

A Case of Interstitial Cutaneous Sarcoidosis

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ABSTRACT

A 57-year-old African-American woman with pulmonary sarcoidosis presented to the emergency room with a large solitary violaceous plaque on her right lower leg. The lesion, initially diagnosed as cellulitis, was ultimately diagnosed as interstitial cutaneous sarcoidosis. Classically, sarcoidosis is characterized histologically by non-caseating granulomas with a paucity of inflammatory cells (“naked granulomas”); however, in 16–20% of cases, an interstitial histiocytic pattern is noted under the microscope. Various treatment regimens have been described for cutaneous sarcoidosis, including the use of tetracycline and its derivatives. The patient described in this report was treated with oral minocycline (Minocin[®]) and topical clobetasol propionate (Dermovate[®]) ointment, with significant improvement in both the appearance and symptomatology of the lesion.

KEYWORDS: *cutaneous sarcoidosis, cutaneous infection, necrobiosis lipoidica, granuloma annulare, minocycline, clobetasol propionate*

A 57-year-old African-American woman, with known pulmonary sarcoidosis, was seen in a Toronto emergency department with a one-day history of redness, swelling, and intense burning pain in her right lower leg. A large violaceous plaque had been present on the extremity for two years time and had been slowly increasing in size. The lesion was occasionally painful, and periodically the leg became edematous; however, the patient had never before experienced this degree of pain or swelling.

The patient’s past medical history was remarkable only for pulmonary sarcoidosis, which was currently stable, and for which she was being followed by a respirologist. At the time of presentation, the patient was not experiencing any shortness of breath, cough, or sputum production; she was experiencing only minimal non-specific chest discomfort, a symptom which had remained unchanged for several years. She was not taking any medications, and her pulmonary function tests had remained stable over the previous six months.

Initially, the emergency room physician suspected an underlying deep vein thrombosis based on the symptoms of redness, swelling, and pain in the lower limb. However, when a venous ultrasound revealed normal and patent vessels in the limb, a diagnosis of “dermatitis with superimposed cellulitis” was made. The patient was given a seven-day prescription for cephalexin (Keflex[®]), at a dose of 500 mg daily, and an urgent referral to a Toronto University Dermatology clinic was made.

When assessed in the dermatology clinic shortly thereafter, the patient reported no improvement in the appearance or symptomatology of the limb while on cephalexin (Keflex[®]). The lesion was noted to be a large, well-demarcated violaceous

SOAP Note.

Subjective

One-day history of redness, swelling, and burning pain in right lower leg. Extensive lesion present on the extremity for two years time, slowly increasing in size. No current medications.

Objective

Large, well-demarcated violaceous plaque, delineated by an erythematous border. Significant induration with mild tenderness to palpation. No evidence of local or systemic infection. Negative tissue cultures. Histology: interstitial dermal histiocytic infiltrate, with no well-formed granulomas.

Assessment

Interstitial cutaneous sarcoidosis.
DDx: cutaneous infection, necrobiosis lipoidica, and granuloma annulare.

Plan

Minocin[®], at a dose of 100 mg twice daily, for one month’s time.
Dermovate[®] ointment, to be applied once daily, for one month.
Indefinite use of Minocin[®] and Dermovate[®] ointment at a reduced dose.
Regular follow up with a dermatologist.

plaque, which measured 15 cm x 25 cm in size and also was present circumferentially around the lower leg. The plaque was significantly indurated, delineated by an erythematous border, and mildly tender to palpation. Photographs of the lesion were taken (Figure 1).

Because the patient was known to have systemic sarcoidosis, a diagnosis of cutaneous sarcoidosis seemed likely. Based on the clinical appearance of the lesion, a diagnosis of erythema nodosum—a non-specific manifestation of cutaneous sarcoidosis—was favored.^{1,2} A punch biopsy was performed in order to confirm this diagnosis, and tissue cultures (including

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Figure 1. Large indurated violaceous plaque present circumferentially around the patient's right lower leg.

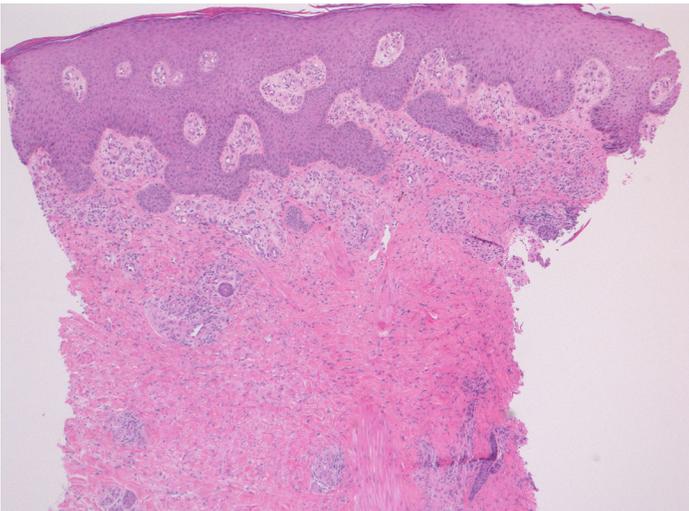


Figure 2. H&E stain of the skin biopsy at low magnification, demonstrating a diffuse dermal histiocytic infiltrate, consistent with interstitial sarcoidosis. No plasma cells, which would be seen in necrobiosis lipoidica, were noted.

