Clinical Section

President Norman Tanner FRCS

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Cases

Idiopathic Pulmonary Hæmosiderosis with Unusual Features

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First reported by Ceelen (1931) in two children with severe anæmia, idiopathic pulmonary hæmosiderosis is being recognized with increased frequency both in children and adults. Boyd (1959) reviewed 29 cases in patients over 16 years of age, including 3 of his own, and Bronson (1960) reviewed the radiological appearances in 34 adults, the majority in the second and third decade. The main presenting symptoms are recurrent hæmoptysis and anæmia; most cases run a rapid course but remissions of several years' duration have been recorded. The condition is separate from cardiac hæmosiderosis (Lendrum *et al.* 1950) and is believed to have no connexion with hæmochromatosis. The pathogenesis is not well understood – the deposition of hæmosiderin in the lungs is thought to be due to intra-alveolar bleeding or diapedesis of red cells; hypersensitivity with the lung as a shock organ was postulated by Steiner (1954).

History: A man aged 32 was admitted to hospital (5.4.61) with an acute respiratory infection. For four months he had had general malaise and joint pains in the hands, feet and shoulders. His parents and two paternal aunts have rheumatoid arthritis.

On examination: There was slight swelling of finger joints but no abnormal signs in the chest.

Investigations: Chest radiographs showed fine granular mottling of both lung fields, especially the lower two-thirds (Fig 1). Hb 100%. E.S.R. 55 mm in the first hour (Westergren). Serum iron 80 μg/100 ml. Sternal marrow normal. Rose-Waaler test: positive (D.A.T. 1 : 512). Radiographs of joints showed bilateral marginal erosions in the first metatarsophalangeal joints but were otherwise normal. Electrophoresis: slight fall in albumin with raised α_2- and γ-globulins. Mantoux 1 : 1,000 positive. Bronchogram: no significant abnormality. Respiratory function tests (Dr R Marshall): large functional residual capacity and reduced diffusing capacity (14 ml/min/mm Hg – normal 22–32). No abnormality found in urine, serum calcium, liver function, search for L.E. cells, electrocardiograms, gastric lavage or cervical gland biopsy.

Bronchoscopy: normal appearances. Bronchial biopsy from the right middle lobe carina contained a fragment of lung which showed hæmosiderosis. This finding was confirmed by open lung biopsy (lingula) and at thoracotomy (Mr C Grimshaw) comment was made on the brown and granular appearance of the lung.

Histology (Dr E H Hemsted): Sections taken from the bronchial biopsy and lung biopsy show areas of lung in which the alveolar spaces are filled with cells, approximately the size of a macrophage and

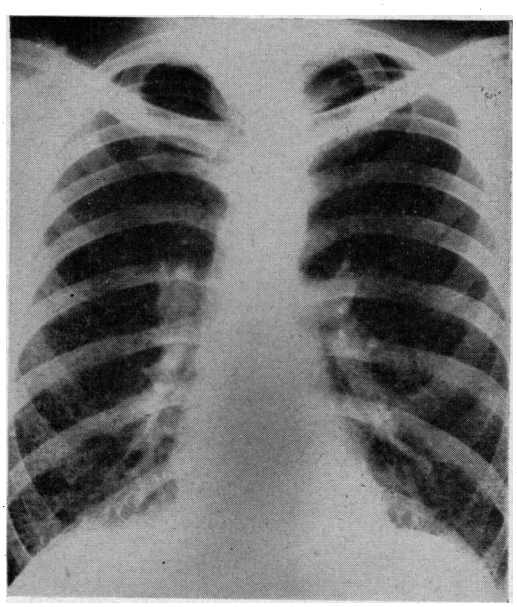

Fig 1 *Chest radiograph showing fine granular mottling in mid and lower zones of both lung fields*

