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A 'burnt-out' case of sarcoidosis

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SARCOIDOSIS has a strong tendency to spontaneous resolution, and there is good evidence that sarcoid granulomas can disappear leaving no evidence of their former presence. The granulomas may persist for several years without becoming fibrotic, apparently still capable of resolution; but if they fail to resolve, they generally undergo hyaline fibrosis. In this fibrosis, there may eventually be little or no recognizable remnant of the original epithelioid cell granuloma. Necropsy findings at this very late stage of the disease may be non-specific or inconclusive, even though correlation with the observed clinical course may leave no reasonable doubt of the diagnosis. This paper reports a case which illustrates this point.

Case report

In October 1933, a nurse, aged 25 years, was admitted to the Brompton Hospital for investigation. After a cold which had led to cough and loss of weight, a chest radiograph had shown widespread irregular shadows, especially in the middle zones, and these persisted (Fig. 1). By

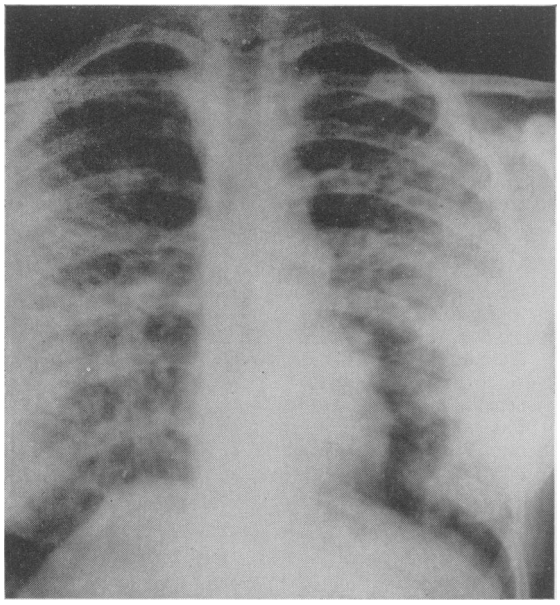

FIG. 1. Radiograph of chest, 1933, showing widespread linear and coarsely mottled opacities, densest in the middle zones of the lungs.

the time of admission, she denied all symptoms except slight dyspnoea on exertion. A Mantoux test with 1:100 Old Tuberculin was negative, no tubercle bacilli were found in the sputum, and the erythrocyte sedimentation rate was normal. No firm diagnosis was reached, and as she was free from evidence of progressive disease, she returned to work. During the second world war, she served overseas in the nursing service of one of the Armed Forces. In 1943 after a respiratory infection leading to a transient mild bronchitis, the chest was X-rayed for the first time since 1933, and reported to show 'pulmonary fibrosis, of no significance'. After the war, she continued her nursing career abroad. In 1957, after an attack of purulent bronchitis she noticed breathlessness on exertion which became more severe after an operation for varicose veins in 1959. Nevertheless, she managed to continue at work, and it was not until early in 1963 that increasing dyspnoea led to further investigation of her case, including a lung biopsy. A diagnosis of 'interstitial fibrosis of the lungs' was made; treatment with betamethasone was followed by oedema of the ankles and sacral region without relief of dyspnoea, and in consequence was withdrawn. She was invalided to England, and admitted to the Brompton Hospital in August 1963. On admission, she was cyanosed, with raised venous pressure and oedema of the feet, and dyspnoeic on slight exertion. There was only a trace of mucoid sputum. The fingers were not clubbed; there were a few crepitations at the bases of the lungs, a parasternal right ventricular impulse, an apical systolic murmur and loud pulmonary component of the second heart sound, and ECG evidence of right ventricular hypertrophy. Radiographically, the heart shadow was enlarged, with a prominent pulmonary conus and irregular linear and mottled opacities in the lung fields suggestive of widespread patchy fibrosis (Fig. 2). The blood showed a haemoglobin concentration of 17·0 g/100 ml, and normal leucocyte count, sedimentation rate and electrolyte levels. The skin showed no reaction to a Mantoux test with 1:1000, but an 8-mm reaction to 1:100 O.T. The vital capacity was 1500 ml, of which 900 ml could be expired in the first second, and these values were unchanged after isoprenaline. Arterial blood showed an oxygen saturation of 81%, pressure 47 mm, and carbon dioxide pressure 35 mmHg. The very long his-

