



The Morphologic Spectrum of Cutaneous Sarcoidosis

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At our weekly Grand Rounds conference, first-year residents are responsible for presenting the cases of the week, along with a comprehensive differential diagnosis. After each case, the attendings are asked if they would like to add or remove items from our lists, frequently disputing some of the more unlikely or exotic conditions that we try our best to rationalize. One disease that seems to always be listed and rarely argued against is sarcoidosis. Cutaneous sarcoidosis can present in numerous ways with morphologic types including papular, subcutaneous, ulcerative, hypopigmented, erythrodermic, ichthyosiform, morpheaform, and mucosal, among others. Accordingly, the disease can mimic more common conditions, present atypically, and often requires histopathology to clarify the diagnosis.

Recently, a patient with a history of systemic sarcoidosis presented to our clinic for an evaluation of numerous severely pruritic, erythematous, annular plaques on the trunk and lower extremities (Figure 1). Because of our knowledge of her medical history, the lesions were suggestive of cutaneous sarcoidosis and a biopsy revealed multiple sarcoid granulomas, confirming our suspicion. However, in patients without a known history of sarcoidosis, the cause of the eruption would be less clear, and the diagnosis, appropriate workup, and necessary treatment could be delayed. My goal is to provide residents with an overview of the several possible common and uncommon cutaneous sarcoidosis variants so that we have a better understanding of the condition and appreciate when it should be considered in the differential diagnosis. Additionally, it is easy to include sarcoidosis within a broad differential, and I hope to provide some distinguishing factors that might help residents clarify the diagnosis from other more common conditions.



Figure 1. Annular sarcoidosis.

Background

Sarcoidosis is a multisystem granulomatous disease of unknown etiology that can involve all organ systems but most commonly affects the lungs, eyes, lymph nodes, and most notably the skin in 9% to 37% of cases.^{1,2} It occurs in all races, both genders, and all ages, but it is most frequently seen in black women aged 30 to 39 years.^{2,3} Skin disease can occur in association with systemic involvement or in isolation, and it often is characterized as a nonspecific or specific eruption.⁴ Nonspecific lesions of sarcoidosis include erythema nodosum (EN), which does not histologically contain granulomas and is considered to be a reactive process to sarcoidosis present elsewhere. Specific lesions of sarcoidosis, including papular, subcutaneous, and ulcerative variants, are characterized by the presence of noncaseating granulomas at the site of the lesion and often present in the setting of a chronic disease course.

Common Cutaneous Manifestations

Erythema Nodosum—Erythema nodosum represents the most common nonspecific eruption associated with sarcoidosis and typically presents with

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ill-defined, erythematous, tender nodules on the bilateral lower extremities that resolve with bruise-like lesions over the course of 1 to 2 weeks.⁵ When occurring together, sarcoidosis with EN is referred to as Löfgren syndrome, which is an acute and often benign form of sarcoidosis affecting younger adults in association with fever, polyarthralgia, uveitis, fatigue, and bilateral hilar adenopathy. Löfgren syndrome most commonly occurs in white Scandinavian patients and is rare in black patients with an estimated prevalence of 10 to 12 per 100,000 patients, a peak incidence between 20 and 39 years of age, and a predilection in women.^{6,7} The presence of EN or bilateral ankle peri-arthritis alone in combination with bilateral hilar adenopathy typically is sufficient to make a diagnosis. The condition often is self-limited, remitting spontaneously with rare recurrences, and usually responds to nonsteroidal anti-inflammatory drugs.⁶

Papular Sarcoidosis—Papular sarcoidosis is the most common specific manifestation of cutaneous sarcoidosis and usually presents with asymptomatic papules on the face (Figure 2),⁸ often on the periorbital skin.^{5,9} The lesions are firm, 2 to 5 mm, and have a yellow-brown discoloration on a background of erythema.⁹ Clinically, the lesions of papular sarcoidosis can be distinguished from other conditions by the use of diascopy in which firm application of a glass slide over one of lesions causes the erythema to blanch, accentuating the yellow-brown or “apple jelly” appearance. The lesions typically respond to treatment or spontaneously resolve on their own.⁹

