

Sarcoid pleural effusion: three cases and review of the literature

A J NICHOLLS, J A R FRIEND, AND J S LEGGE

From the Chest Clinic, City Hospital, Aberdeen

ABSTRACT Pleural sarcoidosis is rare—it is little recognised in Britain although several cases have been reported in the international literature. Three white men with pleural effusions caused by sarcoidosis have been seen in a two-year period when approximately 60 new cases of thoracic sarcoidosis have presented. In one patient a recurrent massive effusion was only diagnosed as being caused by sarcoidosis after thoracotomy, and in two further patients small symptomatic pleural effusions were present at the onset of typical sarcoidosis. Two patients were successfully treated with steroids and the third improved spontaneously. Percutaneous biopsy is not always helpful in diagnosing pleural sarcoidosis, but a lymphocytic, often blood-stained, pleural aspirate is highly characteristic. While other diseases may coexist, a pleural effusion in a patient with histologically proven sarcoidosis is more likely to be caused by the primary disease than by any other condition.

Pleural involvement in sarcoidosis has been regarded as exceptional in the British literature.^{1 2} Although recent reports have described acute pleurisy without effusion³ and retrosternal pain,⁴ sarcoidosis is not widely regarded as a cause of pleural effusion in the United Kingdom.

In Britain there has only been one published case occurring in a West Indian living in London,⁵ whereas there have been many well-documented cases of pleural sarcoidosis with effusion in the international literature, several of which have been reviewed Chusid and Siltzbach⁶ and by Wilen and colleagues.⁷

We present here three cases of sarcoidosis in white men living in Scotland, all of whom developed symptomatic pleural effusions not caused by other conditions.

Case reports

CASE 1

A 28-year-old Scottish white male oil-rig engineer developed right uveitis in March 1976. His chest radiograph showed bilateral hilar and paratracheal lymphadenopathy and lower zone pulmonary infiltration. Sarcoidosis was diagnosed and prednisolone 40 mg daily was given. His uveitis cleared within a month.

In April 1976 he was asymptomatic, steroids

having been stopped. His tuberculin reaction (10 TU) was negative, having been Heaf grade III positive in 1963. Spirometry, lung volumes, and diffusing capacity were normal, but there was mild hypoxaemia (P_{aO_2} 9.68 kPa). No further treatment was given and he remained well for the next six months.

In October 1976 this patient developed left cervical and bilateral axillary lymphadenopathy and hepatosplenomegaly. His radiograph was unchanged and a blood count was normal. Both a liver biopsy and a cervical lymph node biopsy showed non-caseating granulomata typical of sarcoidosis. Pulmonary function testing was unchanged and no treatment was given. He remained well for the rest of 1976.

In January 1977 he complained of left pleuritic chest pain and progressive dyspnoea. He had a large left pleural effusion (fig 1) and increased hepatosplenomegaly. There were no signs of venous disease in the legs. Pleural aspiration yielded a litre of bloodstained fluid containing eosinophils, lymphocytes, and neutrophil polymorphs which was sterile on culture. A Mantoux test (10 TU) was negative. A further three litres of fluid were aspirated at subsequent thoracenteses, with the same negative bacteriology. Pleural punch biopsy did not yield specific histology. Sputum was repeatedly negative for acid-fast bacilli on direct film and culture. Bone marrow obtained by aspiration showed reactive changes,

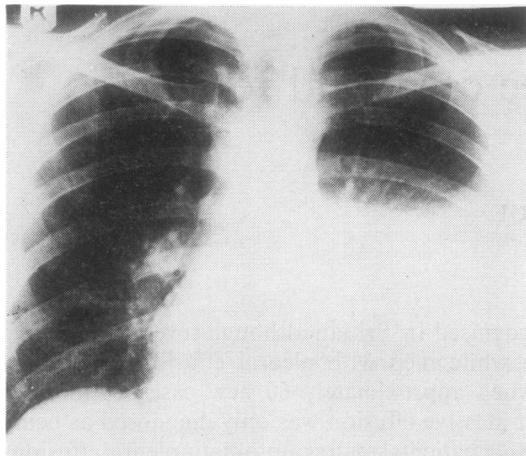


Fig 1 Case 1. January 1977, showing a large left pleural effusion.

and was sterile on culture. A repeat Mantoux test with 100 tuberculin units was negative.

