Chapter 13
Sarcoidosis in Aging Skin

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Introduction

Sarcoidosis is an idiopathic multisystem granulomatous inflammatory disease which commonly presents with manifestations in the lungs, skin, eyes and lymph nodes, although various organs may be affected. Cutaneous involvement is seen in approximately one-third of patients with systemic illness [1], and isolated skin disease occurs in roughly one-fourth of all patients [2]. The hallmarks of sarcoidosis include an accumulation of mononuclear phagocytes and infiltration of affected tissues by noncaseating granulomas (NCGs). Several eponyms have been used to characterize skin involvement in the disease, such as “Boeck’s sarcoidosis,” “Darier–Roussy sarcoidosis,” “lupus pernio of Besnier,” “Heerfordt’s disease,” and “Löfgren’s syndrome,” as well as more visually descriptive terms including papular, macular, annular, psoriasiform, verrucous, hypomelanotic, ichthyosiform, lymphedematous, and so forth. Labeled one of the “great imitators,” cutaneous sarcoidosis may exhibit a myriad of different morphologic lesions and pose a challenge to accurate diagnosis. This chapter will discuss the background of cutaneous sarcoidosis with an emphasis on elderly patients, as well as the principal morphologic forms of skin lesions in relation to differential diagnostic considerations. A brief summary on treatment options will also be presented.

Epidemiology

Sarcoidosis occurs worldwide with a roughly equal incidence of 1–40/100,000 in both sexes [3], with individuals under 40 years of age being most commonly affected [4]. A second peak in incidence occurs in women aged 45–65 years [5, 6], and in Europeans the age at disease onset tends to average in the fifth decade [3]. A much greater incidence of sarcoidosis is seen in blacks (particularly females) in the United States and South Africa, as well as in Scandinavian and Irish populations [7]. In Europe, white individuals are more commonly affected, as are western Europeans [3]. African-American patients generally present at a younger age than individuals of other ethnic groups, and may experience a more widely involved and advanced disease course, while in whites the opposite tends to occur [8]. The
incidence of sarcoidosis in those older than 60 years of age at diagnosis has been estimated at approximately 8% [9, 10]; however, it has been suggested that the paucity of cases reported among older patients may actually be an underestimate of the true incidence, when compared to more common diseases afflicting the elderly such as pulmonary tuberculosis or lung carcinoma [10]. Cutaneous sarcoidosis tends to occur with greater frequency in elderly females than in males [10–12].

**Clinicopathologic Characteristics**

The precise etiology of sarcoidosis is unknown. However, immune dysregulation has been implicated, likely due to persistence of a low-virulence antigen incompletely cleared by the immune system, resulting in a chronic T-cell response with granuloma formation. Postulated antigens consist of infectious agents including Mycobacteria, viruses and fungi; environmental triggers such as metals, pollens and dust; as well as auto-antigens [3, 8].

An accumulation of CD4+ T cells and increased levels of interleukin 2 (IL-2) occur at sites of disease activity, along with elevated levels of Th1 cytokines including interferon, and increased production of tumor necrosis factor (TNF) and TNF receptors [13]. Elevated B-cell activity and immunoglobulin production have also been noted, and increased antigen presenting cells and circulating immune complexes may also play a role [13, 14]. Genetic susceptibility has also been postulated to play an etiologic role, as familial clusters of the disease correlating with certain class I and II HLA alleles on chromosome 6 have been documented, including HLA-B8, HLA-A1 and HLA-D3 [3, 8, 14].

Although patients most commonly present with bilateral hilar lymphadenopathy, pulmonary infiltration, and skin or eye lesions, organ involvement in sarcoidosis can range from localized to widespread, mild to severe, and cause a self-limited to chronic disease course, depending on the impact of NCG formation on involved organ systems. In addition to pulmonary and cutaneous disease, sarcoidosis can manifest with ocular, lymph node, bone marrow, endocrine, hepatic, cardiac, musculoskeletal, neurologic and renal involvement. Roughly 5% of cases are asymptomatic and discovered incidentally by chest radiograph, while systemic and pulmonary symptoms are noted in approximately 45 and 50% of cases, respectively [13]. One-third of sarcoidosis patients develop lymphadenopathy, roughly 25–50% develop ocular disease, and approximately 5–10% experience neurologic or cardiac involvement [3, 14].

The extent of cutaneous lesions in sarcoidosis does not seem to correlate well with the extent of systemic involvement, but the mode of disease onset may be more closely associated with its course and prognosis [15, 16]. Patients who experience an acute onset of illness with development of erythema nodosum generally undergo a more self-limited course and spontaneous resolution of their disease, while those who experience a more insidious onset have a greater likelihood of developing progressive pulmonary fibrosis [17]. Spontaneous remission of disease occurs in