Sarcoidosis

26

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Contents

26.1 Epidemiology

Sarcoidosis has a worldwide distribution affecting all races and both sexes. Annual incidence has been reported as high as 64/100,000 in Sweden and lowest in Spain and Japan, with a reported rate of 1.4/100,000 [1]. There is significant racial variation of sarcoidosis in the United States with 10–14/100,000 in whites and 36–64/100,000 in African Americans. Rybicki et al. studied the incidence of sarcoidosis in the Detroit, MI, metropolitan area and findings were the following: African American females, 39/100,000; African American males, 30/100,000; white females, 12/100,000; and white males, 9/100,000. African American women, aged 30–39, had the highest incidence, at 107/100,000 [2].

26.2 Etiology

The etiology of sarcoidosis is unknown; however, hypotheses include infectious, genetic, and immunologic etiologies. Several studies have implicated mycobacteria as causative agents; however, detection of mycobacteria DNA in sarcoidal tissue has been inconclusive, and it has never been cultured from sarcoidal tissue [3]. Martinetti et al. [4] found a positive association of HLA-1, HLA-B8, and HLA-DR3 with sarcoidosis in a study of European patients. Rybicki et al. [5] found that familial clusters occurred more commonly in African Americans. The immunologic theory is that an unknown antigen is presented to CD4+, Th1 subtype T-helper cells by macrophages, bearing MHC class II molecules. Cytokines from CD4+ T-cells, IL-2, and interferon gamma stimulate lymphocytes and induce granuloma formation in the target organ. The recruitment of CD4+ T-cells from the circulation leads to a decreased delayed-type hypersensitivity reaction. Anergy is often seen in patients in the early stages of the disease. Cytokines also stimulate B-cells, leading to hypergammaglobulinemia [6].

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26.3 Clinical Findings

Sarcoidosis involves the skin in 25 % of cases [7], and dermatologists are often involved in confirming the diagnosis. Cutaneous lesions are divided into specific (those containing granulomas) and nonspecific or reactive (those without granulomas). Classic specific skin lesions are asymptomatic red-brown papules, nodules, and plaques. These lesions are commonly found on the face, lips, neck, upper back, and extremities (Figs. 26.1, 26.2, 26.3, 26.4, 26.5, and 26.6). Lupus pernio is the most common cutaneous presentation, consisting of red-brown to violaceous papules and nodules on the nose, lips, cheeks, and ears which can lead to scarring (Figs. 26.7 and 26.8). Lupus pernio is most common in African Americans and is usually associated with chronic, fibrotic sarcoidosis of the upper respiratory tract, nasopharynx, and lungs (Figs. 26.9 and 26.10). Sarcoidosis is often called the "great imitator" because of its wide variety of presentations. Other less common cutaneous lesions include subcutaneous nodules, ichthyosiform dermatitis, psoriasiform plaques, hypopigmented macules and plaques (Fig. 26.11), cicatricial alopecia, lichenoid papules and plaques, erythroderma, and ulcers.

Erythema nodosum is a nonspecific presentation of sarcoidosis. Sarcoidosis is referred to as Lofgren's syndrome when presenting as erythema nodosum and accompanied by hilar adenopathy, fever, iritis, and migratory arthritis. Erythema nodosum associated with sarcoidosis spontaneously resolves in 83 % of patients within 2 years. Other nonspecific cutaneous lesions include onychodystrophy and clubbing of the fingers, with or without bone cysts.