Over time, the papules of sarcoidosis may coalesce to form larger plaques that appear round, oval, or annular with more pronounced erythema and deeper granulomatous induration.^{9,10} These plaques often occur on the face, extremities, scalp, back, and buttocks, and are more likely to result in scarring.^{9,11}



Figure 2. Papular sarcoidosis of the nose. Reprinted with permission from *Cutis*. 2007;79:289-290. ©2007, Quadrant HealthCom Inc.⁸

Annular lesions, as seen in our patient, often display central clearing with hypopigmentation, atrophy, scarring, and central cicatricial alopecia when they appear on hair-bearing areas.¹²

Subcutaneous Sarcoidosis—Subcutaneous sarcoidosis, also known as Darier-Roussy sarcoidosis, typically presents as multiple, asymptomatic to mildly tender, firm, flesh-colored nodules on the extremities with involvement of the face, head and neck, trunk, and buttocks less frequently.^{13,14} It most commonly occurs in middle-aged white patients, with a slight female predominance.^{1,15} The presence of these lesions is highly correlated with the occurrence of bilateral hilar lymphadenopathy, and approximately 15% of patients also exhibit uveitis, parotitis, arthritis, mucositis, dactylitis, neurologic and renal involvement, or hepatosplenomegaly.¹³ Nonetheless, it is suggested that subcutaneous sarcoidosis has a relatively good prognosis; one study of 10 cases showed no development of long-term or severe complications.¹⁶

Scar Sarcoidosis—Scar sarcoidosis is another common variant that presents with erythematous to violaceous infiltration and elevation of tattoos and scars, preferentially occurring within scar tissue, traumatized skin sites, and around foreign material (Figure 3).^{9,10,17-23} It has been shown to be present in 29% of patients with cutaneous involvement and can sometimes be the only cutaneous manifestation of systemic disease.^{9,24} The lesions may be tender or pruritic and typically resolve slowly or spontaneously.^{9,25} A biopsy may be needed to distinguish scar sarcoidosis from granulomatous hypersensitivity reactions to tattoo pigment and hypertrophic scars.

Lupus Pernio—Lupus pernio characteristically involves the face and presents as shiny, indurated, reddish brown to purple plaques on the nose, cheeks (Figure 4), ears, and lips.^{6,8,10,26,27} As reported by Spicknall et al,⁸ the condition was first described in 1889 by the French dermatologist Besnier²⁸ who noted on the nose of one of his patients “a general infiltration with very ill-defined borders, with marked thickening” and subsequent “spread in all directions . . . extending to the adjacent parts of the cheeks.”²⁹ Nine years after his initial presentation, his patient was left with “total destruction of the tip [of the nose], while the livid lupus infiltration spread over the 2 cheeks” in what he described as a “perfect example” of the natural evolution of this condition.²⁹ Based on this description, the characteristic morphology of lupus pernio is of ill-defined induration or plaquelike lesions on the face, rather than macular, papular, or nodular lesions. It is important to make this distinction because lupus pernio typically is present in patients with extensive systemic involvement and a chronic disease course.^{8,30}



Figure 3. Large erythematous violaceous plaque of sarcoidosis that developed over a prior scar. Reprinted with permission from *Cutis*. 2006;78:418-422. ©2006, Quadrant HealthCom Inc.²³



Figure 4. Lupus pernio. Reprinted with permission from *Cutis*. 2007;79:289-290. ©2007, Quadrant HealthCom Inc.⁸

Rare Cutaneous Manifestations

Ulcerative Sarcoidosis—Rarely, cutaneous sarcoidosis can present with ulcerations, arising either de novo or within another specific preexisting lesion.⁹ These ulcerations most commonly occur in black women and often present on the lower extremities.^{31,32} Although the morphology of these lesions is nonspecific,

histopathology of the ulcerations and surrounding skin characteristically reveals noncaseating granulomas.^{9,32} As with lupus pernio, ulcerative sarcoidosis often is accompanied by systemic involvement.³¹

