

Commentary

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The case reports by Loughney and Higgins and Hughes and McGavin raise several points of relevant clinical interest. Although pleural involvement by sarcoidosis is relatively infrequent, the evaluation, nature and extent of any pleural thickening or pleural effusion will vary according to the appearances seen on plain film, computed tomographic (CT) scan, or at thoracoscopy. Pleural pain may be absent or less severe than might be anticipated. Effusions may be large and occasionally bilateral; they may present without evidence of mediastinal or pulmonary abnormality, or occur concomitantly with or shortly after the appearance of bilateral hilar lymphadenopathy, without overt evidence of lung changes. Conversely, they may develop several months or even many years after the diagnosis of sarcoidosis. The granulomatous nature of the pleural involvement may be confirmed by pleural biopsy; needle biopsy may be unsatisfactory since, in the presence of the effusion, it may yield only a small piece of parietal pleura. Characteristically, the effusions are exudative with a specific gravity of 1.018–1.035, a protein content of 4.0–6.0 g, and predominantly lymphocytic cellularity. Transudates may occur in sarcoidosis in which only occasional cells and a few lymphocytes are present, although such features may give rise to doubt as to their cause. Rarely, in the absence of any evidence of malignancy, effusions may be bloodstained other than by tap. Where a pleural effusion presents prior to the advent of apparent lung disease with or without mediastinal involvement, it is especially important to determine the specific gravity, protein content, and cell count of the pleural fluid, and to allow for the fact that, particularly in those with transient effusion, there may be pleural granulomas but with a relatively acellular transudate pleural fluid. Effusions may occur during the course of sarcoidosis among patients of all ethnic groups, but culture of the pleural fluid for AAFB is essential in all cases. Tuberculin sensitivity may be reduced or absent in a sick patient. If there is doubt, and in the absence of other features of sarcoidosis, it may therefore be wise to institute appropriate antitubercular cover, adding steroids later if required. Conversely, clearly evident tuberculin sensitivity does not necessarily mitigate against a diagnosis of sarcoidosis; two cases reported by Mikhail et al clearly illustrate the difficulties in differentiation between a pleural effusion associated with sarcoidosis or one due to Mycobacterium tuberculosis.

Small effusions may resolve spontaneously or following treatment with prednisolone and are usually accepted as being due to sarcoidosis without recourse to pleural biopsy. Conversely, in patients with chronic sarcoidosis they may persist for months or years, proving relatively unresponsive to suppressive therapy, and leading to substantive pleural thickening.

In the case reported by Loughney and Higgins the chest radiograph showed mediastinal adenopathy but no evidence of hilar lymphadenopathy or parenchymal disease, although CT scanning revealed an associated lymphadenopathy affecting the superior mediastinal, hilar, and subcarinal nodes. Both the pleural mass and the nodes showed non-caseating granulomas in the biopsy specimen. CT examination and biopsy thereby clarified the situation; however, atypical presentations of this nature may give rise to doubt as to the possibility of coexistent malignant lymphoma and this pathology may be associated with the generalised granulomatosis attributable to the sarcoidosis or to the propensity of a malignant lymphoma to be associated with a relatively extensive but so-called local granulomatous response in the mediastinal nodes. In such cases it is advantageous to define the histology at various mediastinal levels, and to submit the biopsy tissues for culture for AAFB and for other organisms as may be relevant to diminish the possibility of overlooking other infectious or malignant disease associated with an extensive but localised granulomatous response or a malignant lesion co-existing with sarcoidosis.

An overlap syndrome of sarcoidosis and primary biliary cirrhosis with a co-existing myositis is described by Hughes and McGavin; their clinical assessment is supported by comprehensive investigations. First described by Myers et al, sarcoïd myopathy is rare. Symptomatic patients typically have a chronic slowly progressive muscle disease that closely resembles chronic polymyositis or muscular dystrophy. Other symptomatic forms include palpable muscle nodules and acute myositis. Asymptomatic muscle involvement is thought to occur in 50–80% of cases, and random muscle biopsy tissue has, in the past, routinely provided a method of tissue diagnosis in sarcoidosis. It is against this background that difficulty may arise in determining the aetiology
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of an associated myopathy which may be attributable to a disorder other than sarcoidosis. Wolfe et al reported four patients with muscle weakness and reviewed the clinical features of 75 previously reported cases of sarcoid myopathy. The least common form of symptomatic sarcoid muscle disease is the palpable nodule which may cause pain, stiffness, and cramps. An acute myositis may occur but it is rare: in such cases, creatine kinase levels are usually raised. It is the least frequent form of sarcoid muscle involvement with only 18 cases having been reported in the English language literature. Most patients are female and black and present with fevers and myalgias over a period of weeks or months and may simulate the presentation of acute polymyositis. All show predominant proximal muscle weakness, most commonly of the hips and shoulders. A single case of acute sarcoid myositis affecting the respiratory muscles has been reported and was responsive to prednisolone with the resolution of symptoms and improvement of lung function tests. Al-Saffar et al have reported acute sarcoid myositis in a West Indian woman with pulmonary sarcoidosis who showed markedly increased creatine kinase levels associated with eosinophilia for which no other cause could be found. She was treated with prednisolone and showed considerable improvement of muscle strength with rapid return of the eosinophilia and creatine kinase levels returned to normal.

In this context it is important to note that eosinophils may not infrequently outnumber plasma cells in biopsy specimens of sarcoid tissue and that, rarely, in patients with sarcoidosis a significant peripheral blood eosinophilia may be noted for which no other related cause can be found. Chronic myopathy is most frequently seen and is a slowly progressive, often symmetrical, disease involving the proximal muscles of the extremities, trunk and neck, often with muscle wasting. Distal muscle involvement may be secondary to peripheral neuropathy. Chronic myopathy usually occurs in older patients, predominantly in postmenopausal women. Muscle enzymes are often increased and electromyography shows a myopathic pattern. Pseudohypertrophy is occasionally seen.

The association of sarcoidosis with myasthenia gravis is rare. Sarcoidosis has developed during regression of myasthenia gravis in some cases and during resurgence of sarcoidosis in others. Regression of myasthenia gravis and sarcoidosis after thymectomy has also been reported. Takanana et al have described such an association in which, as one would expect, myasthenia gravis became less severe after thymectomy, but sarcoidosis did not. The recent discovery of a family of autoantibodies which appears almost exclusively in patients with myositis has led to a deeper analysis of humoral autoimmunity in this clinically heterogeneous family of diseases.

In the comprehensive investigation of their patient with sarcoidosis, primary biliary cirrhosis and a coexisting myositis, Hughes and McGavin point to the finding of a strongly positive mitochondrial M2 antibody that has been shown to be more highly specific for primary biliary cirrhosis than the AMA test. Yeaman et al found that serum samples from 38 of 40 patients with established clinical, biochemical, and histological features of primary biliary cirrhosis reacted positively, whereas those from 39 controls gave a negative response, but the well known capacity for the natural enhancement of a wide range of humoral antibody titres in patients with sarcoidosis may have to be taken into account in a further assessment of their prevalence and significance in overlap syndromes.

Pleural sarcoidosis: Sarcoidosis and primary biliary cirrhosis.

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