

Acute pleurisy in sarcoidosis

I. T. GARDINER AND J. S. UFF

From the Departments of Medicine and Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS, UK

Gardiner, I. T., and Uff, J. S. (1978). Thorax, 33, 124-127. Acute pleurisy in sarcoidosis. A 47-year-old white man with sarcoidosis presented with a six-week history of acute painful pleurisy. On auscultation a loud pleural rub was heard at the left base together with bilateral basal crepitations. The chest radiograph showed hilar enlargement as well as diffuse lung shadowing. A lung biopsy showed the presence of numerous epithelioid and giant-cell granulomata, particularly subpleurally. A patchy interstitial pneumonia was also present. He was given a six-month course of prednisolone, and lung function returned to normal.

Pleural involvement by sarcoid was thought to be very infrequent (Chusid and Siltzbach, 1974) until one recent report which gave an incidence of nearly 18% (Wilen *et al.*, 1974). However, histologically confirmed cases remain small in number, even from very large series. Beekman *et al.* (1976) have stressed that it is so unusual that pleural disease in a patient with sarcoidosis is very likely to be due to a condition other than the sarcoidosis.

We present the case of a European man with acute painful pleurisy in whom the diagnosis of sarcoidosis was confirmed histologically.

Case report

A 47-year-old white man presented with a six-week history of right parasternal pleuritic pain with no other respiratory symptoms. He was given antibiotics, and the pain subsided but one week later appeared on the left side. A chest radiograph showed left middle and lower lobe shadowing, thought to be infective in nature. He was given further antibiotics, but one month later the radiograph showed the shadows to be bilateral. He had an unproductive cough and complained of 'not being able to get enough air into the chest'. He was admitted to hospital for investigation, and a recurrence of pleural pain was accompanied by a loud pleural rub at the left base, together with bilateral basal crepitations. The chest radiograph showed bilateral hilar enlargement and there was a diffuse haze around both hilae. The middle and lower zone lung fields had a fine granular 'ground-glass' appearance. A Mantoux test was negative (100 TU) and, because all sputum and blood tests

were unhelpful, an open lung biopsy was performed on 19 July 1974. Small white nodules, 1 mm across, were scattered over the visceral pleura, and the lung felt firmer than normal. The hilar lymph nodes were enlarged and a biopsy specimen was taken from one.

Two weeks later he was started on prednisolone, 30 mg per day. This was gradually reduced and eventually stopped six months later when the lung function (Table) had returned to normal levels; it has remained so since that time.

Table Lung function

	26 June '74	17 July '74	8 Nov. '74	Predicted values
Forced expiratory volume (1 sec)	3.5	2.7	3.4	3.2-4.2 litres
Vital capacity	4.3	3.2	4.2	4.1-5.3 litres
Alveolar volume	4.2	4.0	4.7	
Transfer coefficient (K _{CO})	1.44	1.31	1.61	1.54-2.12 mmol/min/mmHg × 1.36 = mmol/min/kPa
Total lung capacity	6.6	4.7	6.2	6.1-7.9 litres

Conversion factor: CO uptake ml/min/mmHg × 1.36 = mmol/min/kPa.

Material and method

Lung and lymph node tissue for light microscopy was fixed in formalin, processed in the standard way, and embedded in paraffin. Sections were stained with haematoxylin and eosin, Weigert's impregnation for elastin counterstained with van Gieson, reticulin stain (Gordon and Sweet), and Ziehl-Neelsen's stain.

Lung tissue for electron microscopy was fixed in glutaraldehyde, post-fixed in osmium tetroxide, and embedded in resin.

Results

The lymph node contained numerous small epithelioid and giant-cell granulomata, typical of sarcoid. There was no caseation and no tubercle bacilli were identified. Macroscopically the lung was peppered with numerous small, firm, white nodules, the largest 1 mm in diameter. These were present throughout the specimen but were particularly noticeable on the pleural surface. The lung contained numerous granulomata, similar to those in the lymph node, both subpleurally (Fig. 1) and adjacent to pulmonary arteries (Fig. 2). The granulomata in the lung parenchyma were larger and were surrounded by a zone of inflammatory cells, which were mainly lymphocytes with small numbers of macrophages, eosinophils, and plasma cells. This infiltrate extended into the surrounding tissue, frequently producing a localised non-destructive vasculitis in the adjacent pulmonary vessels (Fig. 2). Unassociated with the granulomata, there was a patchy interstitial pneumonitis. The septa contained a mild chronic inflammatory infiltrate, and there were many macrophages within the alveoli (Fig. 3).

Electron microscopy confirmed that these cells were macrophages and that the alveolar septa were lined by type II pneumocytes. Direct immunofluorescence showed an occasional fleck of IgG within the granulomata and numerous inflammatory cells with intracytoplasmic IgG, IgM, and IgA around the granulomata and in the alveolar septa. No complement components were detected, and there was no evidence of immunoglobulins within vessels, even in areas showing vasculitis.