Hypopigmented Sarcoidosis—Hypopigmented sarcoidosis is another rare variant of cutaneous sarcoidosis that is characterized by hypopigmented macules ranging from a few millimeters to more than a centimeter in diameter, favoring the extremities.^{9,12} These lesions are most noticeable in darkly pigmented patients, and although they visually appear to be macules, they often have an appreciable dermal or subcutaneous component on palpation. The diagnosis can be difficult, as granulomas often are less apparent on histopathology in this variant and repeat biopsies may be needed.^{9,33}

Erythrodermic Sarcoidosis—Erythrodermic sarcoidosis does not present as a generalized exfoliative erythroderma but rather with large yet localized erythematous to brown-red patches and plaques with superficial desquamation.^{9,34,35} The condition can be clinically distinguished from more common causes of erythroderma by diascopy, which reveals the characteristic apple jelly appearance with blanching of the underlying erythema. Histopathologically, reported cases have demonstrated diffuse noncaseating granulomas in the dermis with a sparse surrounding perivascular and periadnexal infiltrate.^{34,35}

Ichthyosiform Sarcoidosis—Cutaneous sarcoidosis also can manifest as an acquired ichthyosis and presents with ichthyosis vulgaris-like scale, most commonly on the lower extremities.^{9,36} The scale often has a characteristic pasted on appearance with adherent centers and less adherent edges.⁹ In previously reported cases in the literature, ichthyosiform sarcoidosis has exclusively occurred in dark-skinned races with no reported cases in white patients, with almost all cases being associated with systemic involvement.^{36,37} The diagnosis can be established by the histologic findings of ichthyosis and sarcoid granulomas. These patients require long-term follow-up to evaluate the potential development of systemic involvement.³⁸

Morpheaform Sarcoidosis—Cutaneous sarcoidosis resembling morphea is another possible but uncommon variant.^{12,39} The cases described generally have been indistinguishable from true morphea, with cutaneous induration and fibrosis that often occurs in a linear fashion.^{39,40} These lesions can occur at any time during the disease course and histopathologically show prominent dermal sclerosis with sarcoid granulomas. They respond well to antimalarial agents.^{39,40}

Mucosal Sarcoidosis—Mucosal involvement in sarcoidosis is unusual but can occur, affecting most areas of the mouth including the tongue, buccal mucosa, lips, and palate.⁴¹ Mucosal sarcoidosis typically

presents with asymptomatic, focal, firm nodules or with diffuse submucosal enlargement, with other less common presentations including superficial ulcerations or papules.⁴¹ In general, the presence of intraoral sarcoidosis is associated with established widespread systemic involvement; however, there have been reports of oral lesions as the presenting sign of systemic disease.⁴¹⁻⁴³ It is important to keep mucosal sarcoidosis in the differential diagnosis when a patient presents with an oral lesion of unknown cause.

Conclusion

Although the data are somewhat conflicting, the presence of certain sarcoid skin lesions may offer some prognostic clues.⁴⁴ For example, when cutaneous lesions are predominantly macules and papules, it often corresponds to a more acute form of disease with radiologic stage I pulmonary involvement and a disease duration in most patients of less than 2 years.^{1,44-46} Similarly, subcutaneous sarcoidosis is mainly seen in patients with stage I lung involvement and a disease duration of less than 2 years.^{16,46-49} Plaquelike lesions and lupus pernio often are seen in chronic forms of sarcoidosis with more than 2 years of disease activity and tend to be more persistent and recurrent, which frequently requires systemic corticosteroid therapy.^{1,45,46,50,51} Additionally, bone involvement has been found to be more common in patients with lupus pernio, but otherwise specific skin lesions rarely provide clues for sites of extracutaneous involvement.¹

The morphologic spectrum of sarcoidosis is broad, and this review does not even mention the lichen nitidus-like papules, pustular lesions, polymorphous light eruption-like lesions, discoid lupus erythematosus-like plaques, palmar erythema, genital lesions, and verrucous lesions that also have been reported to occur with sarcoidosis.⁹ I hope this review provides some perspective on the diversity of the common and uncommon cutaneous manifestations of sarcoidosis and offers some guidance on when to consider sarcoidosis as a potential diagnosis.

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