Derma Dilemma

Stephanie H. Ward, MD, MPH
Marie O. Uberti-Benz, MD

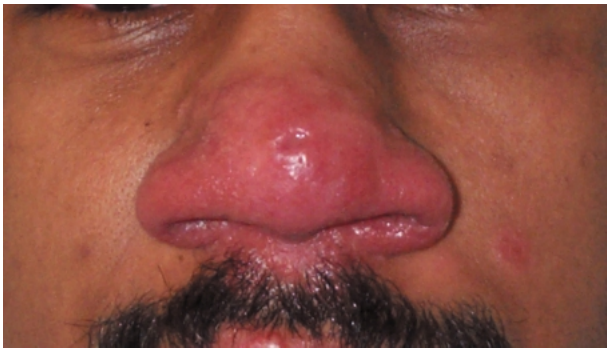

Figure 1. Diffuse indurated erythematous infiltration of the nose and a firm, hyperpigmented nodule on the cheek.

CASE PRESENTATION

A 29-year-old African-American man with a history of alcohol abuse is admitted to the psychiatry unit for depression and substance abuse. A medical consultation is requested for an erythematous rash and swelling of his nose that has been worsening over the past 6 months. He reports a similar rash on his nose 1 year ago, which improved significantly with a short course of oral corticosteroids. The patient denies pain and pruritus at the affected site, and has no systemic complaints. He has no other past medical history and takes no medications. Physical examination reveals diffuse indurated, erythematous infiltration of the nose as well as scattered firm, hyperpigmented nodules on the cheeks and upper lip (**Figure 1**).

What is your diagnosis?

(A) Rosacea
(B) Sarcoidosis
(C) Acne vulgaris
(D) Lupus erythematosus

What is the most appropriate initial treatment?

(A) Retinoids
(B) Antibiotics
(C) Antimalarials
(D) Topical/intralesional corticosteroids

Dr. Ward is a resident in internal medicine, University of Pennsylvania Health System, Philadelphia, PA. Dr. Uberti-Benz is clinical professor and chief of the division of dermatology, University of Pennsylvania–Presbyterian Medical Center, Philadelphia, PA.

ANSWERS

The correct answers are (B) sarcoidosis and (D) topical/intralesional corticosteroids. Figure 1 shows lupus pernio, one of the many manifestations of cutaneous sarcoidosis, infiltrating the nose, and a subcutaneous nodule is seen on the cheek. Although rosacea is characteristically localized to the face, it appears as persistent erythema with papules, telangiectases, and/or tiny pustules. Acne vulgaris also has a predilection for the face and a variety of clinical manifestations, but most commonly presents as comedones (open or closed), papulopustules, nodules, or cysts. Facial lesions in patients with lupus erythematosus are often seen in a "butterfly" distribution, and appear acutely as sharply demarcated erythema with minimal scaling. Chronic discoid lesions of lupus are well-defined erythematous, hyperkeratotic plaques with adherent scale.

In the absence of systemic disease or widespread, disfiguring lesions, topical or intralesional steroids are the most appropriate initial treatment for most types of cutaneous sarcoidosis.

SYSTEMIC SARCOIDOSIS

Sarcoidosis is a multisystem disease characterized by the formation of noncaseating granulomas. Although the etiology remains unclear, environmental, genetic, infectious, and immunologic influences have been implicated.

Sarcoidosis occurs worldwide in all races, both sexes, and in all age groups but has been found to be more prevalent among US blacks, Irish, and Scandinavians.[1] The clinical manifestations vary greatly depending on which organs are involved and the extent of granulomatous inflammation in those organs. All organ systems can be affected, but the lungs are most commonly involved. Patients may also experience systemic symptoms, including fever, malaise, fatigue, anorexia, and weight loss. The course of sarcoidosis can be self limited, but it is more commonly chronic, with flares waxing and waning over time.

CUTANEOUS SARCOIDOSIS

Approximately 25% of patients with systemic sarcoidosis have cutaneous involvement. Skin lesions can occur at any stage but are most frequently present at disease onset and may also occur in the absence of systemic disease.[2,3]

Cutaneous lesions of sarcoidosis vary markedly in morphology and clinical appearance, and it is possible to see more than one type of lesion in a single patient. Lesions are classified as specific or nonspecific. Specific lesions reveal granulomatous inflammation on biopsy, whereas nonspecific lesions are reactive processes that may be seen in a variety of clinical settings, including systemic sarcoidosis.

