Cutaneous Sarcoidosis Presenting as Leonine Facies

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GOAL

To gain a complete understanding of cutaneous sarcoidosis

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss the clinical presentation of cutaneous sarcoidosis.
2. Describe the histologic characteristics of cutaneous sarcoidosis.
3. Explain the differential diagnosis of cutaneous sarcoidosis.

CME Test on page 44.

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Cutaneous sarcoidosis often masquerades as many other disease entities. We describe the case of a 56-year-old African American man with a 1-year history of progressively enlarging nodules and plaques of the face resulting in a leonine appearance and madarosis. The diagnosis of cutaneous sarcoidosis was made after skin biopsy results revealed noncaseating granulomas without evidence of foreign body, mycobacteria, or deep fungal infection. A thorough systemic workup was void of other comorbidities. The reports of tumoral sarcoidosis or sarcoidosis presenting with leonine facies are rare, and those cases that have been reported have been linked to other systemic findings.

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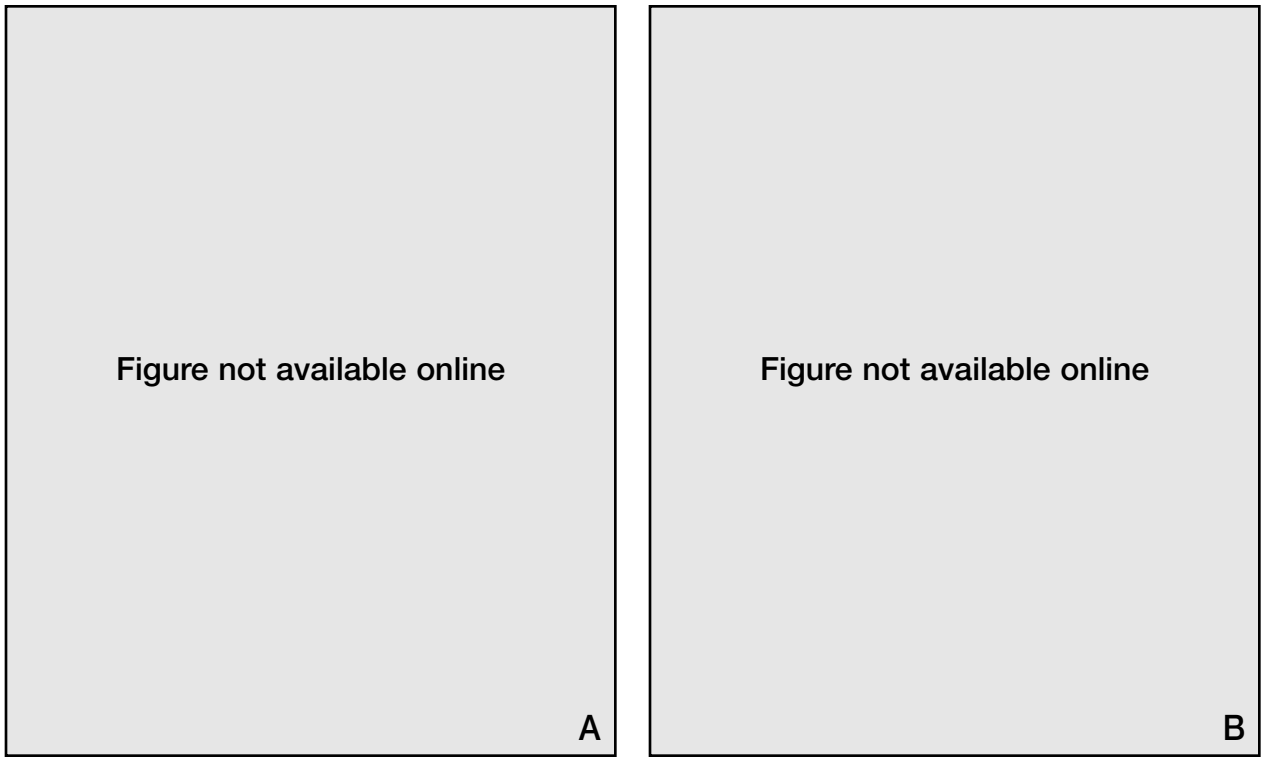

Figure 1. Cutaneous tumors on the face (A) and loss of the lateral eyebrows (B) at the time of initial presentation.

