Sarcoidosis Mimicking Lipodermatosclerosis

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The clinical presentation of cutaneous sarcoidosis is highly variable. Rare presentations include ulcerated plaques, morpheaform lesions, and unilateral lower extremity edema. We report the case of a woman who presented with unilateral ulcerating sarcoidosis of the lower leg with progressive fibrosis and edema mimicking lipodermatosclerosis. This case is unique in that the patient exhibited all 3 of the rare manifestations of sarcoidosis; to our knowledge, this presentation has not been previously reported in the literature.
Cutis. 2005;75:322-324.

Systemic sarcoidosis is a chronic granulomatous disease that involves the skin in 25% of affected patients. The clinical presentation of cutaneous sarcoidosis is variable and includes both specific and nonspecific lesions. Specific lesions contain granulomas and include lupus pernio, infiltrative scars, papules, nodules, subcutaneous nodules, and plaques.[1] Nonspecific lesions, which do not contain granulomas, include erythema nodosum, calcinosis cutis, and nail clubbing. Less frequent clinical manifestations of cutaneous sarcoidosis have been reported, such as ulcerative, psoriasiform, hypopigmented, verrucose, ichthyosiform, lichenoid, eruptive, erythrodermic, pustular, atrophic, perforating, umbilicated, and anular lesions,[1-3] as well as folliculitis, faint erythema, scarring alopecia, cheilitis granulomatosa, palmar erythema, angiolupoid lesions, and lupus erythematosuslike and rosacealike lesions.[1-9] Rare presentations include ulcerated plaques, morpheaform lesions, and unilateral lower extremity edema.[4-7]

Accepted for publication June 9, 2004.
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The authors report no conflict of interest.
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We describe the case of a woman who presented with unilateral ulcerating sarcoidosis of the lower leg with progressive fibrosis and edema mimicking lipodermatosclerosis. The presentation is unique in that the patient exhibited all 3 of the rare manifestations of sarcoidosis (ulceration, unilateral edema, and fibrosis), with morphologic similarity to lipodermatosclerosis. To our knowledge, this unique presentation has not been previously reported in the literature.

Case Report

A 52-year-old African American woman with a 5-year history of a slowly enlarging lesion on the left lower leg reported tenderness, swelling, and burning in the area. She had a history of pulmonary sarcoidosis, and the diagnosis was confirmed by results of transbronchial biopsy; she had been taking prednisone 20 to 40 mg/d for the pulmonary sarcoidosis. The patient could not recall the temporal relation between prednisone intake and onset of her skin lesions.

Findings of the physical examination included a firm brown plaque with an irregular surface and a few small punched-out ulcers circumferentially involving the left ankle and foot. A few scattered, smooth, faintly erythematous, brownish papules a few millimeters in diameter were noted over the neck and hips.

Histologic results of multiple biopsy samples from papular lesions revealed nodular collections of epithelioid histiocytes and a few multinuclear cells, characteristic of sarcoidosis. The results of a histologic examination of the biopsy sample from the leg lesion revealed collections of histiocytes and multinuclear cells forming granulomas at all levels of the dermis, characteristic of sarcoidosis (Figure 1). Biopsy results also revealed marked fibrosis in the deep dermis (Figure 2). The available fat was unremarkable. There was no suggestion of an infectious agent. No tissue samples were obtained for cultures.

Treatment with triamcinolone acetonide 0.1% ointment and compression stockings was started. Over the following 7 years, the lesions progressed,