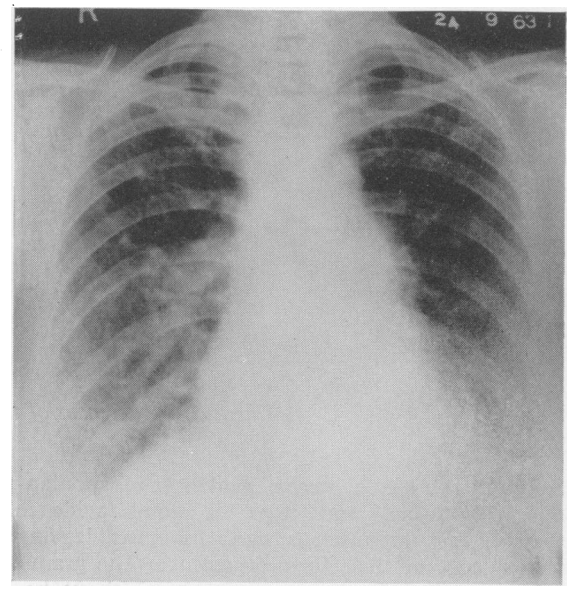

FIG. 2. Radiograph of chest, 1963, showing widespread linear and finely mottled opacities in the lungs and enlargement of the heart shadow with prominence of the pulmonary conus.

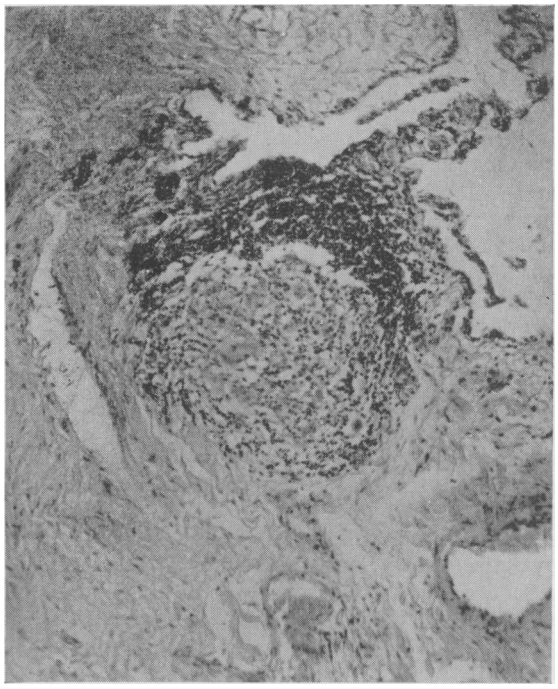

FIG. 3. Lung biopsy, April 1963. Remnant of epithelioid-cell granuloma near a bronchiole in otherwise featureless fibrosis. H & E, × 110.

tory and the absence of finger-clubbing with such a long duration of known radiographic abnormality cast doubt upon the diagnosis of 'idiopathic' interstitial fibrosis, and accordingly the lung biopsy sections were reviewed. These showed severe fibrosis, much of it peribronchiolar, but some in irregular foci among the alveoli; in relation to the bronchioles, occasional remnants of epithelioid-cell follicles and a few giant cells could be found (Fig. 3); and the muscular arteries showed both medial and intimal thickening.

It was evident that the established fibrosis was not susceptible to any treatment. Intensive measures to control the congestive heart failure and anoxia led to only temporary improvement. Because her only relatives lived near that hospital, she was transferred to Broadgreen Hospital, Liverpool, under the care of Dr Colin Ogilvie, and died there in November 1963, 30 years after the first detection of an abnormality in the chest radiograph. Necropsy was performed by Dr John Campbell, to whom I am indebted for sending me a detailed report of the findings and histological sections of the organs. Death had evidently been due to congestive heart failure, secondary to pulmonary hypertension: the heart was enlarged from hypertrophy of the right ventricle, whose wall was 10 mm thick, the pulmonary arteries were atheromatous as far as the peripheral branches visible on the cut surface, and there were thrombi, some recent, in both arteries and some veins. The lungs showed irregular fibrosis, especially in the lower lobes, with some fine emphysema, and paratracheal, hilar and subcarinal lymph-nodes were enlarged. Microscopically, the lungs showed changes similar to those found in the biopsy, except that the remnants of epithelioid-cell follicles were extremely scanty; one of those found contained a Schaumann conchoidal inclusion body (Fig. 4). Apart from the changes associated with congestive heart failure, the only other microscopic abnormalities were the presence of Schaumann bodies, usually in small groups, in the spleen (Fig. 5) and in small numbers in hilar lymph-nodes.