Pulmonary involvement occurs in 90 % of sarcoid cases and may be asymptomatic or present with cough, dyspnea, or chest pain. Chest x-ray most commonly shows hilar and paratracheal adenopathy, but pulmonary infiltrates may also be seen, with pulmonary fibrosis in end-stage disease. Ocular involvement presenting as acute anterior uveitis, lacrimal gland enlargement, and iritis is seen in 30–50 % of cases. Granulomas occur in the liver and spleen in 50–80 % of patients. Although hepatic granulomas may be asymptomatic, splenomegaly is usually associated with extensive fibrosis of other organs and poor prognosis. Musculoskeletal changes present as bone cysts, arthralgias, and myalgias. Central and peripheral nervous systems as well as the cardiac and endocrine systems may also be involved. Hypercalcemia caused by alveolar macrophage secretion of 1,25-dihydroxyvitamin D3 is seen in 17 % of cases. Cardiac involvement occurs in only 5 % of cases, presenting as an infiltrative myopathy, pericarditis, and even sudden death. Iwai et al. examined racial differences in cardiac sarcoidosis seen at autopsy. Cardiac granulomas were seen in 10–20 % of cases in the United States compared to 67 % in Japan [8].

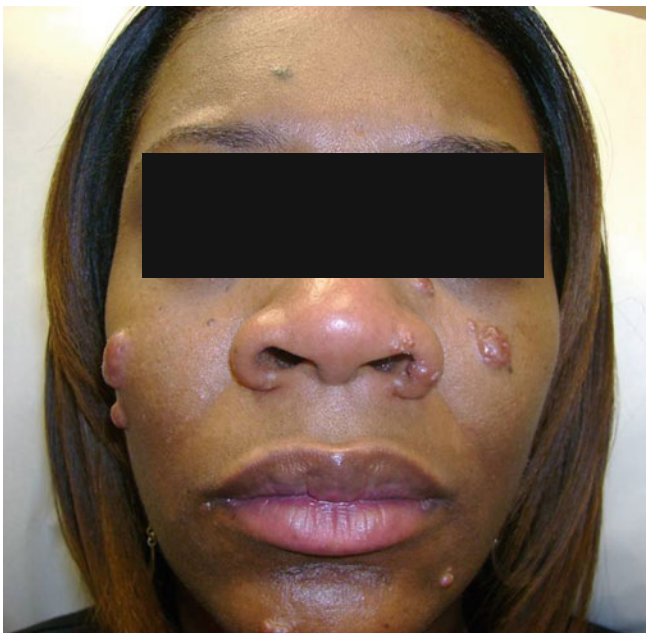

Fig. 26.1 African American female with sarcoidosis on the face

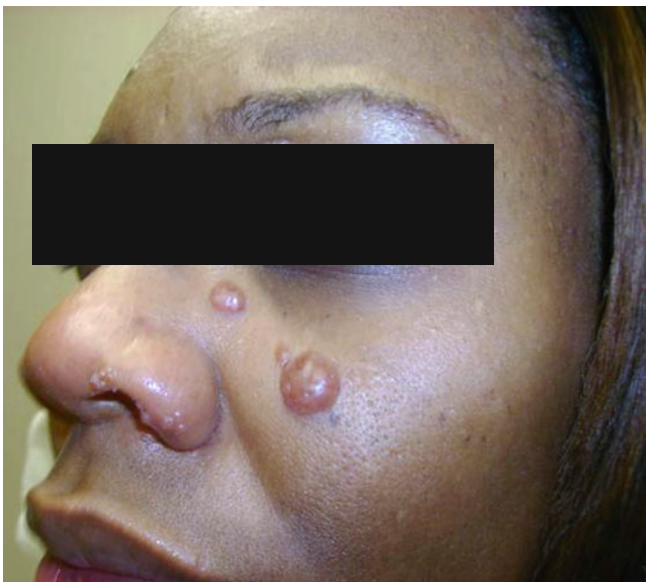

Fig. 26.2 African American female with sarcoidosis on the left cheek