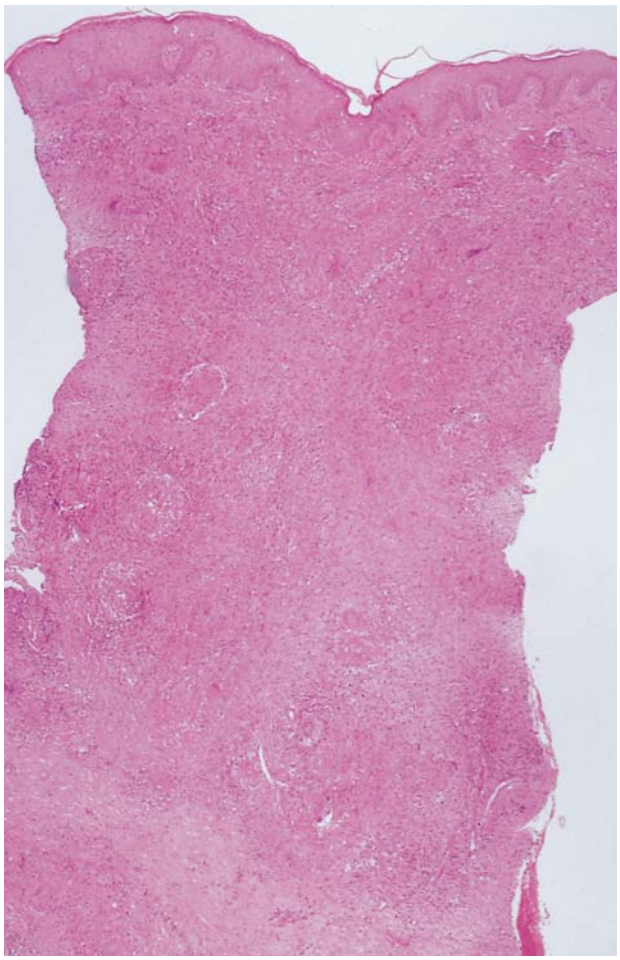

Figure 1. Diffuse sarcoidal granulomas (H&E, original magnification ×40).

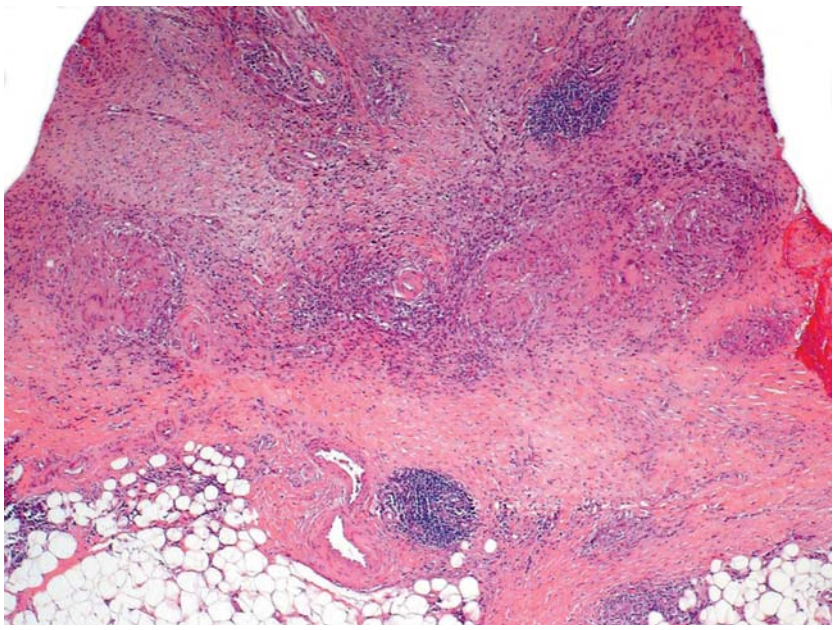

Figure 2. Sarcoidal granulomas and fibrosis in the deep dermis (H&E, original magnification ×100).

extending farther to the medial ankle and dorsum of the left foot. A few punched-out ulcers were present. In addition, there was marked fibrosis of the left ankle, which markedly decreased range of motion. The lesions were treated with intralesional injections of triamcinolone acetonide 10 mg/mL approximately every 4 months for the next 2 years. The patient also was treated with methotrexate and prednisone for her pulmonary disease. The lesions continued to progress, leading to severe constriction of the ankle and lower leg. In addition, marked edema developed proximal to the area of fibrosis and constriction. The findings were similar to the inverted champagne bottle appearance seen in lipodermatosclerosis (Figure 3).

Comment

This case was unique because the patient exhibited the 3 rare clinical features of sarcoidosis—ulceration, unilateral edema, and fibrosis—mimicking lipodermatosclerosis. Ulcerative sarcoidosis is rare and more common in women than in men.[4] The lower extremity is the most common site of development. Ulcers generally develop in papulonodular lesions, but they also may arise de novo. The unilateral edema may be secondary to proximal nodal involvement with sarcoidosis and lymphatic obstruction.[9] Although cases of sarcoidosis with fibrosis (morpheaform sarcoidosis) have been previously reported, the degree of fibrosis and the association with constriction seen in this patient were very unusual.