An open pleural and lung biopsy was performed in view of further accumulation of fluid—2600 ml of serosanguinous fluid was aspirated and culture was again sterile. The lung and parietal pleura were slightly reddened and fibrinous exudate was present, but no obvious superficial pulmonary lesion was seen. Lung histology showed the changes of sarcoidosis underlying the visceral pleura (fig 2) and the parietal pleura showed non-specific inflammatory change.

Treatment with prednisolone 40 mg daily was started and in addition conventional doses of rifampicin, isoniazid, and ethambutol were given as the results of the the tuberculosis cultures were not available by then. The effusion did not recur and the lymphadenopathy and hepatosplenomegaly regressed partially. Two years later he remains in good health on 5 mg prednisolone daily, although liver and spleen remain palpable 5 cm below the costal margins. His chest radiograph shows persistent lower zone shadowing, but pulmonary function tests have not changed significantly.

CASE 2

A 27-year-old Scottish white male stonemason developed erythema nodosum and a dry cough in February 1978. Two months later he complained of left-sided pleuritic chest pain and became progressively more breathless. Physical examination was normal apart from signs of a left pleural effusion. A chest radiograph confirmed the effusion and also showed bilateral hilar lymphadenopathy.

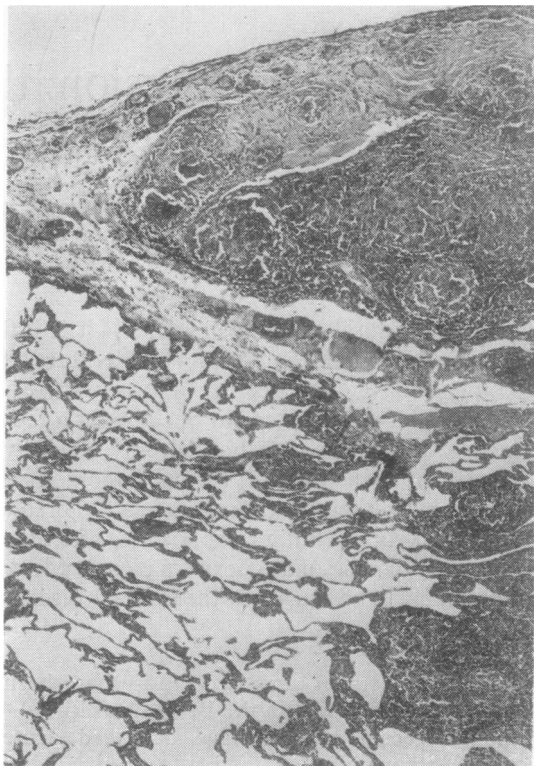


Fig 2 Case 1. Epithelial cell granulomata in pleura and underlying lung. Haematoxylin and eosin, original magnification $\times 64$.

Pleural aspiration yielded a litre of slightly bloodstained fluid containing lymphocytes, histiocytes, and mesothelial cells. Pleural punch biopsy showed fibrinous granulation-like tissue, but no granulomata were identified. A Mantoux test was negative at 10 TU, but positive (20 mm diameter induration) at 100 TU. Culture of the pleural fluid was negative for tubercle bacilli and other organisms, and no sputum was produced. A Gallium scan showed diffuse uptake in the mediastinum, liver, and abdominal lymph nodes, compatible with a lymphoma or sarcoidosis. A Kveim test (Colindale K 19/1/13) subsequently showed typical sarcoid granulomata on biopsy.

He received no drug therapy and returned to work three weeks later with a little residual fluid still present. By November 1978, nine months after the onset of his symptoms, he was completely well with a normal chest radiograph.

CASE 3

A 25-year-old white male labourer, American by birth and of Italian ancestry, presented in April

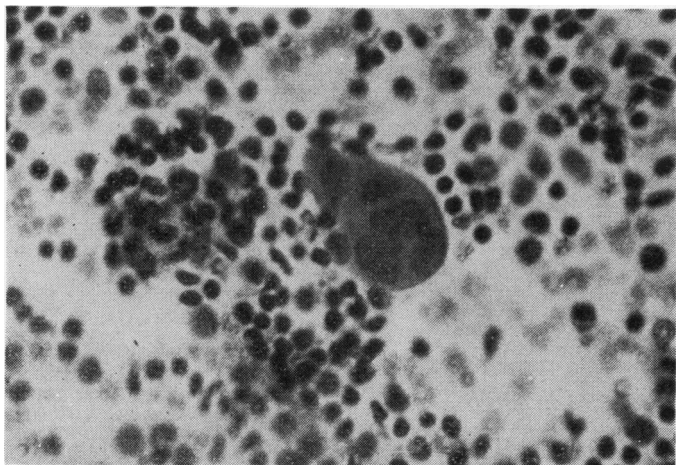


Fig 3 Case 3. Pleural fluid cytology showing a multinucleate giant cell surrounded by numerous lymphocytes and erythrocytes. Papanicolaou stain.