Comment

In this case, the early part of the clinical history is more compatible with the hypothesis that the mottling in the chest radiograph observed first in 1933 was due to sarcoidosis, than to any of the other possibilities. The slightness

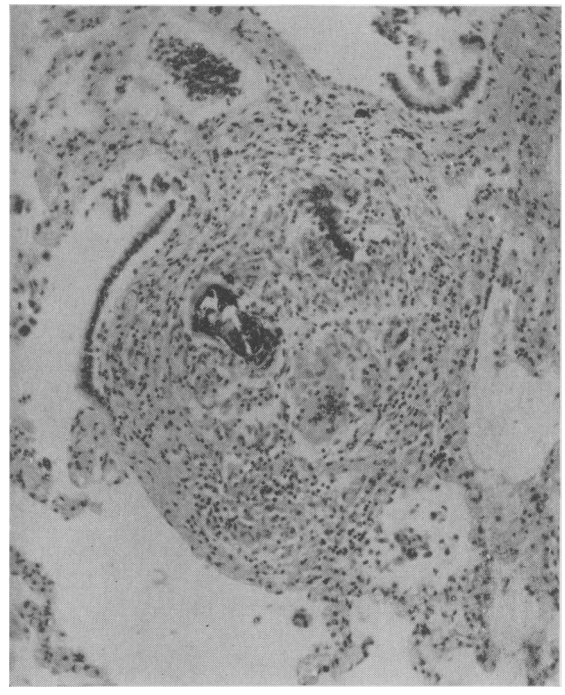

FIG. 4. Lung at necropsy, November 1963. Giant cells and a Schaumann body. H & E, × 110.

of the symptoms at that time and for many years afterwards, the negative tuberculin test, and the absence of clubbing at any time make any form of 'idiopathic' fibrosing alveolitis (diffuse interstitial fibrosis of the lungs) very unlikely (Grant, Hillis & Davidson, 1956; Rubin & Lubliner, 1957; Scadding, 1960, 1964; Livingstone *et al.* 1964; Scadding & Hinson, 1967). The only other possibility besides sarcoidosis that remains to be considered is histiocytosis X or eosinophilic granuloma, which may give rise to a very indolent infiltration of the lungs, with only slight symptoms initially, but eventually developing into extensive honeycombing and severe effects on function (Parkinson, 1949; Lewis, 1964); and at this late honeycombed stage, as in occasional cases of sarcoidosis, all trace of the specific granuloma may have disappeared. In the present case, the persistence of a few remnants of epithelioid-cell granulomas in the lung biopsy, and of Schaumann inclusion bodies in the lungs, spleen and lymph-nodes at necropsy makes it highly probable that the defining characteristics of sarcoidosis, non-caseating epithelioid-cell tubercles in several organs or tissues (Scadding, 1967), had been present during the earlier stages of the disease. Diminution in the number of remnants of epithelioid-cell tubercles in the lungs at necropsy as compared with the biopsy specimen was probably due in part to the effect of the cortiocosteroid treatment which was given immediately after the biopsy, and in part to the natural progression of the hyalinization.

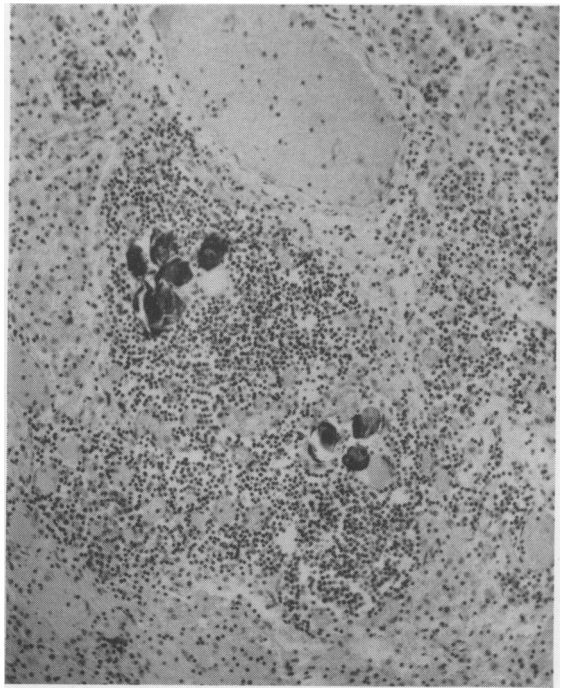

FIG. 5. The spleen at necropsy. Groups of Schaumann bodies. H & E, × 110.

The disappearance of specific granulomas in the late fibrotic stage of sarcoidosis has been well documented. Ustvedt (1948) described the case of a woman who died 11 years after a typical uveoparotid syndrome with bilateral hilar adenopathy, and at necropsy showed only hyaline fibrosis in lungs and lymph-nodes. Smellie & Hoyle (1960) observed three patients with long-standing sarcoidosis, in whose lungs only dense hyalinized fibrosis was found. In addition to the case here described, I have seen two others, in which after the disease had been known to be present for 15 years and 6½ years, only scanty remnants of epithelioid tubercles and a few persisting Schaumann bodies were left as evidence of the original sarcoid infiltration at the time of necropsy (Scadding, 1967).

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