Pulmonary Sarcoidosis

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KEYWORDS

• Sarcoidosis • Lung • Pathology • Pulmonary function • Evolution

KEY POINTS

- Modes of onset of pulmonary sarcoidosis are various and often unspecific, leading to diagnosis delay.
- Noncaseating granulomas are shown at a high rate through bronchial flexible endoscopy and represent an important element for confirming diagnosis in the context of typical clinical-radiographic presentation with bilateral hilar lymphadenopathy or micronodular lesions with typical distribution along lymphatic vessels.
- Monitoring evolution has to be scheduled every 3 to 6 months with clinical evaluation, chest radiography, and pulmonary function tests.
- The evolution of pulmonary sarcoidosis may be variable, with different evolution patterns from rapid spontaneous recovery to progressive inexorable respiratory insufficiency that is insensitive to treatments.

INTRODUCTION

Sarcoidosis is a systemic disease affecting the lung in almost all cases.[1–3] Whatever the various revealing symptoms, the evidence of abnormal chest radiography is usually a key step for considering diagnosis.[4,5] Bronchial flexible endoscopy allows typical granulomas to be obtained at a high rate.[6–10] The lung is investigated through imaging; pulmonary function; and, when required, 6-minute walk test (6MWT), cardiopulmonary exercise testing, or right heart catheterization.[5,10–13] The impact of pulmonary sarcoidosis may be benign or severe. The evolution of pulmonary sarcoidosis may be variable from rapid spontaneous recovery to progressive inexorable respiratory insufficiency insensitive to treatments.[14,15]

This article focuses on lung disorders, modes of onset, some investigations (especially lung function and bronchoalveolar lavage [BAL]), the prognosis, and the evolution. It does not address pathogenesis, diagnosis of sarcoidosis, chest imaging, severe manifestations, pulmonary hypertension, or treatment, which are also discussed in this issue.

PATHOLOGY

Pulmonary sarcoidosis is a granulomatous interstitial pneumonia, a group of diseases that includes a variety of infectious and noninfectious settings.[16] Observation of the characteristic noncaseating granuloma is essential for the diagnosis of sarcoidosis. Sarcoid granulomas are well formed and

Disclosures: None.

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Clin Chest Med 36 (2015) 631–641
http://dx.doi.org/10.1016/j.ccm.2015.08.006

consist of a compact core of macrophages/mononuclear phagocytes converted into epithelioid cells and giant cells[17,18] (Fig. 1A, B). Epithelioid cells are metabolically active cells, particularly in the synthesis of angiotensin-converting enzyme and 1α-25$(OH)_2$ vitamin D (calcitriol).[19–21] Epithelioid cells are closely associated with $CD4^+$ T lymphocytes, whereas CD8 lymphocytes, $CD4^+$ $FOXP3^+$ T_{reg}, Th17 cells, B lymphocytes, as well as immunoglobulin (Ig) A–producing plasma cells are present in the peripheral area.[22–24] In contrast with other granulomatous interstitial pneumonias, sarcoidosis shows a particularly florid proliferation of granulomas with a trend to coalesce.[18] Sarcoid granulomas occasionally show a focal central coagulative necrosis. Collections of granulomas may form macroscopically small white nodules (micronodules) or large masses (macronodules) with the lung in between relatively spared.[25] The topographic predilection of granulomas for lymphatic routes (collecting lymphatics in pleural interstitium, interlobular septa, and bronchovascular interstitium, as well as intralobular lymphatics) provides a valuable histopathologic diagnostic criterion for pulmonary sarcoidosis[18,26] (see Fig. 1B, C). Such a distribution suggests a critical role of lymphatics in the emergence of these lesions, reinforcing a putative role of airborne particles in the pathogenesis of pulmonary sarcoidosis.[26] In addition to granulomas close to small airways, a peribronchiolitis with a narrowing of the bronchiolar lumen is common (see Fig. 1D).