Discussion

The literature suggests that the typical patient with pleural involvement by sarcoid is a negress who has had sarcoidosis diagnosed for some years, who has extensive radiological pulmonary involvement, and who presents with pleural effusions (Sharma and Gordonson, 1975; Chusid and Siltzbach, 1974). Pleural involvement does not necessarily cause symptoms and may be found only if specifically sought (Beekman *et al.*, 1976; Wilen *et al.*, 1974). Classical pleural pain has been described in sarcoidosis (Wilen *et al.*, 1974), but more common is an atypical pain thought to be due to mediastinal lymph node enlargement (Mayock *et al.*, 1963). Chronic asymptomatic pulmonary involvement is unlikely in our patient because a chest radiograph taken for unrelated reasons a

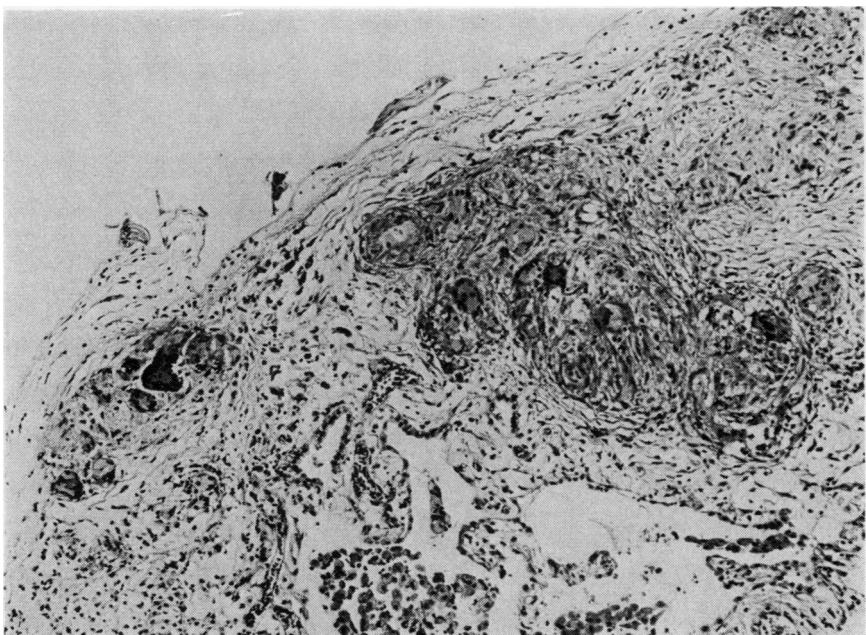


Fig. 1 Multiple small granulomata (some of which have coalesced) beneath the visceral pleura (Haematoxylin and eosin $\times 45$).

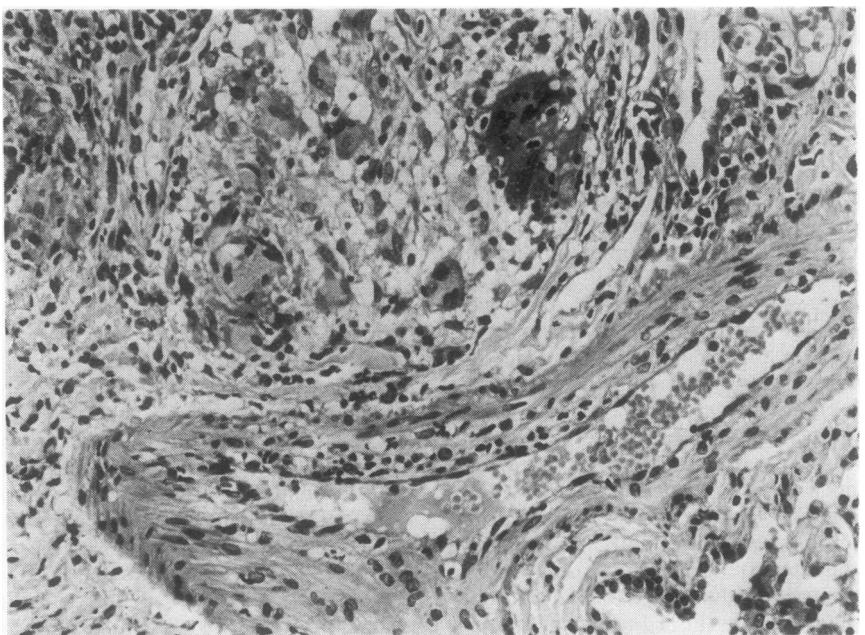


Fig. 2 A granuloma adjacent to a medium-sized pulmonary artery. Inflammation in the intervening wall is well seen with preservation of the elastic plates (*H and E* $\times 300$).