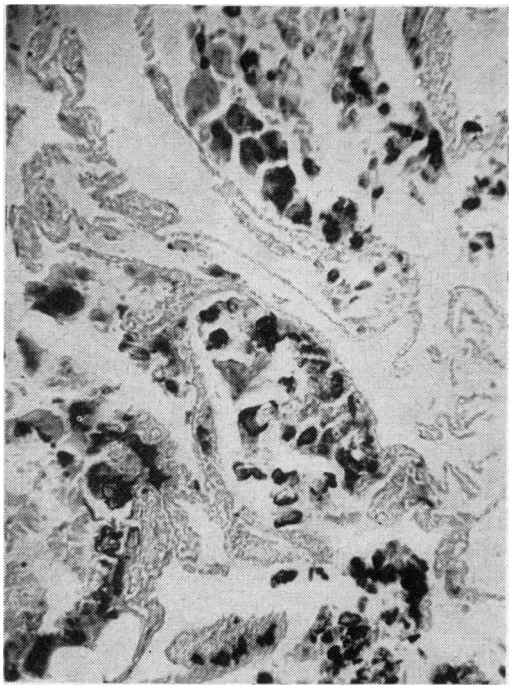

Fig 2 *Section from bronchial biopsy stained with prussian blue showing alveoli containing numerous cells impregnated with hæmosiderin pigment.* ×82

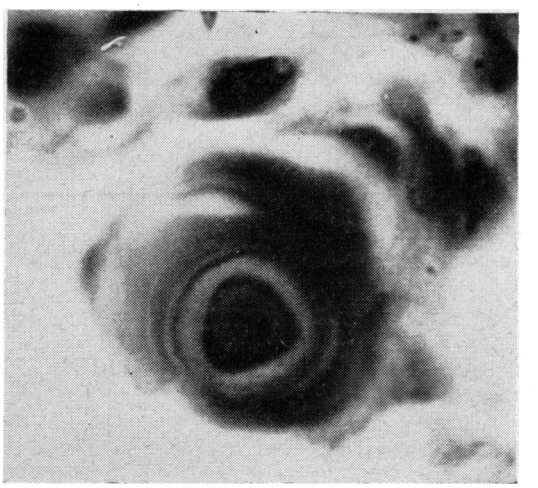

Fig 3 *From bronchial biopsy stained with hæmatoxylin and eosin showing a single corpus amylaceum with both blue and brown laminated rings. Actual diameter 40 μ.* ×1,050

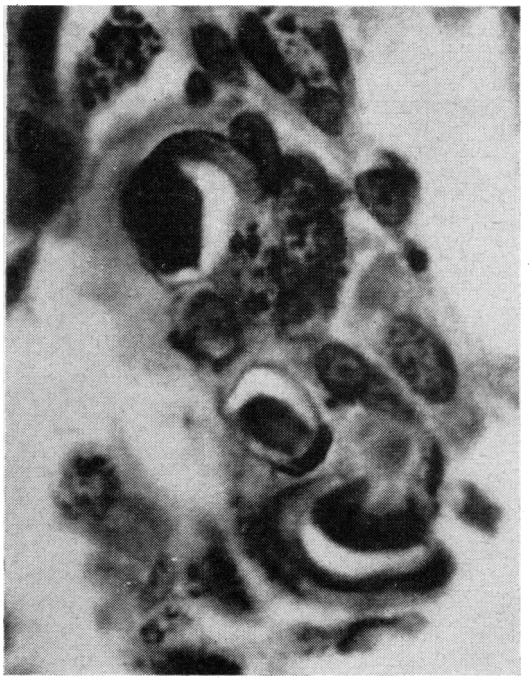

Fig 4 *From lung biopsy stained H & E showing apparent transformation of cells into corpora amylacea.* ×1,050

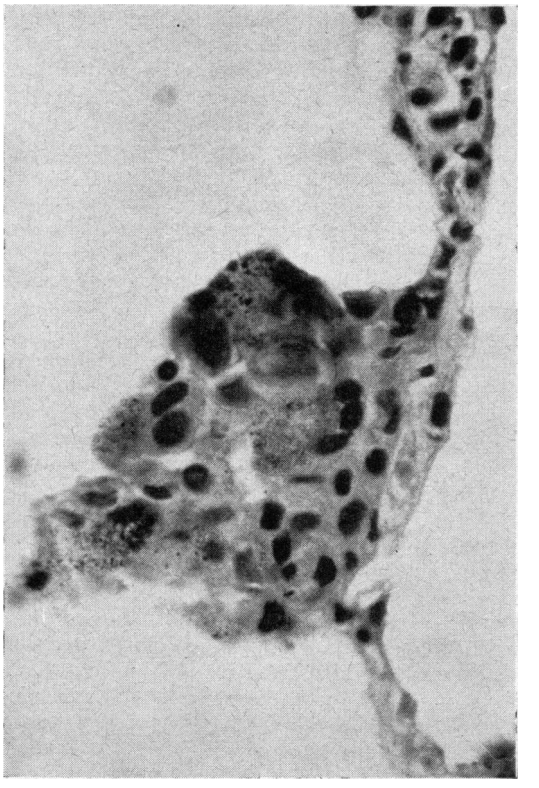

Fig 5 *Section from bronchial biopsy stained with hæmatoxylin and eosin showing involvement of one small portion of alveolar wall.* ×395