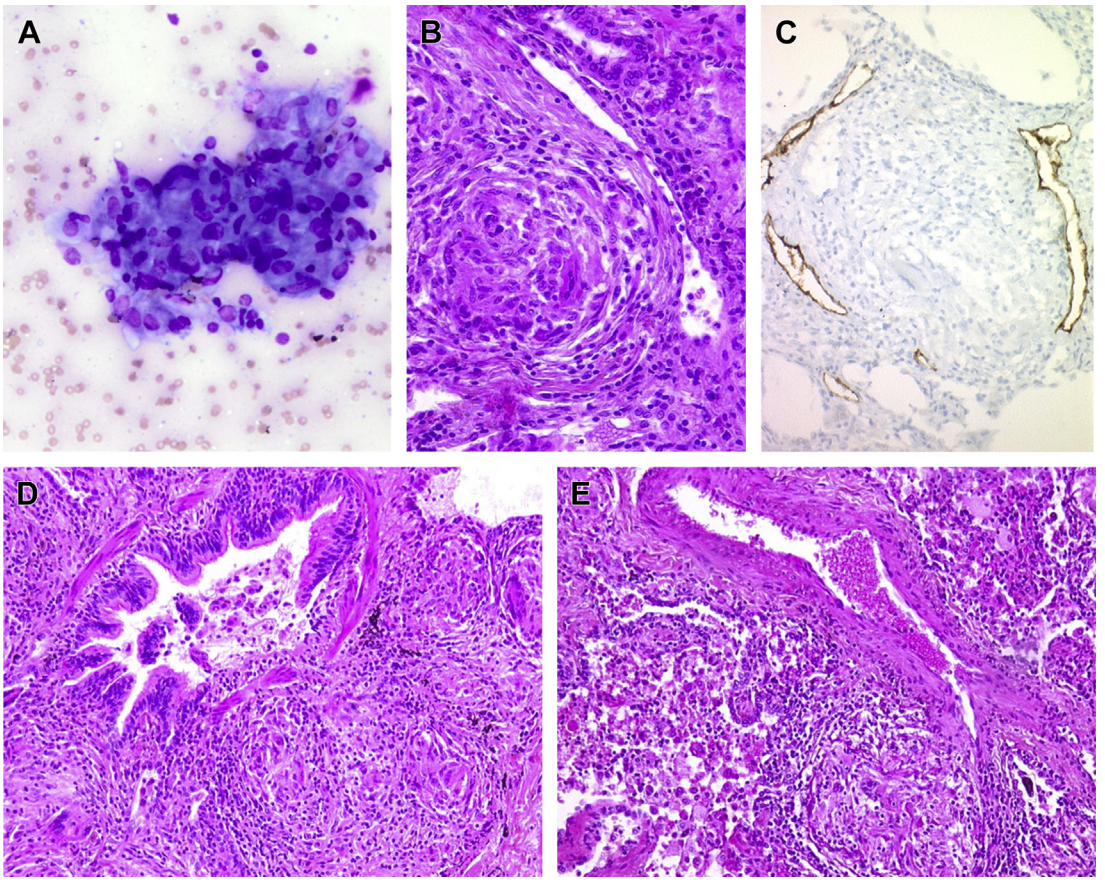

Fig. 1. Examples of the characteristic well-circumscribed noncaseating granulomas made of tightly clustered histiocytes, epithelioid cells, and lymphocytes observed in various situations in pulmonary sarcoidosis. (*A*) A granuloma obtained by fine-needle aspiration using endobronchial ultrasonography of a mediastinal lymph node (May-Grünwald-Giemsa, original magnification × 200). (*B–E*) Images obtained from paraffin-embedded surgical lung biopsies. (*B*, *C*) The characteristic proximity of granulomas and lymphatics observed in pulmonary sarcoidosis (*B*); lymphatic lumen is observed above rhe granuloma (hematoxylin-eosin-saffron [HES], original magnification × 100). (*C*) The lymphatics wrapping a granuloma appear brown after incubation with the lymphatic marker antipodoplanin D2-40 antibody, original magnification × 100). (*D*) The bronchiolar involvement by granulomas (HES, original magnification × 100). (*E*) The vascular involvement by a granuloma in the wall of a pulmonary artery (HES, original magnification × 100). (*Courtesy of* [*A*] Dr J. Fleury-Feith, APHP, Paris.)