The cause of fibrosis in cutaneous sarcoidosis may be similar to that proposed for pulmonary sarcoidosis. In the lung, there is evidence of CD4 cell activation, followed by production of various cytokines of the helper T cell subtype 1 (T_H1) pathway, including interleukin 2 (IL-2), IL-8, interferon γ, and tumor necrosis factor α. These cytokines stimulate proliferation of lymphocytes and activation of other effector cells such as macrophages and natural killer cells. This process results in granuloma formation. Subsequently, there is a shift in cytokine profile from the T_H1 to the T_H2 pathway with IL-4 production; this change results in a fibroproliferative response with deposition of extracellular matrix leading to

hyalinization and fibrosis of the granulomas, which cause scarring.[10]

In this case, the patient initially presented with the ulcerative form of sarcoidosis with histologic features typical of granulomas. The lesions progressed through the chronic inflammatory fibroproliferative phase, resulting in fibrosis that resembled lipodermatosclerosis.

The morphologic similarities between the lesions in this patient and those of lipodermatosclerosis may be secondary to the similarities between the proposed pathogenic mechanisms of both diseases.[11] Lipodermatosclerosis presents as bound-down, tender, sclerotic skin on the lower extremities. The condition affects primarily women (mean age, 62 years).[12] Some patients exhibit vascular abnormalities such as deep vein incompetence. The acute phase of lipodermatosclerosis mimics cellulitis, whereas the late phase is similar to morphea. It is speculated that proinflammatory cytokines, which induce hypercoagulable states and venous hypertension, contribute to the pathogenesis of lipodermatosclerosis.[12] Prolonged venous hypertension increases capillary permeability, allowing leakage of macromolecules, including fibrinogen, into the dermis. Decreased fibrinolytic activity leads to the formation of pericapillary fibrin cuffs, which then impede the exchange of oxygen and other nutrients.[12] These changes result in tissue anoxia and ulceration. There is also evidence that the skin adjacent to ulcers in lipodermatosclerosis synthesizes excess collagen and contains abundant transforming growth factor β, which is a potent stimulus for collagen synthesis.[12] These factors may overlap with those implicated in sarcoidosis.

In conclusion, the clinical differential diagnosis of lipodermatosclerosis should include sarcoidosis, along with morphea, erythema nodosum, other forms of panniculitis, and persistent cellulitis.

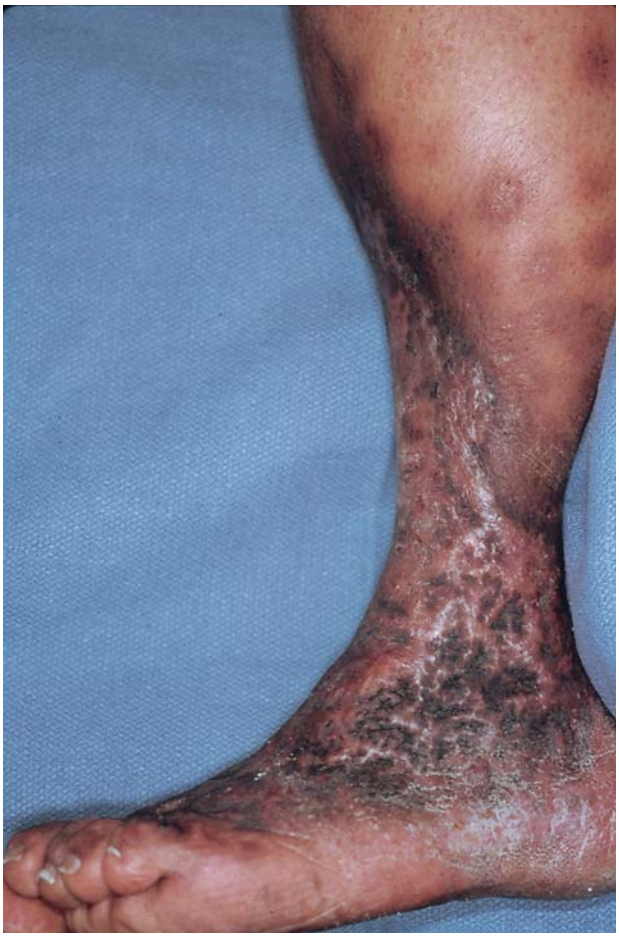

Figure 3. Inverted champagne bottle appearance of left lower extremity after disease progression.

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