Case Report

A 56-year-old African American man presented with lesions on his face that had been progressively increasing in size over the previous year. Physical examination revealed numerous nontender subcutaneous nodules and plaques on his face, particularly in the forehead region. The nodules ranged in size from 1 to 3.5 cm (Figure 1). Generalized thickening of the facial skin along with marked thinning of the eyebrows resulted in a leonine appearance. In addition to the dramatic facial findings, 1- to 4-mm brown papules were noted on the posterior neck and dorsal right hand. There was no lymphadenopathy or hepatomegaly. Physical examination of the lungs and heart also revealed no abnormalities.

The patient's medical history was significant for hepatitis C and asthma. He had a remote history of seizures from previous alcohol abuse. Results of a complete blood count and serum chemistries, including a liver function test, were normal. Results of serologic tests for syphilis using rapid plasma reagin also were negative.

Skin biopsies from the face and dorsal hand were obtained for histopathologic evaluation (Figure 2). Routine staining of both biopsy specimens with hematoxylin and eosin (H&E) revealed a granulomatous dermatitis with numerous noncaseating epithelioid granulomas (Figure 3). Special stains for acid-fast bacilli using both the Ziehl-Nielsen and Fite-Faraco methods were negative on 6 separate sections. No fungal elements were visualized using Gomori methenamine silver staining technique. Results of fungal, bacterial, and acid-fast bacilli tissue cultures were negative. These changes were compatible with sarcoidosis.

The patient was examined by an ophthalmologist and was noted to have no ocular abnormalities. A chest radiograph showed no hilar adenopathy or pulmonary infiltrates. Pulmonary function test results were normal. Radiographic images of the hands were performed, and no bone changes were seen. A liver biopsy revealed no granulomas to indicate hepatic sarcoidosis. The only pathologic findings present were of mildly active chronic hepatitis C.

An otorhinolaryngologist examined the patient with regard to the swelling around the patient's nose and "sinus problems," possibly from local extension of the tumoral lesions. A computed tomography scan of the sinuses revealed anatomic swelling of the osteomeatal complexes bilaterally, mucosal membrane thickening of the uncinate processes, and nasal septal deviation.

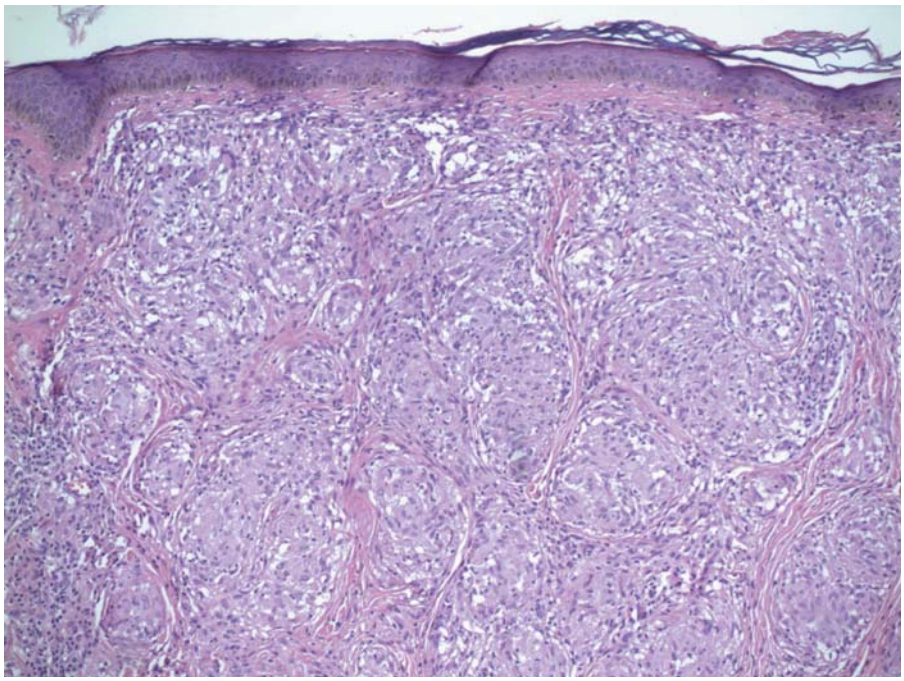

Figure 2. Biopsy specimen from the root of the nose (H&E, original magnification ×10).