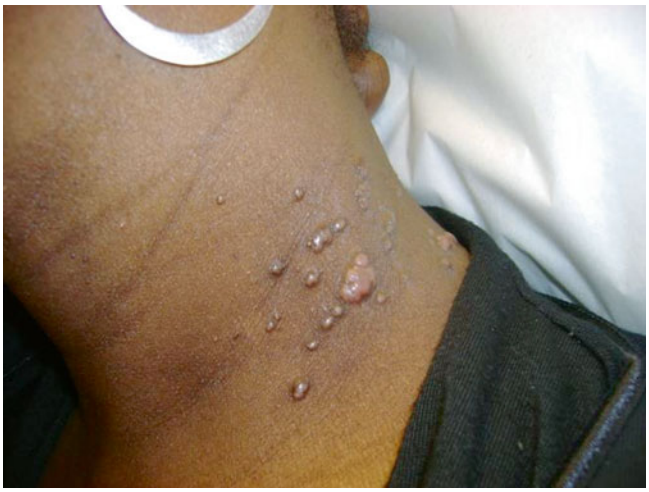

Fig. 26.3 African American female with sarcoidosis on the left neck

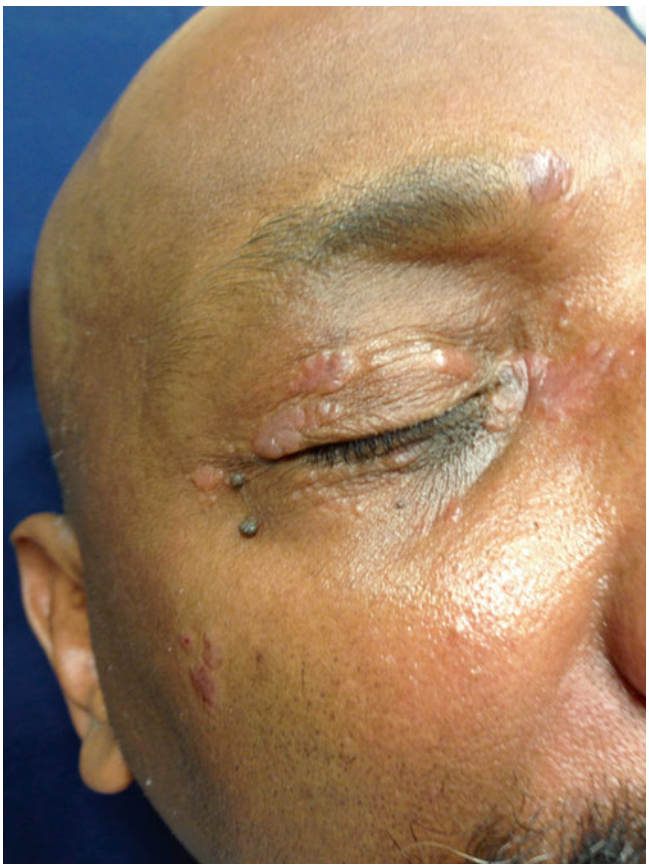

Fig. 26.4 Sarcoidosis in an African American male, right face

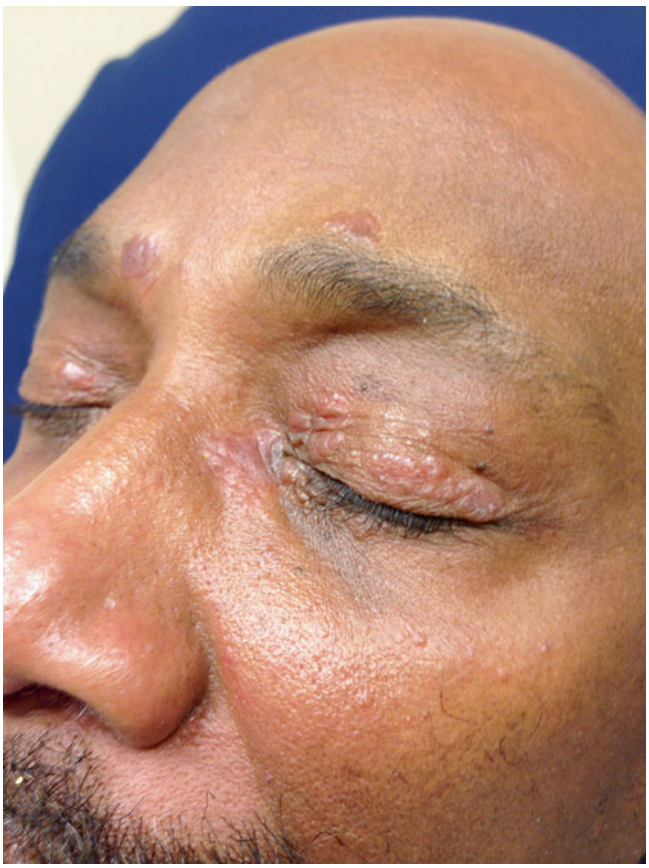

Fig. 26.5 Sarcoidosis in an African American male, left face

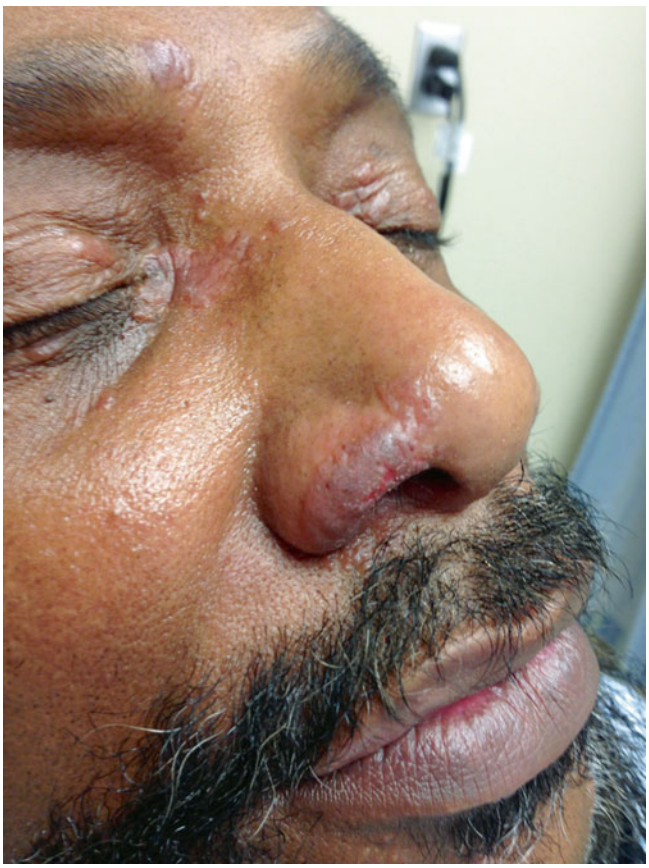

Fig. 26.6 Sarcoidosis in an African American male, right nasal ala

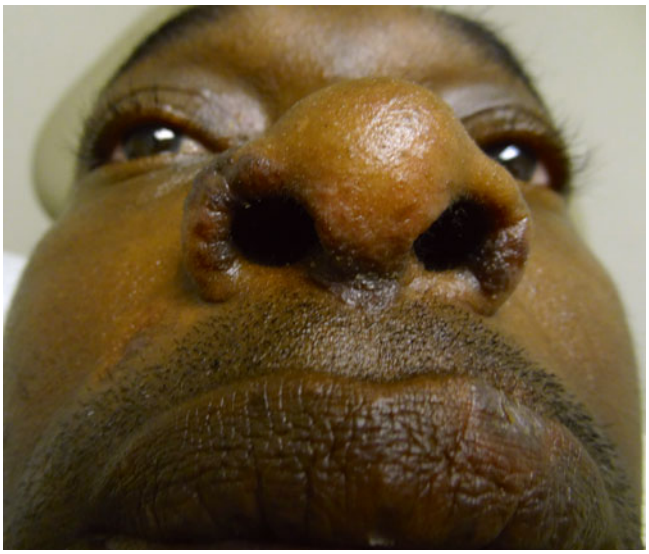

Fig. 26.7 Sarcoidosis in an African American male, nose

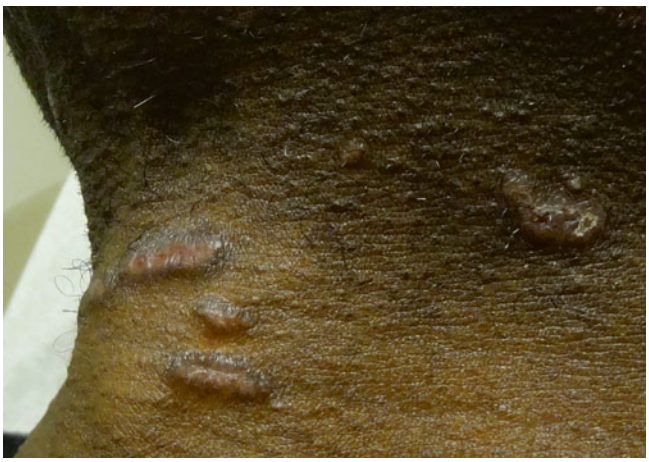

Fig. 26.8 Sarcoidosis in areas of trauma of an African American male, lower beard region of the neck