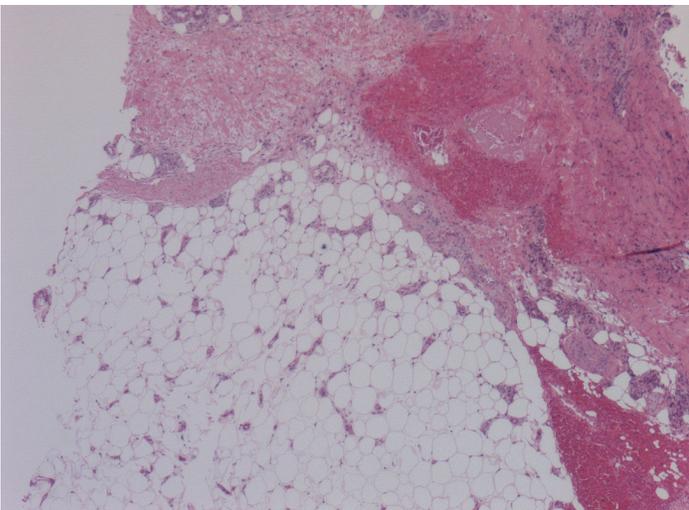


Figure 3. View of the subcutaneous tissue at medium power, demonstrating the absence of panniculitis. Erythema nodosum was excluded based on this finding.

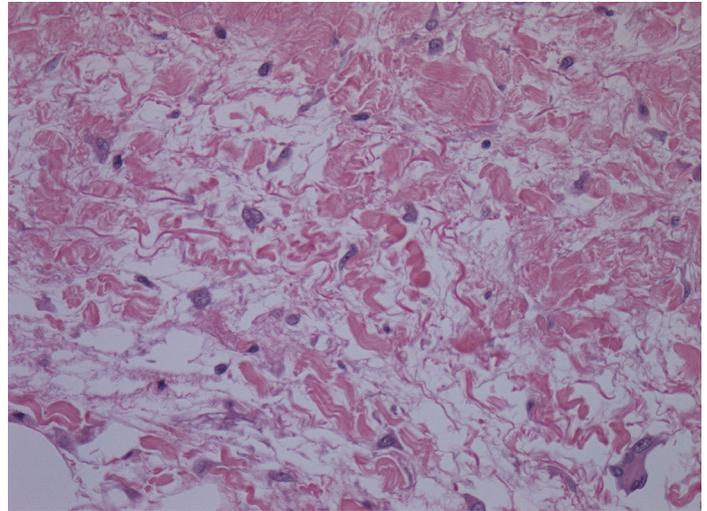


Figure 4. High-powered view of the histiocytic infiltrate within the dermis. This finding, although non-specific, is consistent with atypical cutaneous sarcoidosis.

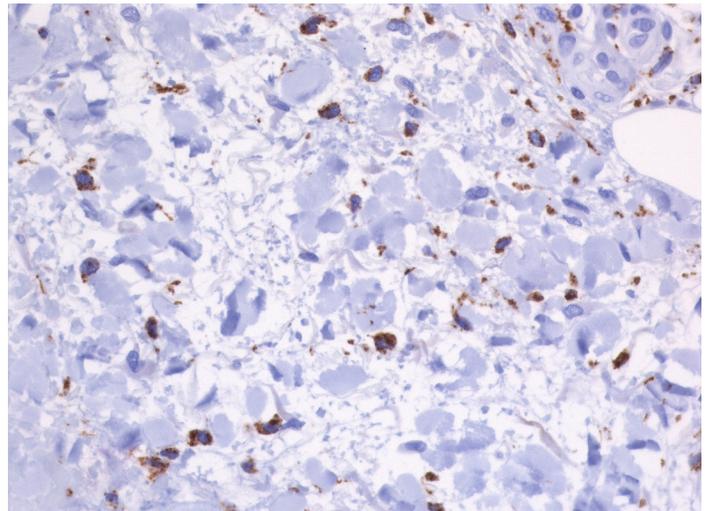


Figure 5. Stain specific for CD68, a glycoprotein expressed on monocytes and macrophages, supporting the presence of dermal histiocytes (40X). Additional stains for mucin, which would be seen in granuloma annulare, were negative.

cultures for fungus and atypical mycobacteria), as well as a Gram stain, were obtained.

