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Sarcoidosis
Sarcoidosis is a granulomatous disease, often systemic, of undetermined cause. A distinction is made between the rare subacute, transient type of sarcoidosis and the usual chronic, persistent type.

In subacute, transient sarcoidosis, erythema nodosum is associated with hilar adenopathy, fever, and, in some cases, … . Occasionally, there is enlargement of some of the subcutaneous lymph nodes, such as the submental or cervical nodes.

In systemic sarcoidosis, cutaneous lesions are encountered in approximately one fourth of patients who are seen in … the only manifestation of sarcoidosis in about one fourth of patients with sarcoidosis seen in dermatologic departments.
In the United States, this disorder is much more common and is more severe in African Americans. It is rare in children. The most common cutaneous lesions of sarcoidosis are brown or purple papules and plaques. Through central clearing, circinate lesions may result. When papules or plaques of sarcoidosis are situated on the nose, cheeks, and ears, the term "lupus pernio" is applied. This presentation has been associated with upper respiratory involvement and greater disease severity.
A rare form of sarcoidosis is its lichenoid variant, in which small, papular lesions occur. Very rare manifestations...
Subcutaneous nodules of sarcoidosis are also rare. Originally described by Darier and Roussy, they may...
occur in association with other cutaneous lesions or alone. Up to 80% to 90% of patients with subcutaneous sarcoidosis have associated skin lesions.
Systemic sarcoidosis occasionally coexists with granuloma annulare. Cutaneous lesions of sarcoidosis may localize to the skin and subcutaneous tissues. Foreign material in approximately 20% of cutaneous sarcoidal lesions from patients with systemic sarcoidosis.

**Histopathology.**

The lesions of erythema nodosum occurring in subacute, transient sarcoidosis have the same histologic...
Like lesions in other organs, the cutaneous lesions of chronic, persistent sarcoidosis are characterized by the presence of circumscribed collections of epithelioid histiocytes—so-called epithelioid cell tubercles—which show little or no necrosis.

The papules, plaques, and lupus pernio-type lesions show variously sized aggregates of epithelioid cells...
and, rarely, also giant cells. Typical sarcoidal granulomas are found in the ichthyosiform lesions, in ulcerated areas, and in atrophic lesions. Verrucous sarcoid exhibits prominent associated acanthosis and hyperkeratosis. Biopsies of hypopigmented sarcoid may reveal granulomas, which may have a perineural component or fail to reveal granulomas. In subcutaneous nodules, larger epithelioid cell tubercles lie in the subcutaneous fat.
In typical cutaneous lesions of sarcoidosis, the well-demarcated islands of epithelioid cells contain few, if any, giant cells.
Classically, sarcoid has been associated with only a sparse lymphocytic infiltrate, particularly at the margins of the granulomas. Occasionally, small foci of fibrin or necrosis showing eosinophilic staining is found in the center of some of the granulomas. A reticulum stain of sarcoid reveals a network of reticular fibers.
Systemic Lesions. The lungs are the most commonly involved organ in the chronic, persistent type of sarcoidosis. The lesions may be either nodular or diffuse with extensive parenchymal fibrosis.
In about 25% of the patients, ocular manifestations occur, most commonly chronic iridocyclitis. Splenomegaly is present in 70%, of peripheral lymph nodes in 30%, and of the liver in 20% of the patients.
Sarcoidosis, although usually a benign disease, is fatal in approximately 5% of patients. The most common cause of death is respiratory failure, due to pulmonary fibrosis or bronchiolitis obliterans. Hypopituitarism from involvement of either the pituitary gland or the hypothalamus is also a rare fatal complication.
The diagnosis of sarcoidosis in a patient with systemic disease is based on clinical presentation, biopsy.
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Pathogenesis

The cause of sarcoidosis is unknown, and the disease may not have the same pathogenesis in all individuals. Alterations in antigen presentation and the immune response have been postulated as a pathogenic mechanism. Mycobacteria, especially cell-wall-deficient forms, have been postulated to represent the antigen source. Mycobacterium tuberculosis has been implicated by some studies, whereas others have suggested atypical mycobacteria. Other infectious causes such as Rickettsia have also been suggested.
Electron microscopic examination of epithelioid cells fails to show any evidence of bacterial fragments, unlike the...
residual bodies of lysosomes. Asteroid bodies consist of collagen showing the typical 64- to 70-nm periodicity. It seems likely that this collagen is trapped between epithelioid cells during the stage of giant-cell formation.

**Differential Diagnosis**

The histologic differentiation of sarcoidosis from lupus vulgaris may be very difficult, and it is occasionally impossible. There is no absolute histologic criterion by which the two diseases can be differentiated with certainty. It is important to exclude tuberculosis because the organisms in lupus vulgaris are scarce and may be difficult or impossible to find.
Foreign-body granulomas can also resemble sarcoidosis. Polariscopic examination in search of doubly refractile material, however, usually demonstrates doubly refractile inclusions in sarcoidosis. Microscopy shows "naked" tubercles indistinguishable from those of sarcoidosis, but unlike sarcoid, they are usually perifollicular.

Tuberculoid leprosy, which may show granulomas in association with only a sparse lymphocytic infiltrate, can also be confused with sarcoidosis.