Cutaneous Sarcoidosis of the Lower Extremity: A Case Report and Review of the Literature

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OBJECTIVES

- Illustrate a multisystem flare of sarcoidosis presenting through co-occurring cutaneous and pulmonary manifestations in a patient with previously inactive disease
- Emphasize the diagnostic importance of dermatological findings as potential indicators of systemic sarcoid activity
- Demonstrate the efficacy of a multidisciplinary diagnostic workup in managing complex cases of sarcoidosis involving the lower extremities
- Evaluate the therapeutic escalation for the successful resolution of cutaneous lesions

INTRODUCTION

Sarcoidosis is a systemic, multisystem inflammatory disease characterized by the formation of non-caseating granulomas. While pulmonary involvement is nearly universal, the disease frequently presents with extrapulmonary manifestations.

- Prevalence Factors: Highest in Caucasians and females [1]
- Risk Profile: Increased prevalence in never-smokers compared to past/current smokers [1]

Sarcoidosis can affect nearly any organ system, with varying frequencies [1]:

- Lungs & Lymph Nodes: 97%
- Liver: 65%
- Skin: 35%
- Eyes: 12–50%
- Nervous System: 10%
- Heart: 5%

Diagnostic accuracy relies on a combination of imaging, biopsy, and laboratory work:

- Differentials: Must differentiate from malignancy and pulmonary infections [2]
- Staging: Disease staging is refined by systematically excluding or identifying extrapulmonary involvement [3]

Treatment is tailored to the severity of organ involvement and symptomatic burden [2]:

- First-Line: Systemic corticosteroids - Prednisone
- Steroid-Sparing Agents - Methotrexate, Azathioprine, or Mycophenolate Mofetil
- Emerging Therapies - Janus Kinase (JAK) Inhibitors

Table 1: Making the Diagnosis of Sarcoidosis [4]

Clinical Presentation	- Dyspnea, cough, chest pain, fatigue, fever, weight loss - Skin: erythema nodosum, lupus pernio - Eyes: uveitis, conjunctival lesions - Joints: arthralgias, arthritis	- Variable presentation - Multiple organ involvement
Radiographic	- Bilateral hilar lymphadenopathy - Parenchymal infiltrates - Fibrosis (advanced disease)	- Chest X-ray / CT
Histopathology	- Non-caseating granulomas	- Usually obtained using biopsy - Needed for diagnosis
Labs	- Elevated serum ACE levels - Hypercalcemia / hypercalciuria - Elevated ESR/CRP - Lymphopenia	- Supportive - ACE levels do not always correlate with the disease

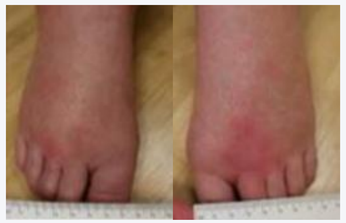

Figure 1 - Clinical Photograph:
Bilateral feet at initial presentation illustrating the maculopapular rash with cutaneous nodules

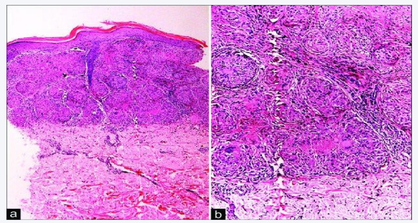

Figure 2 - Representative Photomicrograph Cutaneous Sarcoidosis Skin Biopsy:
(a) Multiple epithelioid cell granulomas in upper/mid dermis (H&E, x100)
(b) Granulomas well-formed, compact, without lymphoid cuffing (H&E, x200) [6]

CASE PRESENTATION

A 49-year-old female with a significant multisystemic medical history presented to the Foot Clinic with new-onset skin eruption on the lower extremities [Figure 1].

The patient's past medical history is notable for pulmonary sarcoidosis, which was diagnosed in 2016 and previously stable/inactive.

- Comorbidities include:
  - **Endocrinologic/Metabolic:** Type 2 Diabetes Mellitus, diabetic polyneuropathy, hypothyroidism, and dyslipidemia
  - **Inflammatory/Autoimmune:** Undifferentiated inflammatory arthritis and endometriosis
  - **Oncologic:** History of breast malignancy (2006) status post-bilateral mastectomy, chemotherapy, and radiation
  - **Surgical/Infectious:** Status post-toe amputation for diabetic ulcer with osteomyelitis
  - **Psychiatric:** Major Depressive Disorder and Bipolar I Disorder

Physical Examination & Clinical Findings

- Integumentary: Bilateral, macular erythematous rashes localized to the dorsal aspect of the lower extremities. Palpation revealed firm, subcutaneous nodules within the affected areas.
- Ancillary Testing: Chest CT was performed to evaluate systemic involvement, which identified active pulmonary sarcoidosis, confirming a multisystem flare.