The results of the biopsy were unexpected. The clinical diagnosis of erythema nodosum was excluded due to the absence of panniculitis (inflammation of the subcutaneous adipose tissue). However, no well-formed granulomas were present either, which would support the diagnosis of classic cutaneous sarcoidosis. Instead, an interstitial histiocytic infiltrate was observed extending from the upper layers of the dermis into the subcutaneous tissue (Figures 2, 3, and 4). The presence of histiocytes was supported by positive staining of the glycoprotein Cluster of Differentiation 68 (CD68) (Figure 5).

Interstitial histiocytic infiltrates are known to occur in skin infections, drug reactions, and infrequently in cutaneous sarcoidosis. The differential diagnosis in this patient included cutaneous sarcoidosis, other granulomatous diseases (such as necrobiosis lipoidica and granuloma annulare), drug reaction, and infection. Given the patient's negative drug history, the absence of growth on tissue culture, and the overall clinical picture, the most

appropriate diagnosis became interstitial cutaneous sarcoidosis.

Sarcoidosis is a systemic disease of unknown etiology that can affect virtually any organ system of the body.³ Although people of any age, and of either sex, can be affected, sarcoidosis occurs more commonly in people of Irish, Scandinavian, and African-American descent.³ Involvement of the skin has been estimated to occur in 20–35% of cases.⁴⁻⁶ Because involvement of the skin commonly occurs early in the course of systemic illness, a skin biopsy can provide opportunity for early diagnosis.⁴⁻⁷ Most commonly, cutaneous sarcoidosis presents as asymptomatic flesh-colored papules. However, the morphologic appearance of sarcoid lesions are notoriously varied.^{2,5,6,8} Because of this, sarcoidosis has earned the reputation of being one of the “great imitators” in medicine.^{2,9} In this particular case, other “great imitators,” such as syphilis, were not investigated.

When cutaneous sarcoidosis is suspected clinically, a skin biopsy should be performed in order to support the diagnosis. The typical histological appearance of sarcoidosis is that of a granulomatous dermal infiltrate, comprised of epithelioid histiocytes.¹⁰ These granulomas tend to involve few or no inflammatory cells and thus are commonly referred to as “naked granulomas.”¹⁰ However, like the clinical presentation of cutaneous sarcoidosis, the histologic presentation of the disease can be diverse, and several atypical patterns have been described, including that of an interstitial histiocytic pattern.¹¹ In two retrospective studies, this particular pattern was seen in 16–20% of cases of cutaneous sarcoidosis.^{10,11} Interstitial sarcoidosis is a diagnosis of exclusion; one must first rule out the more common causes, including skin infection and drug reaction. In this particular case, a differential diagnosis—which also included necrobiosis lipoidica as well as granuloma annulare—was considered. However, the diagnosis of interstitial cutaneous sarcoidosis was favored due to the clinical history of pulmonary sarcoidosis.

Because very few placebo-controlled studies have been conducted, current treatment recommendations for cutaneous sarcoidosis are based on anecdotal evidence and data from uncontrolled case series.² The use of oral corticosteroids has been described for severe cutaneous involvement; however, because of their significant side effects, these agents are not prescribed for extended periods of time.¹² Intra-lesional triamcinolone or high-potency topical steroids may be effective when cutaneous lesions are both small and limited in number.¹³ In several instances, long-term remission has been achieved through the use of high-potency topical steroids under occlusive dressings.¹⁴ Due to their long-term safety profile, tetracyclines and their derivatives are often the treatment of choice, with minocycline having been reported to produce complete remission in up to two-thirds of cases.¹⁵

The patient in this case was seen in follow up shortly after the biopsy results were obtained, and minocycline (Minocin[®]) was prescribed at a dose of 100 mg twice daily for one month. The patient was also instructed to apply clobetasol propionate (Dermovate[®]) ointment to the plaque once daily for the duration of the month. This therapy resulted in rapid and dramatic improvement in the appearance of the lesion. In order to sustain these results, the patient was instructed to reduce the dose of

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minocycline (Minocin[®]) to 100 mg once daily and to apply the clobetasol propionate (Dermovate[®]) ointment only intermittently as required. Regular follow-up with a dermatologist was also recommended.

In conclusion, cutaneous sarcoidosis is a disease that can present in a variety of ways, both clinically and histologically. Awareness of the heterogeneity of cutaneous manifestations will allow clinicians to consider this disease more often, providing increased opportunity for early diagnosis and treatment. The diagnosis of sarcoidosis is one that requires clinical-pathological correlation. In this case, the diagnosis was based on the presence of confirmed systemic sarcoidosis as well as clinical and histologic features that were compatible with atypical cutaneous sarcoidosis. Although no consensus currently exists for the treatment of this condition, the patient in this report responded well to oral minocycline (Minocin[®]) and topical clobetasol propionate (Dermovate[®]) ointment. 

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