusion of other causes of granulomatous inflammation [5].

Treatment is not required in all cases of sarcoidosis. Most cases, particularly those with isolated pulmonary involvement, may be self-limiting. Therapy is indicated when patients experience disabling symptoms or show evidence of progressive organ dysfunction. Glucocorticoids remain the first-line treatment, although the optimal dose and duration are not clearly established. Corticosteroid therapy in a dose of 20-40 mg/day may be considered for 4-6 weeks, with progressive taperinng over the course of up to 12 months, depending on clinical evolution. In refractory cases, immunosuppressive agents such as disease-modifying antirheumatic drugs (DMARDs) may be used, with methotrexate being the most extensively studied. Recent studies have demonstrated the efficacy of TNF-alpha inhibitors -particularly infliximab- in treating refractory sarcoidosis[6,7].

Case Presentation

A 32-year-old male presented to the Rheumatology Department for evaluation of painful erythematous nodules on both lower legs and bilateral ankle swelling. The patient reported difficulty walking, joint pain, and alternating episodes of diarrhea and constipation. The symptoms progressed over a few weeks before presentation. He denied ocular or urinary symptoms and had no significant past

medical history.

One month prior, the patient presented to the rheumatologist with similar complaints. Serological testing for Yersinia and Salmonella antibodies was negative, as was the ANA panel. An inflammatory syndrome was noted, with a C-reactive protein (CRP) level elevated tenfold, an erythrocyte sedimentation rate (ESR) of 48 mm/h, and leukocytosis (12,000/µL). The patient received oral methylprednisolone 16 mg daily for 5 days, followed by 8 mg daily for another 5 days, with clinical improvement. However, symptoms recurred shortly after corticosteroid discontinuation.

During admission, clinical examination confirmed bilateral erythema nodosum, bilateral ankle arthritis, and limited mobility as shown in Figure 1a and 1b. He was afebrile, physical examination revealed no palpable lymphadenopathy or organomegaly. Blood pressure was within normal limits, measured at 120/80 mmHg.

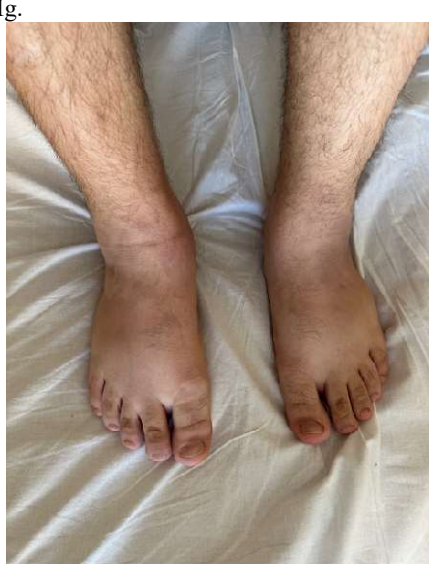


Figure 1a. *showing bilateral swelling of the ankle joints.*

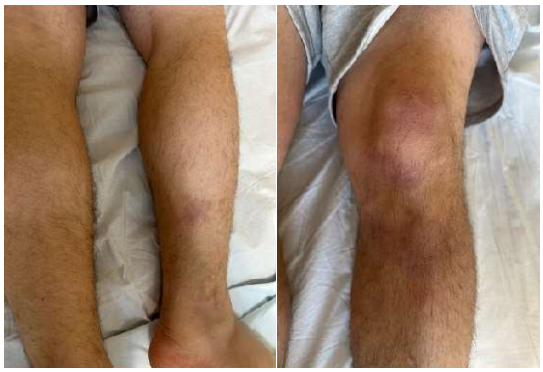
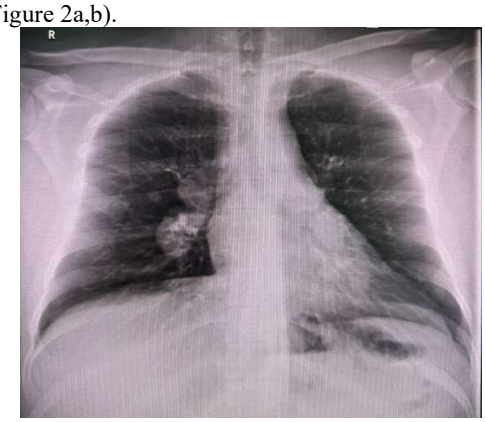