Clinical Course & Management

The patient's treatment was based on diagnostic findings and clinical response:

1. Initial Phase: While awaiting the multidisciplinary workup, the patient was started on Hydrocortisone 2.5% cream twice daily.
2. Systemic Response: Following the CT confirmation of active pulmonary disease, oral Prednisone was initiated. While the foot rash showed initial improvement, the patient developed new erythematous nodules on the upper extremities.
3. Treatment Escalation: Fluocinolone 0.025% cream was substituted for the hydrocortisone.
4. Outcome: This combination led to the full resolution of pulmonary granulomas, the cutaneous rash, and the skin nodules.
5. Maintenance: The patient successfully tapered her systemic steroids and is currently maintained on 5mg of Prednisone daily to ensure continued remission. Although the lesions resolved, minor residual pain at the previous nodule sites was reported.

Table 2: Extra-Pulmonary Manifestations of Sarcoidosis [5]

Organ System	Prevalence (Percentage Range)
Skin	16-32%
Eyes	12-23%
Liver	12-20%
Lymph Node	12-15%
Neurologic	5-9%
Bone Marrow	4-8%
Spleen	7%
Bone & Joints	1-7%
Cardiac	2-5%
Parotid/Salivary Gland	3-4%
Renal	1%
Muscle	0.4-1%

Table 3: Sarcoidosis and the Skin [2, 3, 5, 6]

Specific Sarcoidosis Skin Lesions	Atypical Sites Where Specific Sarcoidosis May Appear	Nonspecific Sarcoidosis Skin Lesions
Papular Sarcoidosis	Scar Sarcoidosis	Erythema Nodosum
Nodular Sarcoidosis	Tattoo Sarcoidosis	Erythema Multiforme
Plaque Sarcoidosis	Nail Sarcoidosis	Nail Clubbing
Lupus Pernio	Scalp Sarcoidosis	Calcinosis Cutis
Hypopigmented Sarcoidosis	Alopecia	Others
Angiolupoid Sarcoidosis	Genital Sarcoidosis	
Psoriasiform Sarcoidosis	Oral Cavity Sarcoidosis	
Verrucous Sarcoidosis		
Others		

DISCUSSION

Pathophysiology and Clinical Presentation

- Sarcoidosis is a multifaceted systemic disease characterized by the formation of non-caseating granulomas. This case illustrates the classic systemic reach of the disorder, where an initially inactive pulmonary diagnosis transitioned into an acute flare involving the lungs, skin, and potentially the joints.
- The hallmark of specific sarcoid lesions is the "naked granuloma" - a cluster of epithelioid cells with a distinct scarcity of surrounding lymphocytic inflammatory activity.

Diagnostic Work-up and Differential Diagnosis

- Diagnosis is frequently a process of exclusion, as sarcoidosis, particularly in its mild or asymptomatic stages, can mimic several conditions. A multidisciplinary approach is essential to differentiate sarcoidosis from mycobacteria tuberculosis, fungal infection, immune deficiency states, and malignancy [Table 1].

Categorization of Cutaneous Lesions

- Cutaneous manifestations, the second most common organ involvement after the lungs [Table 2], are categorized based on histological findings:
  - Specific Lesions: Histology reveals non-caseating granulomas upon biopsy
  - Nonspecific Lesions: Reactive processes that do not contain granulomas [Table 3]

A biopsy was not necessary, as this case demonstrated that in a patient with a known history and clear systemic flare, clinical diagnosis and treatment response can be sufficient. A representative biopsy from the literature is depicted in Figure 2.

Treatment Challenges and Considerations

- Corticosteroid therapy remains the cornerstone for managing acute flares and preventing permanent organ damage. However, this case highlights two critical management barriers:

1. The "Burst and Taper" Cycle: The recurrence of disease during prednisone tapering reflects the chronic, unpredictable nature of sarcoidosis.
2. Comorbidity Management: Long-term steroid use presents a significant risk for this patient due to her Type 2 Diabetes. Steroid-induced hyperglycemia must be balanced against the need for inflammatory control, often necessitating a transition to steroid-sparing agents to minimize metabolic side effects.

Osteopathic Concerns

- Potential Somatic Dysfunctions:
  - Inhalation/exhalation rib dysfunctions and diaphragmatic/cervicothoracic inlet restrictions
- OMM Treatment [7]:
  - Direct/Indirect Myofascial Release: To improve local microcirculation and desensitize nociceptors by freeing the restricted connective tissue of previous nodule sites
  - Suboccipital Release: To balance the autonomic nervous system, which is disrupted in patients with chronic inflammatory conditions and comorbid psychiatric disorders

The aim of treatment was to take on a holistic approach, considering not just the presenting symptoms but also the patient's overall physical, emotional, and social well-being.

CONCLUSION

- Sarcoidosis is a multisystem inflammatory condition that typically starts in the lungs, but can later affect other organs, including the skin.
- This case demonstrates how the disease evolved from pulmonary involvement to skin lesions on the lower limbs, showing its unpredictable presentations.
- Managing the condition required collaboration across multiple specialties and an escalation in the patient's treatment from topical steroids to systemic prednisone, which eventually led to an improvement in symptoms.
- This highlights the need for close monitoring and personalized care plans when treating patients with complex, systemic sarcoidosis.

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