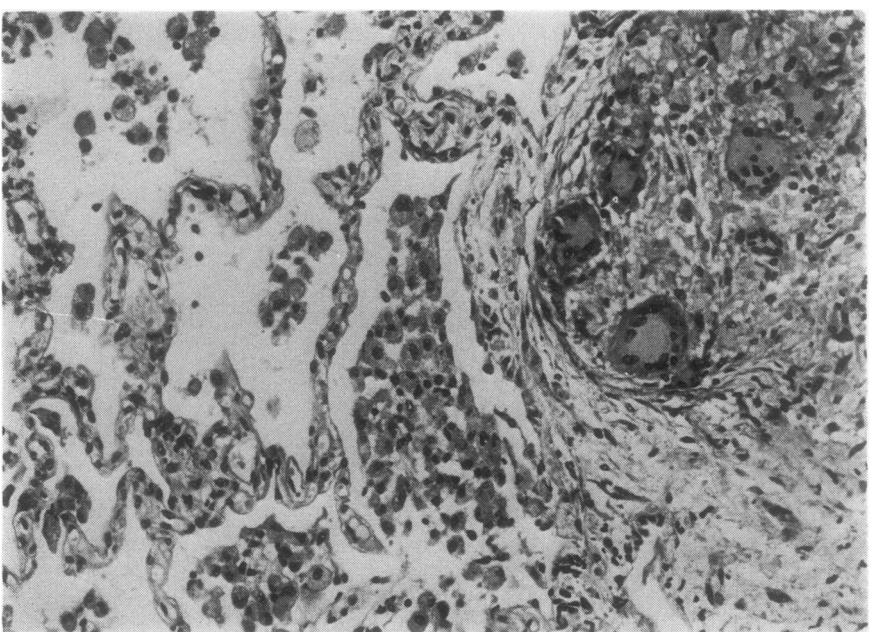


Fig. 3 Many macrophages lying free in alveolar spaces surrounding a well-formed granuloma (*H and E* $\times 300$).

few months before the onset of the presenting illness was normal.

The hilar haze and 'ground-glass' appearance seen on our patient's chest radiograph, suggesting an alveolar and acinar filling process (Ziskind *et al.*, 1963), are unusual but have been described as highly suggestive of sarcoidosis (Rabinowitz *et al.*, 1974). The nature of this alveolar filling process has been unclear. Sahn and colleagues (1974) have described a case of pulmonary sarcoid with an 'acinar' pattern on the chest radiograph. Lung biopsy revealed multiple granulomata, and the alveoli adjacent to these were filled with mononuclear cells. These authors could not determine whether the cells were blood-borne or shed from alveolar walls. Our patient showed similar radiographic appearances, and electron microscopy has shown these cells in alveolar spaces to be macrophages.

The return of the lung function to normal suggests that steroids induced clearing of macrophages from the alveoli, and that there was no significant loss of pulmonary microvasculature due to the vasculitis.

In the case reported here the histological appearance of the granulomata and their distribution within the lung were typical of those described in sarcoidosis. The granulomata were small and discrete with no evidence of central necrosis; no tubercle bacilli nor fungal elements were demonstrated. However, the diagnosis of sarcoidosis cannot be made on histological grounds alone, because the granulomata of sarcoid are not specific. In the present case the diagnosis was made on the combination of typical histological, radiological, and clinical findings.

The vasculitis seen in this case was a bland process. Where granulomata abutted on medium-sized vessels, lymphocytes could be seen between the elastic plates of the adjacent vessel wall. This appearance was different from that of necrotising

sarcoidal angiitis, as there was no necrosis of the vessel wall, no intimal proliferation, nor vascular occlusion.

We are grateful to Dr. G. W. Poole for permission to publish details of a patient under his care. We also thank Mr. W. Hinks for the photomicrographs and Mrs. P. Weller for secretarial help.

References

- Beekman, J. F., Zimmet, S. M., Chun, B. K., Miranda, A. A., and Katz, S. (1976). Spectrum of pleural involvement in sarcoidosis. *Archives of Internal Medicine*, **136**, 323-330.
- Chusid, E. L., and Siltzbach, L. E. (1974). Sarcoidosis of the pleura. *Annals of Internal Medicine*, **81**, 190-194.
- Mayock, R. L., Bertrand, P., Morrison, C. E., and Scott, J. H. (1963). Manifestations of sarcoidosis. *American Journal of Medicine*, **35**, 67-89.
- Rabinowitz, J. G., Ulreich, S., and Soriano, C. (1974). The usual (sic) unusual manifestations of sarcoidosis and the 'hilar-haze'—a new diagnostic aid. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine*, **120**, 821-831.
- Sahn, S. A., Schwarz, M. I., and Lakshminarayan, S. (1974). Sarcoidosis: the significance of an acinar pattern on chest roentgenogram. *Chest*, **65**, 684-687.
- Sharma, O. P., and Gordonson, J. (1975). Pleural effusions in sarcoidosis: a report of six cases. *Thorax*, **30**, 95-101.
- Wilen, S. B., Rabinowitz, J. G., Ulreich, S., and Lyons, H. D. (1974). Pleural involvement in sarcoidosis. *American Journal of Medicine*, **57**, 200-209.
- Ziskind, M., Weill, H., and Payzant, A. R. (1963). Recognition and significance of acinus-filling processes of the lung. *American Review of Respiratory Disease*, **87**, 551-559.

Requests for reprints to: Dr. J. S. Uff, Department of Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12.