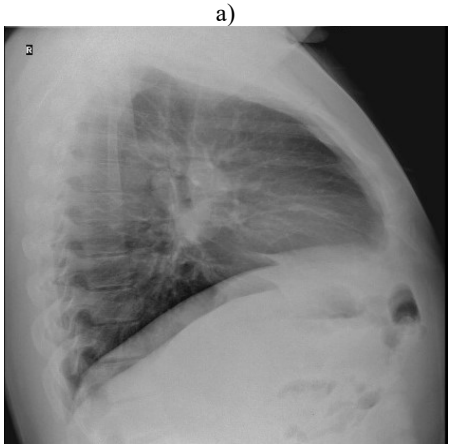
Figure 1b. *Erythema nodosum lesions.*

Laboratory investigations revealed leukocytosis (12,400/µL), elevated CRP of 108 mg/L, and an ESR of 60 mm/h. Uric acid, serum creatinine and calcium levels were within normal limits. Rheumatoid factor (RF) was mildly positive at 22 IU/mL, anti-cyclic citrullinated peptide (anti-CCP) antibodies were negative. Thyroid function tests showed a TSH level of 5.7 µIU/mL (slightly elevated) with a free T4 (FT4) of 1.06 ng/dL (within normal limits), and significantly elevated anti-thyroid peroxidase (ATPO) antibodies at 1600 IU/mL, suggesting autoimmune thyroiditis. Angiotensin-converting enzyme and procalcitonin were negative. The ECG showed no significant abnormalities.

Chest X-ray revealed nodular opacity (17×12 mm) in the medial segment of the right middle lobe, with unclear etiology. Pseudonodular pleural/chest wall opacity (36×18 mm) in the left lateral thoracic region. Bilateral hilar enlargement with polycyclic contours, suggestive of lymphadenopathy → CT recommended (Figure 2a,b).



a)



b)

Figure 2. *Chest X-ray suggestive of lymphadenopathy.*

The contrast-enhanced thoracic CT scan revealed multiple micronodules and small pulmonary nodules, with a maximum diameter of 11×10 mm, diffusely distributed across both lungs, predominantly peripheral and subpleural in location. Additionally, discrete ground-glass opacities were observed, associated with reticular interstitial changes, most evident in the posterobasal and paracardiac segments of the right lower lobe and the anterobasal segment of the left lower lobe. There was no evidence of pleural or pericardial effusion. The examination also identified multiple mediastinal and hilar lymphadenopathies, with enlarged lymph nodes located in the upper and lower paratracheal, subaortic, Barety, infracarinal, and bilateral hilar regions.

(Figure 3a,b).

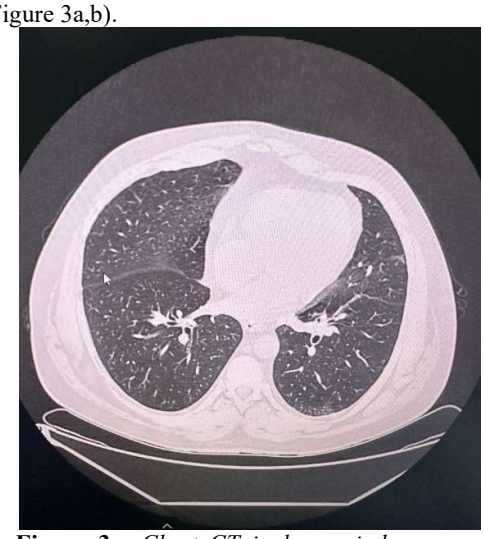


Figure 3a. *Chest CT in lung window revealing ground-glass opacities and pulmonary micronodules*

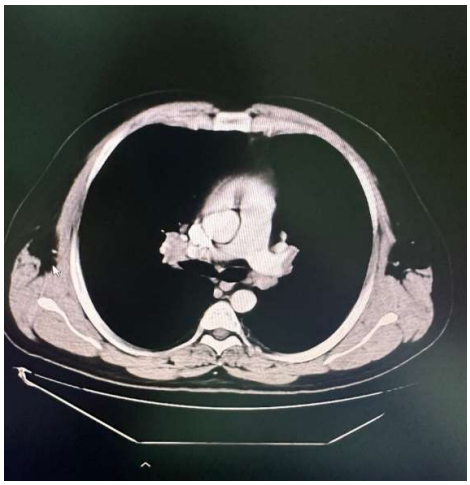


Figure 3b. *Chest CT with mediastinal window showing hilar lymphadenopathy*

Musculoskeletal (MSK) ultrasound of both ankles revealed a minimal amount of fluid in the tibiotalar recess bilaterally, along with significant subcutaneous soft tissue edema (Figure 4).

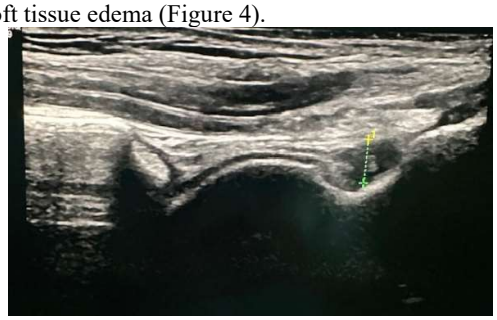


Figure 4. *Minimal amount of fluid in the tibiotalar recess*

Dermatology consult identified erythema nodosum localized to the lower legs. Endocrinology consult revealed chronic autoimmune thyroiditis with a pseudonodular pattern and subclinical hypothyroidism.

