



# Isolated subcutaneous sarcoid-like granulomatous inflammation occurring at injection sites: 3 patients treated successfully with minocycline

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## INTRODUCTION

Subcutaneous sarcoidosis is a rare manifestation of systemic sarcoidosis in which firm asymptomatic-to-tender subcutaneous nodules develop secondary to sarcoidal granulomas involving the panniculus.<sup>1</sup> Sarcoidosis implies systemic disease, but subcutaneous lesions may present with absent or mild systemic involvement. Here we report 3 cases of isolated subcutaneous nodules with sarcoidal granulomas after subcutaneous injections that improved after treatment with minocycline.

## REPORT OF A CASE SERIES

In all 3 patients, sarcoidal granulomas developed at the site of previous iatrogenic injections (allergy shots and leuprolin acetate) in the absence of additional lesions or systemic manifestations. All 3 patients had lesions on their bilateral posterior arms and had a complete response to minocycline. Relevant clinical information, diagnostic workup, and micrographs are presented in [Table I](#) and [Fig 1](#), respectively.

## DISCUSSION

Subcutaneous nodules are rare cutaneous manifestations of sarcoidosis occurring in up to 6% of cases, frequently manifesting on the forearms as

indurated linear bands, although lesions can occur at any site.<sup>1-3</sup> In our patients, lesions developed on the bilateral posterior arms, which correspond to prior inoculation sites and differ from the common locations of subcutaneous sarcoidosis.

Previous reports show that subcutaneous sarcoidosis may be the initial clinical presentation of mild systemic involvement.<sup>2,3</sup> However, because of the isolated nature of many cases, it is debated if these subcutaneous granulomatous lesions truly represent a sarcoidal variant. Nevertheless, these lesions require workup for systemic disease and treatment for physical discomfort and aesthetics.

Although the exact etiology of sarcoidosis remains elusive, the development of granulomas has been attributed to a hypersensitivity reaction with a nonspecific response to extrinsic or intrinsic antigens in a genetically susceptible individual. Exposure to these antigens produces local granulomas and is postulated to initiate systemic disease.<sup>4</sup>

The treatment for subcutaneous sarcoidosis revolves around systemic corticosteroids and immunosuppressive agents.<sup>2</sup> In our patients, a therapeutic response was seen with minocycline as a first-line therapy. All patients had a complete clinical resolution; the 2 patients who had preradiographic and postradiographic studies showed

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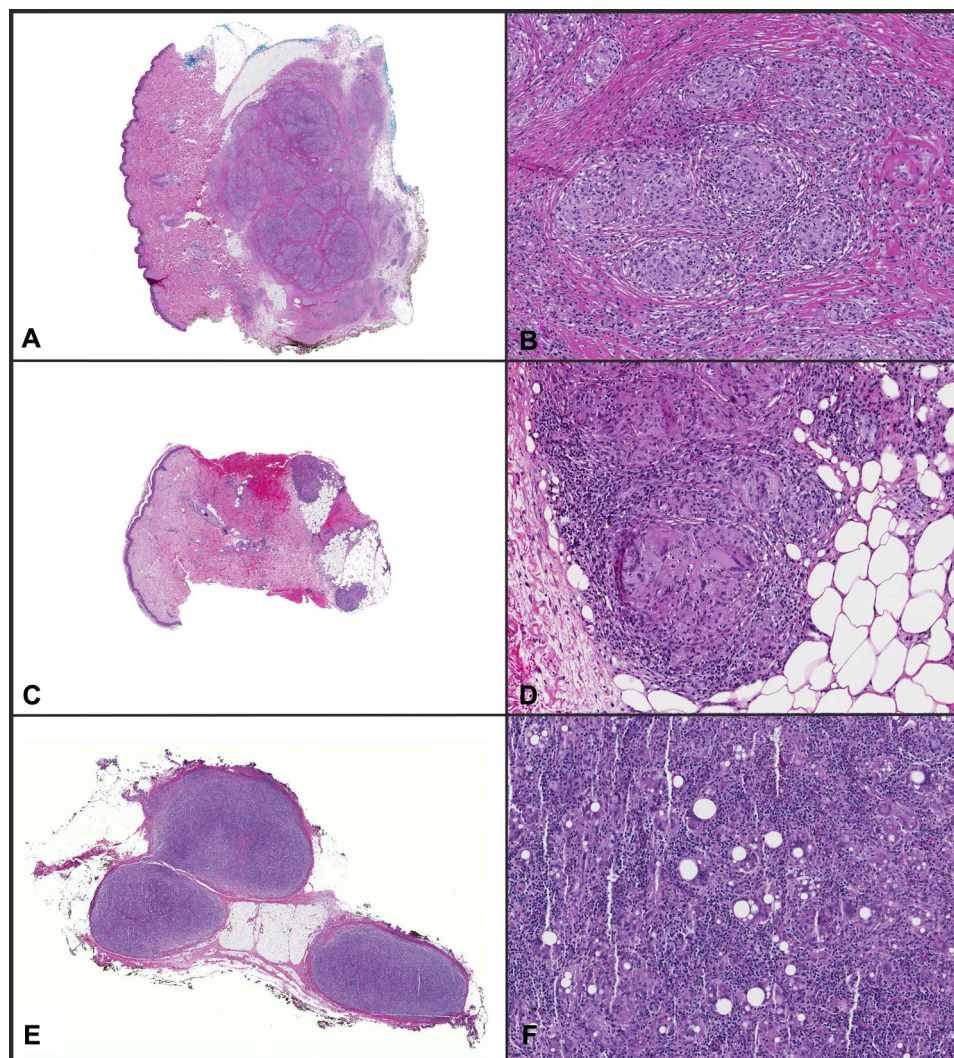
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**Table I.** Clinical features and treatments of cases