Nonspecific Lesions

The most common nonspecific cutaneous lesion of sarcoidosis is erythema nodosum. It is an acute inflammatory reaction to a variety of stimuli, including medications, inflammatory diseases, and infections.[3,4] Erythema nodosum presents as indurated, tender, red subcutaneous nodules, usually occurring on the anterior tibia. The nodules are bilateral but not symmetric.[4] Erythema nodosum is classically associated with acute benign systemic sarcoidosis, which has a high incidence of spontaneous resolution.[2,5] Lofgren's syndrome is the triad of erythema nodosum, hilar lymphadenopathy, and polyarthralgia; it signifies acute systemic sarcoidosis.[3]

Other nonspecific cutaneous manifestations of sarcoidosis include prurigo and erythema multiforme.[2]

Specific Lesions

There are a wide variety of specific lesions of cutaneous sarcoidosis. Lupus pernio is the most characteristic lesion of sarcoidosis.[2] It presents as indurated, red-brown to violaceous skin changes on the nose, lips, cheeks, and ears (Figure 1).[2,6] It is most common in African Americans and is associated with chronic sarcoidosis of the upper respiratory tract, lacrimal glands, and bone.[2,5] Lupus pernio can be extremely disfiguring if not successfully treated.

Maculopapular lesions are the most common specific manifestation of cutaneous sarcoidosis. They present as red-brown to purple papules less than 1 cm in size. They are asymptomatic and usually affect the face, neck, and extremeties.[2,5,6] Although it is possible to see only a few single papules, multiple scattered and confluent lesions are more common.[2,4]

Subcutaneous nodules are painless, firm, mobile lesions that vary from red-brown to violaceous in color.[2,6] They range in size from 0.5 to 2 cm and frequently affect the proximal limbs, torso, and face.[2,5] Nodules are well circumscribed and tend to be indolent.[5]

Plaque sarcoidosis presents as larger infiltrated lesions on the face, back, and extremeties.[3,5,6] Lesions range in color from red to red-brown to purple, and may be annular, polycyclic, or serpiginous.[4]

Sarcoidosis can infiltrate old scars, including surgical scars, tattoos sites, acne, and trauma scars. Previously well-healed scars enlarge and become infiltrated and inflamed with purple, red, or yellowish papules or nodules.[4,5] The pathogenesis of scar sarcoidosis remains

unknown. It may parallel systemic disease activity or appear in isolation.[2,5]

Less common specific cutaneous manifestations of sarcoidosis include psoriasiform, lichenoid, ichthyosiform, ulcerative, and hypopigmented lesions.[2,6]

The relationship between various cutaneous lesions and systemic sarcoidosis is still being investigated. However, it has been recognized that lupus pernio is generally associated with more severe systemic disease and a chronic course, while erythema nodosum indicates acute benign disease.[3,6]

Differential Diagnosis

Cutaneous sarcoidosis varies markedly in its clinical presentations, and has been labeled one the great dermatologic masqueraders.[2] Maculopapular lesions can appear similar to xanthelasma, acne rosacea, trichoepithelioma, lupus erythematosus, adenoma sebaceum, and granuloma annulare.[3,7] The differential diagnoses for plaques include lupus vulgaris, necrobiosis lipoidica, morphea, leprosy, leishmaniasis, gyrate erythema, psoriasis, lichen planus, nummular eczema, and discoid lupus.[3,7] When nodules are present, lymphoma and leukemia cutis must be considered. Finally, lupus pernio may be confused with scar or discoid lupus.[3]

DIAGNOSIS OF SARCOIDOSIS

Sarcoidosis can be a challenge to correctly diagnose as a result of its many manifestations and the lack of a single diagnostic test. Diagnosis is made when compatible clinical or radiologic findings are present combined with histologic evidence of noncaseating granulomas in the absence of other potential causes.[1] Thus, sarcoidosis essentially remains a diagnosis of exclusion. In patients with suspected sarcoidosis, a thorough history should be taken with particular emphasis on environmental and occupational exposures, medication usage, and prior medical history.[1] Physical examination should focus on the lungs, eyes, skin, liver, and heart.[1,2]

Although the clinical presentation may strongly suggest the diagnosis of sarcoidosis, biopsy is recommended in all cases to confirm the presence of noncaseating granulomas and to rule out other causes of granulomatous inflammation.[1] Biopsies should be taken from the most readily available and least invasive site possible. Thus, cutaneous lesions offer not only a visual clue to the diagnosis but also an easily accessible site for biopsy. Punch or incisional wedge biopsies that include the dermis are frequently performed.[3] Histologic examination reveals dermal infiltration of well demarcated islands of epithelioid cells with occasional giant cells and no necrosis (**Figure 2**).[2] Once noncaseating granulomas are identified, polarization for evaluation of foreign bodies should be performed in addition to tissue culture and special stains to rule out bacterial, mycobacterial, and fungal infections.[2]