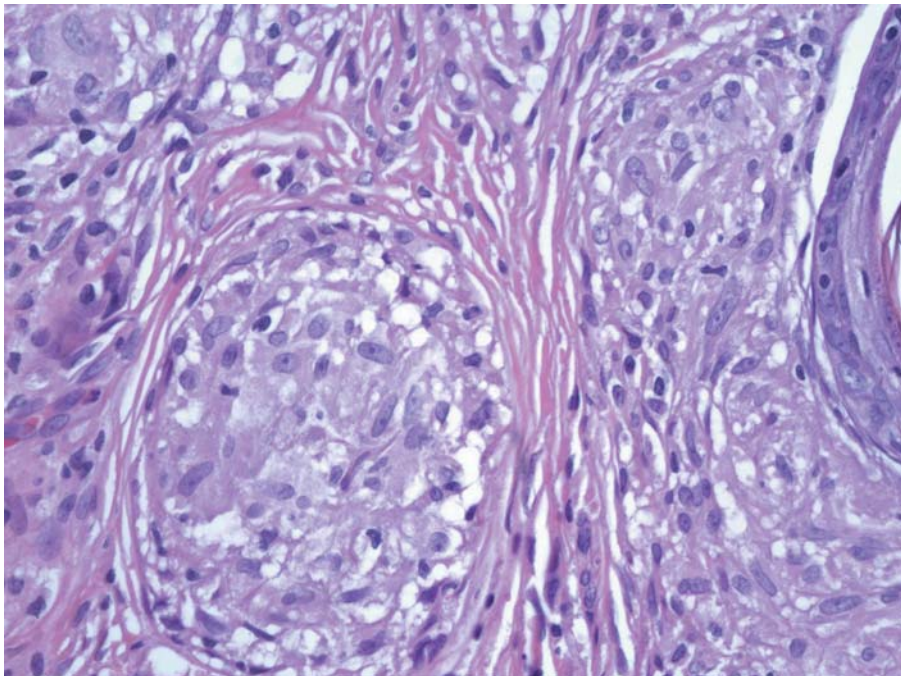

Figure 3. Noncaseating granulomas (H&E, original magnification ×40).

The decision was then made to treat the lesions medically and defer any surgery until after a trial of medical management.

Because of the patient's history of hepatitis C, he was not considered to be a candidate for methotrexate therapy. It was decided to give the patient oral prednisone 40 mg per day (approximately 0.5 mg/kg per day) and hydroxychloroquine sulfate 200 mg twice daily. At the patient's 3-week follow-up visit, all lesions had decreased in size with the exception of one of the nodules at his nasal root. His treatment gradually was tapered to prednisone 5 mg per day, and the larger lesions were treated with intralesional triamcinolone acetonide until clearing was obtained. His condition has been maintained successfully for one year on prednisone

5 to 7 mg per day and hydroxychloroquine sulfate 200 mg twice daily. Discontinuation of the prednisone results in flaring of the patient's skin lesions.

Comment

Approximately 20% to 35% of patients with sarcoidosis have cutaneous disease. Although cutaneous lesions may present at any time during the course of the disease, they often present early after disease onset. The primary lesions most typically found are papules, plaques, nodules, infiltrations of scars, and lupus pernio—a severe, chronic form of cutaneous sarcoidosis with violaceous plaques on the central face.[1-4] Given the multitude of manifestations of sarcoidosis, the disease has become known as one of the "great imitators," masquerading as a wide array of disorders from benign appendageal growths to Kaposi sarcoma.[5]

Of the many descriptions of sarcoidosis, reports of tumoral sarcoidosis are rare. Nodular and other atypical lesions of sarcoidosis most commonly are described in African Americans.[6,7] To our knowledge, the largest sarcoidal tumor that has been reported was a 10×20-cm lumbosacral lesion.[8] A 3-cm tumor on the chin also has been described, but centrally appearing nodules are the exception. Nodules of sarcoidosis generally are (1) located on the extremities, (2) smaller than 2 cm, and (3) late in the course of disease.[8-10]