	Case 1	Case 2	Case 3
Age/sex	30s/male	50s/female	50s/female
Clinical manifestation	6 tender subcutaneous nodules with papules and plaques	Non-tender subcutaneous nodules; right arm involving 1-1.5% BSA	Tender subcutaneous nodules
Location	Bilateral posterior arms	Bilateral posterior arms	Bilateral posterior arms
Subcutaneous injection	Allergy shots (>20 years ago)	Allergy shots (20-30 years ago)	Leuprolin acetate; 1-2 weeks prior to development of lesions
PMH	Noncontributory	Alpha-1-anti-trypsin (MS genotype)	Uterine fibroids, hypothyroid
ACE (U/L)	97 U/L	39 U/L	14 U/L
Vitamin D 1,25-dihydroxy (pg/mL)	79	N/A	N/A
Vitamin D 25-hydroxy (ng/mL)	25	35	N/A
Calcium (mg/dL)	9.6	9.2	9.7
Chest radiograph	Negative	Negative	Negative
Ophthalmology	Normal	N/A	N/A
Magnetic resonance imaging	None	Interdigitating lesion in the subcutaneous fat that measured 5.0 × 4.9 × 3.0 cm and abuts the superficial muscle fascia	Lobulated soft tissue mass of the left deltoid measuring 3.1 × 1.9 × 4.9 cm, extending beyond the fascia with suspicion for malignancy
Pathology	Nonnecrotizing granulomatous inflammation involving the subcutaneous tissue	Granulomatous panniculitis with sarcoidal-type granulomas	Noncaseating granulomatous inflammation involving the subcutaneous adipose tissue
Treatment	Minocycline	Minocycline	Minocycline
Duration of treatment	2 months; discontinued due to transient muscle pain	2 months; no adverse events	5 months; no adverse events
Treatment response	Complete resolution	Complete resolution	Complete resolution

All cases had additional therapeutic workup, but only the pertinent diagnostics to rule out systemic sarcoidosis were included. ACE, Angiotensin converting enzyme; N/A, not applicable; PMH, past medical history.



**Fig 1.** Low- and high-power micrographs of biopsies before treatment. Special stains for micro-organisms were negative on all biopsies. **A** and **B**, Case 1 showed nonnecrotizing granulomatous inflammation involving the subcutaneous tissue. **C** and **D**, Case 2 showed granulomatous panniculitis with sarcoidal-type granulomas, aggregates of epithelioid histiocytes, multinucleated giant cells, and few scattered lymphocytes. **E** and **F**, Case 3 showed noncaseating granulomatous inflammation involving the subcutaneous adipose tissue. (Original magnifications: **A**,  $\times 0.6$ ; **C**,  $\times 1.0$ ; **E**,  $\times 0.5$ ; **B**, **D**, and **F**,  $\times 10$ .)

radiographic resolution mirroring the clinical improvement. Our findings are consistent with those of previous reported use of minocycline in cutaneous sarcoid lesions, with a therapeutic response in 74% of patients with 22% having complete remission.<sup>5</sup>

We observed localized subcutaneous granulomatous lesions that developed at previous injection sites without systemic involvement. These patients' lesions represent an entity that is clinically and histologically compatible with subcutaneous

sarcoidosis and, as such, require the same evaluation, including assessment for systemic disease and management. Whether these patients are ultimately thought to have isolated single-organ subcutaneous sarcoidosis or subcutaneous sarcoid-like granulomas depends on the evolving definition of sarcoidosis and acceptance of a single-organ sarcoid variant. Isolated cutaneous reaction to iatrogenic injections should remain on the differential diagnosis of subcutaneous granulomas. An optimal treatment regimen remains to be identified;

however, our experience shows minocycline to be an effective option for subcutaneous granulomatous nodules.

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