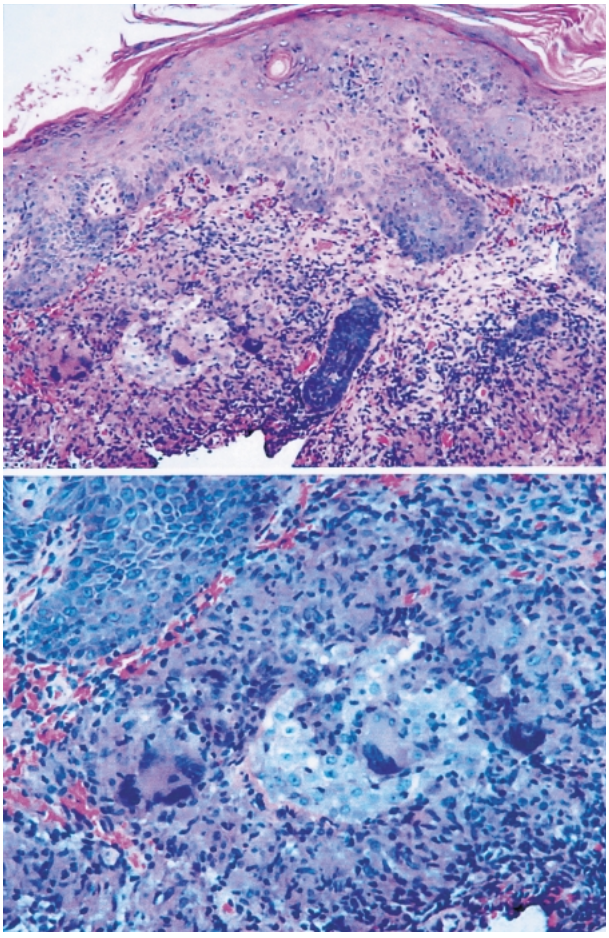

Figure 2. Skin biopsy at low and high power demonstrating dermal infiltration of a noncaseating granuloma.

All patients diagnosed with cutaneous sarcoidosis should undergo an initial work-up for systemic disease and then be periodically screened for systemic involvement. The initial investigation should include a complete history and physical examination, chest radiograph, pulmonary function testing, electrocardiogram, ophthalmologic evaluation (including slit-lamp and funduscopic examinations), and baseline laboratory evaluations, including hepatic and renal function testing and measurement of serum calcium level. Measurement of serum angiotensin-converting enzyme levels is not generally recommended as they are of limited value. Serum angiotensin-converting enzyme levels are elevated in only about 60% of patients with sarcoidosis,

and elevated levels can be identified in other conditions such as diabetes and alcoholic liver disease.[6]

TREATMENT

Treating sarcoidosis, both cutaneous and systemic, can be frustrating for clinicians. The variations in manifestations, uncertain course of disease, and potential side effects of treatment add to the challenge of managing this disorder.[1] Cutaneous lesions may be either refractory to treatment or recur after apparent successful treatment. In addition, the potential for spontaneous improvement exists.[1,3] Up to 60% of patients, especially those with acute inflammatory manifestations such as erythema nodosum, may experience spontaneous improvement or resolution of cutaneous lesions.[2]

Few guidelines exist on whether or when to initiate treatment. Initiation of therapy for systemic sarcoidosis usually depends on disabling symptoms or organ dysfunction.[2] The primary indication for treatment of isolated cutaneous lesions is disfigurement.[2] In general, cutaneous sarcoidosis responds to therapy for systemic disease; however, therapies targeted directly at cutaneous lesions also exist.[7]

The data available on various therapies for specific cutaneous lesions are primarily anecdotal with few if any randomized clinical trials. Corticosteroids are the mainstay of initial therapy for both systemic and cutaneous sarcoidosis. However, there are no specific dose and duration recommendations.[1] Weekly treatment with a topical corticosteroid and hydrocolloid dressing, or monthly intralesional injections with triamcinolone, are effective for localized lesions of sarcoidosis and are the most appropriate initial therapies.[1,3] Other nonoral preparations include superpotent topical steroids, topical hydrocortisone 5% powder in hydrophilic ointment, and monthly intralesional chloroquine.[2] Carbon dioxide or pulsed dye laser treatments have been used for lupus pernio.[2]

Systemic therapies for isolated cutaneous sarcoidosis are reserved for widespread, large disfiguring lesions or lesions that are refractory to topical treatment or impair function.[2,3] Again, there are few randomized, controlled clinical trials on the use of various medications for cutaneous sarcoidosis; however, smaller anecdotal reports suggest efficacy.[3] Hydroxychloroquine and weekly pulsed therapy with methotrexate have both been shown to be beneficial for refractory lesions.[1] Oral corticosteroids have been used at slow tapering doses while following the patients' response to therapy. The main drawback to this regimen is the well-known side effects of long-term corticosteroid use. In addition, many patients will experience flare-ups as the corticosteroids are tapered.[3] Oral steroids are, therefore, reserved for lesions refractory to topical or intralesional therapies or antimalarial drugs unless there is systemic involvement or significant disfiguration. Several other treatments have been used for refractory cases, including allopurinol, thalidomide, tranilast, and psoralen–ultraviolet A phototherapy (PUVA).[2,3,5,7] **HP**

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