With regard to facial manifestations of sarcoidosis, the most mutilating varieties have been described in the lupus pernio type. In contrast to other forms of sarcoidosis, this type is more closely associated with pulmonary fibrosis, upper respiratory tract involvement, bone lesions, and chronic, persistent disease.[1,11,12] One report of an unusual presentation of lupus pernio describes a mutilation of the face with massive plaques and 2- to 3-cm nodules of the infraorbital region of the cheeks. These findings were in conjunction with significant systemic involvement of the upper respiratory tract, lungs, and phalanges.[13]

The concept of leonine facies traditionally has been described with regard to lymphomas and pseudolymphomas.[14,15] We could only find 2 previous reports of sarcoidosis with leonine facies in the literature.[16,17] Each of these cases was marked by a significant comorbidity presenting in conjunction with either severe, complete heart block or laryngeal and bone involvement, respectively.

Our patient's presentation was highly unusual in the large tumoral nature and the site of his skin lesions (nodules >2 cm on the face rather than on the extremities), and the disfiguring leonine appearance with madarosis. These significant skin findings, combined with the absence of a severe comorbidity, have not been reported to our knowledge.

The dramatic tumoral nature of the patient's skin lesions warranted consideration of several other disease entities in the clinical differential diagnosis: leprosy, granulomatous rosacea, lymphoma, various histiocytoses, lupus vulgaris, lupoid leishmaniasis, and other infectious granulomas. The diagnosis in this case was supported by the histologic finding of noncaseating granulomas along with a lack of demonstrable foreign bodies, acid-fast organisms, or fungal organisms; however, similar histologic changes can be seen in other diseases, making the diagnosis of sarcoidosis one of exclusion.

Of the disease entities in the clinical differential diagnosis, granulomatous rosacea and infection can be the most difficult to distinguish from sarcoidosis on histology. Granulomatous rosacea often can mimic sarcoidosis clinically because patients present with yellow-brown papules and nodules that are most prominent on the malar cheeks but also can be seen around the mandible and periorally. Granulomatous rosacea was considered less likely in our patient because his skin lesions included the posterior neck and dorsal hand in addition to his facial lesions.[18] Also, the histology of granulomatous rosacea shows dermal edema with vascular dilatation and a mixed inflammatory infiltrate with a predilection for the vessels and pilosebaceous units. Granulomas in sarcoidosis generally are without surrounding inflammation (termed *naked*) and are well-circumscribed. Granulomas in granulomatous rosacea generally are not naked as they are in sarcoidosis, rather they have surrounding inflammation with caseation necrosis sometimes present. They also tend to be less well-circumscribed. These features more commonly are referred to as the tuberculoid type of granuloma.[18,19] The results of our patient's biopsy had none of these findings. In addition, although some patients with rosacea initially improve with steroids, continued use invariably results in exacerbation of the disease. Our patient has responded well to steroids.

Infections, particularly tuberculosis, leprosy, and leishmania, are other important considerations in our patient. Clinically, tuberculosis in the skin can manifest in multiple ways depending on both the initial site of infection and the immune status of the patient. The type of tuberculosis that most often would be confused with sarcoidosis clinically is lupus vulgaris. It manifests as red-brown coalescing papules and plaques that are covered by scales. Most of the time, these lesions appear on the head and neck. Regardless of the

type of cutaneous tuberculosis, unlike sarcoidosis, there generally is some epidermal change to the lesions, such as scale, verrucous change, or suppuration. In addition, patients often have lymphadenopathy.[20,21] Leishmania is another disease that is important to consider. This disease is endemic in Asia Minor, parts of the Middle East, and in countries around the Mediterranean Sea. In the Western Hemisphere, leishmania is found in South America and Central America. Like tuberculosis, these lesions generally exhibit epidermal changes such as ulceration or a verrucous appearance.[22-24] With leprosy, most patients present with numbness, with temperature sensation and light touch affected first. Progressive nerve involvement can lead to wasting of the muscles served by the involved nerve. With leprosy, a unique feature that can be associated with skin lesions when they do appear is the loss of hair. On histology, there are distinct subtypes that correlate with the clinical disease spectrum. The histologic type most difficult to distinguish from sarcoidosis is the tuberculoid form in which the numbers of organisms that can be seen on special stains are few or absent. There are numerous granulomas throughout the dermis composed of epithelioid cells, lymphocytes, and Langerhans giant cells. Granulomas can erode into the epidermis or extend into peripheral nerves, both suggestive of leprosy rather than sarcoidosis.[25,26]