1978 with left-sided pleuritic chest pain, night sweats, and dyspnoea on mild exertion. He had lost 10 kg in the previous few months.

Clinical examination revealed signs of a small left pleural effusion, but was otherwise normal. A chest radiograph confirmed the effusion, and also showed hilar and paratracheal lymphadenopathy and pulmonary infiltration in the left mid zone and right base. Aspiration of the effusion yielded 200 ml of sterile serous fluid containing eosinophils and lymphocytes. Cytological examination of the fluid showed occasional giant cells (fig 3). Sputum was negative for tubercle bacilli on direct film and culture, and a Mantoux reaction (100 TU) was negative. Pulmonary function tests showed a restrictive ventilatory defect with reduced total lung volume and diffusing capacity. A paratracheal lymph node removed at mediastinoscopy showed typical features of sarcoidosis. Pleural punch biopsy was unsuccessful.

The effusion had not recurred by June 1978, but in view of persistent left pleuritic pain, breathlessness, and abnormal lung function prednisolone 20 mg daily was started. His symptoms resolved, the lung volumes improved, and the single breath carbon monoxide transfer factor rose from 7.3 to 10.55 mmol/min/kPa (predicted 12.8). He remains on prednisolone 5 mg daily and the effusion has not recurred.

Discussion

Pleural involvement with sarcoid granulomata is unusual, but has been recognised since 1933 when Schaumann⁸ described it as a necropsy finding in a 45-year-old white man. Although sporadic case reports have appeared since then and have been

the subject of several recent reviews,^{9 7 9 10} the incidence of the condition is not always apparent from the case reports. However, several authors have quoted their findings for the prevalence of pleural sarcoidosis, and these are summarised in table 1. It should be noted that this is a heterogeneous collection of data, and the criteria for diagnosis of pleural sarcoid are not always stated. Nonetheless, most authors find a prevalence of 0–5% for the condition although Wilen *et al*⁷ and Brun *et al*²² suggest it is much more common. Our own experience suggests a prevalence of around 5%, for the three cases described in this paper have been seen out of a series of approximately 60 new cases of thoracic sarcoidosis attending a chest clinic over two years.

The diagnosis of pleural sarcoidosis depends initially on histological demonstration of the disease in biopsies from conventional sites (liver or lymph node), or by a Kveim test. Thereafter, definitive evidence of pleural granulomata may

Table 1 Reported prevalence of pleural sarcoidosis

Author(s)	Number of patients	Cases of pleural sarcoidosis (%)
Chusid and Siltzbach ⁶	950	7 (< 1)
Ellis and Renthal ¹¹	127	1 (< 1)
Freundlich <i>et al</i> ¹²	300	4 (1.3)
Israel and Sones ¹³	160	3 (2)
Kirks <i>et al</i> ¹⁴	150	5 (3)
Longcope and Freiman ¹⁵	160	2 (1.3)
McCort <i>et al</i> ¹⁶	28	2 (4)
Maycock <i>et al</i> ¹⁷	140	0 (Nil)
Nitter ¹⁸	90	0 (Nil)
Rabinowitz <i>et al</i> ¹⁹	198	10 (5)
Scadding ¹	234	2 (< 1)
Sharma and Gordonson ²⁰	100	6 (6)
Siltzbach ²¹	311	3 (3)
Wilen <i>et al</i> ⁷	223	23 (11)
Brun <i>et al</i> ²²	Anecdotal evidence	(~ 10%)

Table 2 Pleural fluid characteristics in cases where details are stated (NS=not stated)