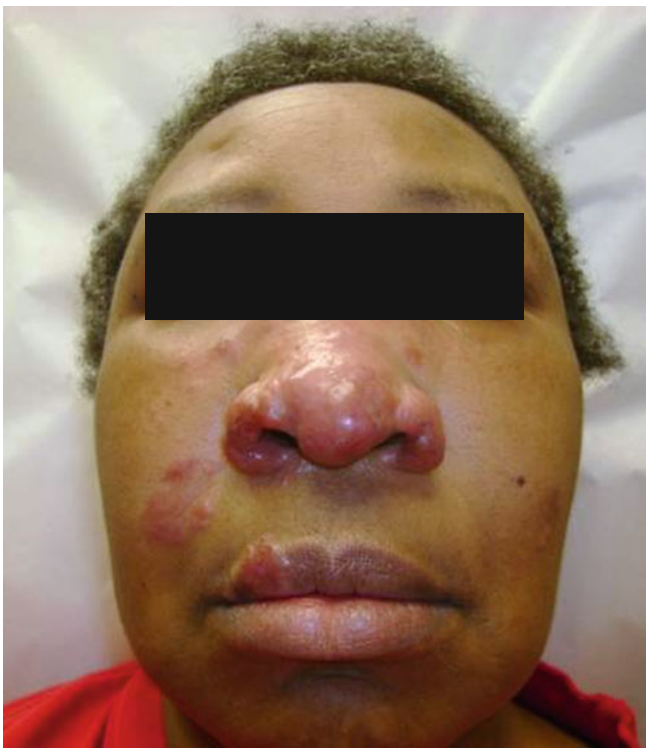

Fig. 26.9 Lupus pernio in an African American female

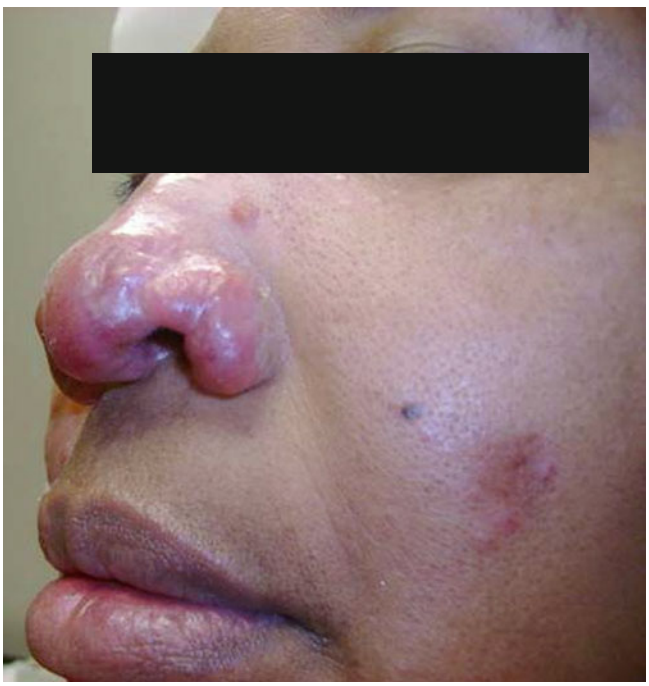

Fig. 26.10 Lupus pernio in an African American female, left face

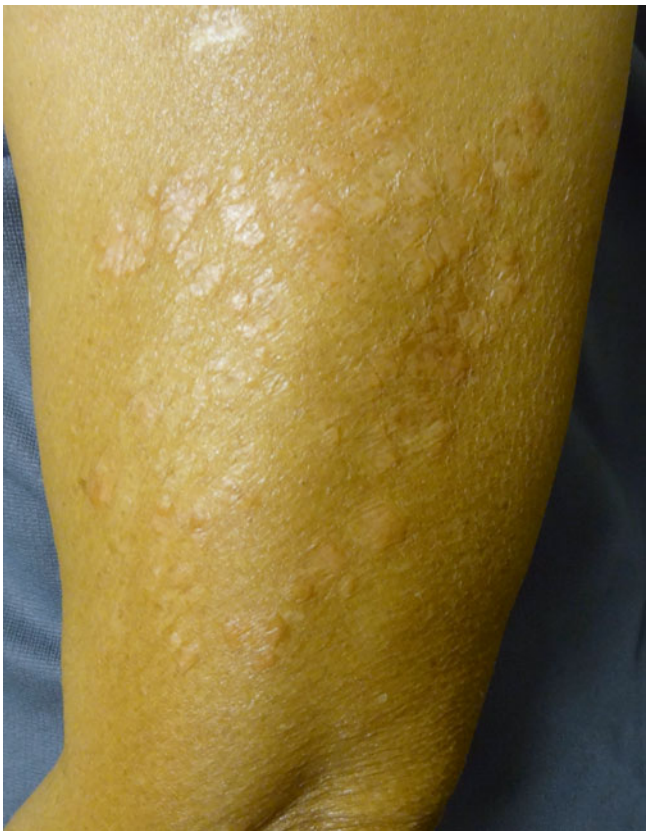

Fig. 26.11 Sarcoidosis of the left upper arm in a Hispanic female

26.4 Diagnosis

Diagnosis of sarcoidosis is one of the exclusions and should include a supportive history and histological evidence of noncaseating granulomas in the tissue, typically in the skin or paratracheal nodes. Histology shows noncaseating epithelioid granulomas with a sparse lymphocytic infiltrate at the periphery of the granulomas and occasional giant cells. Biopsies should be polarized to rule out foreign body reactions and tissue cultures done to rule out an infectious etiology. Workup should include chest x-ray, pulmonary function tests, CBC, ESR, creatinine, hepatic tests, calcium, ACE, and G6PD if antimalarials are considered. ACE levels may be elevated but are not diagnostic of sarcoidosis and have a false-negative rate of 40 %.

26.5 Treatment

Treatment of sarcoidosis is dependent on the severity of the patient's symptoms and the extent of organ involvement. Localized cutaneous lesions are often treated with topical corticosteroids or intralesional triamcinolone 5–10 mg/ml injections performed monthly. Systemic corticosteroids are used for more extensive cutaneous lesions or systemic sarcoidosis [7]. Other therapies include hydroxychloroquine, chloroquine, methotrexate, allopurinol, isotretinoin, infliximab, adalimumab, and thalidomide [9]. Patients with sarcoidosis may have spontaneous resolution of disease in 50–60 % of cases and even as high as 86 %, when presenting with erythema nodosum. The disease is chronic and progressive in 20 % of affected patients. African Americans generally have more prolonged disease, requiring more aggressive therapy, compared to Caucasians. Because of a higher incidence of G6PD deficiency in the skin of color patients, G6PD should be checked prior to initiating antimalarials. Caution should be used in vitamin D supplementation in sarcoidosis patients due to risk of hypercalcemia.

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