As with granulomatous rosacea, the granulomas seen on histology in all of these infectious disease entities are of the tuberculoid type. If the index of suspicion is high clinically and the diagnosis cannot be made by special stains on histology, polymerase chain reaction techniques can be employed to identify the causative organism. Our patient had no epidermal change to his lesions, no lymphadenopathy, no sensory changes, and no other findings to make us highly suspicious of an infectious cause of his disease. No infectious agent could be found on numerous biopsy sections stained for acid-fast bacilli using both the Ziehl-Nielsen and Fite-Faraco methods; furthermore, tissue cultures were negative. Finally, our patient improved markedly with intralesional and oral steroids, which would not be expected in the case of an infectious etiology.

An important aspect of our patient's history is represented by the presence of chronic hepatitis C. To our knowledge, there are no reports in the literature of granulomatous skin disease such as that in our patient, which was caused by hepatitis C. If our patient's skin disease was related to his underlying hepatitis, we might have expected to see a change in the course of his skin disease as his hepatitis C viral load changed. Although there have been reports implicating the onset of sarcoidosis with the initiation of interferon alfa therapy for treatment of hepatitis C,[27,28] our patient had undergone no prior treatment for hepatitis. His underlying hepatitis, however, did limit treatment options for the sarcoidosis by restricting the use of methotrexate.

Treatment of sarcoidosis depends on the extent of the disease. Topical or intralesional glucocorticosteroids often are used for limited cutaneous involvement. Intralesional corticosteroids given at 3-week intervals have proven to be much more effective than the suprapotent topicals because the latter does not provide adequate amounts to the granulomas in the reticular dermis.[3,13,29] The most effective systemic agents for the treatment of sarcoidosis are glucocorticoids, reserved for the treatment of widespread lesions, or those that impair function.[1] Other agents that have been used with success are methotrexate,[30] thalidomide,[31] antimalarials,[32,33] isotretinoin,[34] allopurinol,[35] and tranilast.[36] In 2 case reports of mutilating lupus pernio of the central face, the only treatment for the cutaneous lesions that resulted in a cosmetically acceptable outcome was surgical excision.[13,37] Despite the many agents that have purportedly been used with success, controlled and randomized trials are lacking.

REFERENCES

1. Mana J, Marcoval J, Graells J, et al Cutaneous involvement in sarcoidosis: relationship to systemic disease. *Arch Dermatol.* 1997;133:882-888.
2. Newman LS, Rose CS, Maier LA. Sarcoidosis. *N Engl J Med.* 1997;336:1224-1234.
3. Samtsov AV. Cutaneous sarcoidosis. *Int J Dermatol.* 1992;31:385-391.
4. Fink SD, Kremer JM. Cutaneous and musculoskeletal features, diagnostic modalities, and immunopathology in sarcoidosis. *Curr Opin Rheum.* 1994;6:78-81.
5. Katta R. Cutaneous sarcoidosis: a dermatologic masquerader. *Am Fam Physician.* 2002;65:1581-1584.
6. Morrisom JGL. Sarcoidosis in the Bantu: necrotizing and mutilating forms of the disease. *Br J Dermatol.* 1974;90:649-655.
7. Albertini JG, Tyler W, Miller OF III. Ulcerative sarcoidosis: case report and review of the literature. *Arch Dermatol.* 1997;133:210-215.
8. Koessler A, Grosshans E, Samian F, et al. Sarcoïdose tumorale. *Ann Dermatol Venereol.* 1995;122:783-785.
9. Vainsencher D, Winkelmann RK. Subcutaneous sarcoidosis. *Arch Dermatol.* 1984;120:1028-1031.
10. Ruiz de Erenchun F, Vazquez-Doval FJ, Idoate M, et al. Subcutaneous nodules as the first clinical manifestation of sarcoidosis. *Clin Exp Dermatol.* 1992;17:192-194.