Author(s)	Naked eye appearance	Protein content	Cells
Tice and Sweany ²³	Serosanguinous	NS	NS
Brun <i>et al</i> ²²	Serofibrinous	"exudate"	80% lymphocytes
Berte and Pfothenauer ²⁴	Serosanguinous	51 g/l	67% lymphocytes 29% eosinophils
Plancherel ²⁵	Sanguinous	NS	NS
Silviera and Benevides ²⁶	Turbid	NS	NS
Lebacqz ²⁷ (three cases)	All serous	all "transudates"	NS
Kovnat and Donohue ²⁸	Straw-coloured	50 g/l	occasional erythrocytes
Macquet <i>et al</i> ²⁹	Serofibrinous	NS	93% lymphocytes
Press <i>et al</i> ³⁰	Serous	"transudate"	62% lymphocytes
Selroos ³¹ (four cases)	(i) Serous	40 g/l	98% lymphocytes
	(ii) Serous	"exudate"	NS
	(iii) Serous	"exudate"	NS
	(iv) Serous	20 g/l	88% lymphocytes
Aberg <i>et al</i> ³²	Chylous	NS	NS
Budillon <i>et al</i> ³³	Straw-coloured	"exudate"	NS
Everett and Overholt ³⁴ (two cases)	Both serous	NS	NS
Nelson and Loudon ³⁵	Serous	"exudate"	98% lymphocytes
Kirks <i>et al</i> ¹⁴ (five cases)	NS	all "exudates"	NS
Wilen <i>et al</i> ⁷ (eight cases)	All serous	all < 23 g/l	three cases—occasional lymphocytes five cases—no cells
Chusid and Siltzbach ⁶ (four cases)	(i) Yellow	"exudate"	100% lymphocytes
	(ii) Yellow, turbid	"exudate"	99% lymphocytes
	(iii) Sanguinous	"exudate"	NS
	(iv) Serosanguinous, turbid	"exudate"	100% lymphocytes
Beekman <i>et al</i> ⁵ (two cases)	(i) Sanguinous	49 g/l	66% lymphocytes
	(ii) Yellow	40 g/l	61% lymphocytes
Mikhail <i>et al</i> ⁵	NS	NS	many lymphocytes
Sharma ¹⁰ (eight cases)	(i) Cloudy yellow	65 g/l	90% lymphocytes
	(ii) Straw	38 g/l	"lymphocytes"
	(iii) Straw	40 g/l	no cells
	(iv) Serous	57 g/l	no cells
	(v) Turbid	46 g/l	"predominantly lymphocytes"
	(vi) Serosanguinous	56 g/l	NS
	(vii) Serous	36 g/l	a few mononuclear cells
	(viii) Yellow	48 g/l	no cells
Present study (three cases)	(i) Sanguinous	53 g/l	lymphocytes, eosinophils
	(ii) Serosanguinous	42 g/l	lymphocytes, eosinophils, histocytes
	(iii) Serous	46 g/l	90% lymphocytes giant cells
All cases	9/47 Sanguinous or serosanguinous	28/41 exudates	22/31 predominantly lymphocytic 8/31 no cells

sometimes be obtained by percutaneous biopsy, but this technique is not specially reliable. Our finding of non-diagnostic biopsies in all three cases agrees with the experience of Sharma¹⁰ who found positive pleural histology in only two of his eight cases. However, pleural fluid analysis can be of a greater value, as table 2 shows. The effusion is not infrequently bloodstained, usually an exudate, and (when cellular) contains predominantly lymphocytes. Thus, although there are no distinguishing features specific for sarcoidosis or different from tuberculosis, other possible causes for the effusion are effectively ruled out. While sarcoidosis and tuberculosis can coexist,¹ such an occurrence is rare, and no cases have been reported in which a pleural effusion in a patient with histologically proven sarcoidosis has been shown to be the result of tuberculosis. Thus once conventional bacteriological investigations have excluded tuberculosis, the diagnosis of pleural sarcoidosis can be made with confidence. It has been suggested that pleural sarcoidosis is rare in

the absence of widespread parenchymal lung disease,¹⁴ but this is not a constant enough feature to be of diagnostic value. It remains to be shown, however, if pleural disease can exist as the sole manifestation of sarcoidosis.

The management of a sarcoid pleural effusion depends on the symptoms and biopsy evidence of disease. In the absence of symptoms one can expect an effusion to resolve spontaneously²⁰ but if the effusion is symptomatic or recurrent, resolution will occur with steroid therapy. If a biopsy has given unequivocal evidence of pleural non-caseating granulomata, no other treatment is needed. But if a histology is non-specific, it may be wise to add antituberculous therapy until negative bacteriological results are obtained.

Sarcoidosis is undoubtedly a cause of pleural effusion in Britain as it is in the rest of the world, and awareness of the entity should increase its diagnosis. Indeed, sarcoidosis is the most likely cause of an effusion in patients with other evidence of the disease.

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