Based on the clinical and imaging findings, corticosteroid therapy was reinitiated with oral prednison at a dose of 20 mg daily, for 4 weeks alongside proton pump inhibitors. Also, methotrexate (MTX) was started at 10mg/week and escalated to 20 mg/week by 12 weeks. To increase tolerance, it was recommended folic acid supplementation in a single dose of 5mg/week. After endocrinology evaluation, the patient was recommended to administer levothyroxine therapy (25 μg daily) for subclinical hypothyroidism. The patient showed significant clinical improvement after two weeks, with resolution of joint pain and reduction in skin lesions. He was discharged with a tapering schedule of corticosteroids and referred for pulmonology follow-up.

Discussions

Löfgren syndrome (LöS) is a rare, acute form of sarcoidosis first described by Sven Löfgren in 1953, seen in 5% to 10% of sarcoidosis cases. It is characterized by the triad of erythema nodosum, bilateral hilar lymphadenopathy and acute polyarthritis. Diagnosis does not require all three classic features to be present [8,9].

LöS usually carries a favorable prognosis. Most patients respond well to corticosteroid therapy, but a few may require more intensive treatment [10].

Cutaneous involvement is frequent in sarcoidosis, with the skin being the second most commonly affected organ after the lungs. Skin lesions often represent the initial clinical manifestation, and one study found that in 80% of patients, these cutaneous signs appeared either prior to or concurrent with the diagnosis of systemic sarcoidosis [9].

Erythema nodosum (EN) in sarcoidosis is linked to a favorable prognosis and typically presents as tender, erythematous nodules on the lower legs [11]. Patients with EN often show lower radiological stages of pulmonary sarcoidosis, indicating less severe lung involvement [12].

Sarcoidosis diagnosis requires clinical compatibility, histological evidence of noncaseating granulomas, and exclusion of other causes [5]. The only exceptions for requirement of histopathologic confirmation are: stage I pulmonary sarcoidosis that can be diagnosed based on bilateral hilar adenopathy alone after ruling out other causes and Löfgren syndrome [13].

Serum markers play a limited role in diagnosing sarcoidosis. Although elevated serum angiotensin-converting enzyme (ACE) levels were initially considered specific and correlated with disease activity, subsequent studies have demonstrated a sensitivity of approximately 40%, with poor specificity and false-positive rates up to 15%. Elevated ACE levels may also occur in other conditions such as systemic storage disorders, hepatic disease, diabetes mellitus, autoimmune or granulomatous diseases, and certain infections [6,8]. Elevated serum ACE levels may be useful in monitoring disease progression, as

they reflect the total granuloma burden in the body and correlate with the number of affected organs [14].

The correlation between sarcoidosis and autoimmune thyroiditis has been well studied. A meta-analysis found that thyroid disease is significantly more common in sarcoidosis patients compared to controls (OR 3.28). The link between sarcoidosis and thyroid disease may involve common immunopathogenic pathways, including Th1/Th17 cell activation and sarcoidosis patients with hypothyroidism tend to have more multi-organ involvement [15].

In our case, clinical presentation together with the radiological findings and laboratory results are suggestive of sarcoidosis in the absence of alternative diagnosis. The chest CT revealed bilateral hilar and mediastinal lymphadenopathy associated with pulmonary micronodules, a pattern frequently observed in stage I-II pulmonary sarcoidosis [6]. Other potential causes, such as tuberculosis, lymphoma, autoimmune diseases (e.g. seronegative rheumatoid arthritis, vasculitis), and inflammatory bowel disease, were systematically excluded through laboratory testing and imaging. The therapeutic response to systemic corticosteroids, alongside normalization of CRP and improvment of the skin and joint symptoms, further supports the diagnosis.

Conclusions

Sarcoidosis is a complex disease with diverse clinical presentations that often mimic other conditions, posing significant diagnostic and management challenges. A definitive diagnosis requires excluding other causes of granuloma formation, such as tuberculosis, fungal infections, foreign body reactions, autoimmune diseases (including granulomatosis with polyangiitis and Crohn's disease), and drug-induced allergies, as these can have similar histopathological features [6]. Once diagnosed, patients should undergo a comprehensive evaluation to determine the extent of organ involvement [5]. Close monitoring and regular follow-up are essential because sarcoidosis carries a risk of relapse or recurrence. Spontaneous remission occurs in about half of patients within two years, and in many more within five years; however, the chance of remission decreases after this period. Mortality due to sarcoidosis is relatively low, affecting 1-5% of patients, with respiratory failure, neurosarcoidosis, and cardiac complications being the most common causes of death [14].

Conflicts of Interest: The authors declare no conflicts of interest.

Informed consent

Written informed consent was obtained from the patient. The identity of the patient has been kept anonymous in accordance with ethical standards.

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Received: 11.03.2025

Accepted: 29.03.2025