11. James DG. Lupus pernio. *Lupus*. 1992;1:129-131.
12. Selroos O, Niemisto M. Sarcoidosis of the nose including a report on a patient with large sarcoid polypi of the nasal mucosa. *Scand J Respir Dis*. 1977;58:57-62.
13. Dumitrescu S, Schwartz R, Baredes S, et al. Mutilating facial sarcoidosis. *Dermatology*. 1999;199:265-267.
14. Vocks E, Hertenberger B, Worret WI, et al. An unusual cutaneous T cell lymphoma presenting as leonine facies. *Eur J Dermatol*. 2000;10:309-312.
15. Stein L, Lowe L, Fivenson D. Coalescing violaceous plaques forming leonine facies. *Arch Dermatol*. 1994;130:1552-1553.
16. Moulonguet I, Duterque N, Bamberger N, et al. Sarcoïdose pseudo-tumorale avec faciès léonine: deuxième présentation. *Ann Dermatol Venereol*. 1989;116:816-817.
17. Ford PG, Jorizzo JL, Hitchcock MG. Previously undiagnosed sarcoidosis in a patient presenting with leonine facies and complete heart block. *Arch Dermatol*. 2000;136:712-714.
18. Helm KF, Menz J, Gibson LE, et al. A clinical and histologic study of granulomatous rosacea. *J Am Acad Dermatol*. 1991;25:1038-1043.
19. Mullanax MG, Kierland RR. Granulomatous rosacea. *Arch Dermatol*. 1970;101:206-211.
20. Barnes PF, Barrows SA. Tuberculosis in the 1990s. *Ann Intern Med*. 1993;119:400-410.
21. Chong LY, Lo KK. Cutaneous tuberculosis in Hong Kong: a 10-year retrospective study. *Int J Dermatol*. 1995;34:26-29.
22. Convit J, Kerdel-Vegas F. Disseminated cutaneous leishmaniasis. *Arch Dermatol*. 1965;91:439-447.
23. Sangueza OP, Sangueza JM, Stiller MJ, et al. Mucocutaneous leishmaniasis: a clinicopathologic classification. *J Am Acad Dermatol*. 1993;28:927-932.
24. Peltier E, Wolkenstein P, Deniau M, et al. Caseous necrosis in cutaneous leishmaniasis. *J Clin Pathol*. 1996;49:517-519.
25. Modlin RL, Rea TH. Leprosy: new insight into an ancient disease. *J Am Acad Dermatol*. 1987;17:1-13.
26. Ramasoota T, Johnson WC, Graham JH. Cutaneous sarcoidosis and tuberculoid leprosy: a comparative histopathologic and histochemical study. *Arch Dermatol*. 1967;96:259-268.
27. Eberlein-Konig B, Hein R, Abeck D, et al. Cutaneous sarcoid foreign body granulomas developing in sites of previous skin injury after systemic interferon-alpha treatment for chronic hepatitis C. *Br J Dermatol*. 1999;140:370-372.
28. Teragawa H, Hondo T, Takahashi K, et al. Sarcoidosis after interferon therapy for chronic active hepatitis C. *Intern Med*. 1996;35:19-23.
29. Khatri KA, Chotzen VA, Burrall BA. Lupus pernio: successful treatment with a potent topical corticosteroid. *Arch Dermatol*. 1995;131:617-618.
30. Webster GF, Razsi LK, Sanchez M, et al. Weekly low-dose methotrexate therapy for cutaneous sarcoidosis. *J Am Acad Dermatol*. 1991;24:451-454.
31. Lee JB, Koblenzer PS. Disfiguring cutaneous manifestations of sarcoidosis treated with thalidomide: a case report. *J Am Acad Dermatol*. 1998;39:835-838.
32. Zic JA, Horowitz DH, Arzubiaga C, et al. Treatment of cutaneous sarcoidosis with chloroquine. review of the literature. *Arch Dermatol*. 1991;127:1034-1040.
33. Jones E, Callen JP. Hydroxychloroquine is effective therapy for control of cutaneous sarcoidal granulomas. *J Am Acad Dermatol*. 1990;23:487-489.
34. Waldinger TP, Ellis CW, Quint K, et al. Treatment of cutaneous sarcoidosis with isotretinoin. *Arch Dermatol*. 1983;119:1003-1005.
35. Pollock JL. Sarcoidosis responding to allopurinol. *Arch Dermatol*. 1991;127:1034-1040.
36. Yamada H, Ide A, Sugiura M, et al. Treatment of cutaneous sarcoidosis with tranilast. *J Dermatol*. 1995;22:149-152.
37. Shaw M, Black MM, Davis PK. Disfiguring lupus pernio successfully treated with plastic surgery. *Clin Exp Dermatol*. 1984;9:614-617.