often with their nuclei crowded together to form giant cells. Many are heavily impregnated with hæmosiderin pigment (Fig 2) and calcium salts to form laminated bodies 10–40 μ in diameter. Stained with hæmatoxylin and eosin these laminations appear as blue or brownish rings (Fig 3), the latter being the natural colour of hæmosiderin pigment; they also stain pale pink with purpurin and brown with Von Kossa. These cells appear to be derived from the septal cells (Fig 4); they proliferate and gradually fill up the alveolar space, either as individual cells or as sheets of cells. Their cytoplasm is often ill-defined and impregnated with dust-like particles of hæmosiderin pigment. In some areas the proliferation of these cells appears to be confined to one part of the wall of an alveolus (Fig 5), the involved area showing local thickening though little evidence of an increase in collagen fibre. In areas more extensively involved there is often a surrounding zone of inflammatory cells composed of plasma cells and lymphocytes. The bronchial epithelium would appear to play no part in the disease process.

The blood vessels appear normal; elastic fibres are not increased and are not impregnated with hæmosiderin or calcium salts. Reticulin fibre is increased wherever the alveolar walls are thickened and the capillary outline cannot always be seen in such areas. Many alveoli adjacent to these affected areas show no apparent abnormality; the air spaces are free from stainable material and cells.

A difference is noted in comparing the lung biopsy with the bronchial biopsy. More hæmosiderin pigment is present in the lung biopsy than in the bronchial biopsy, and it is more granular in appearance; cells impregnated with calcium salts are more clearly seen in the bronchial biopsy, though present in both.

Comment on Pathology

The laminated bodies found in both lung specimens appear to be corpora amylacea, first described in the lung by Friedreich (1856) but more often found in the prostate and in the brain. Both their origin and chemical content are matters of controversy but polysaccharides are an important component (Steele *et al.* 1952). They may be extensively calcified, in which case they resemble the microliths of alveolar microlithiasis (Finkbiner *et al.* 1957). It is a matter of interest that one of Friedreich's three patients, a woman aged 43, considered to be tuberculous because of hæmoptysis, was found at autopsy to have tight mitral stenosis and 'exquisite' brown induration of the lungs, or, in modern language, cardiac hæmosiderosis. Friedreich, a lecturer at the University of Würzburg, was of course aware of the latter condition described by his colleague Virchow in 1851; he thought that corpora amylacea were caused by small-scale hæmorrhages due to stagnation of blood in the lesser circulation. Lubarsch & Plenge (1931) found pulmonary corpora amylacea in 15 autopsy cases, 5 of which had brown induration of the lungs. Ceelen (1931), in Bonn, also states that these bodies are frequently found in brown induration. It would seem, therefore, that corpora amylacea are frequently present in cardiac hæmosiderosis, but ours is the first case in which they were described in idiopathic pulmonary hæmosiderosis.

Diffuse interstitial fibrosis in pulmonary hæmosiderosis was noted by Wyllie *et al.* (1948), who reviewed 23 cases in children, but this finding was not confirmed by most other authors. Our own sections show many thickened interalveolar walls but little fibrosis. It may be relevant, therefore, that our patient's diffusing capacity is seriously reduced, a feature typically found in the Hamman-Rich syndrome and other conditions with interstitial pulmonary fibrosis.

Clinical Comment

The patient is symptomless apart from joint pains; he has never had hæmoptysis or known anæmia, though his serum iron (80 μg/100 ml) is rather low. The diagnosis was largely incidental and was made on radiological appearances and lung biopsy. It may be that the condition is more frequent than at present thought and that marked radiological abnormalities sometimes precede the development of overt disease.

It seems probable that he has early rheumatoid arthritis (D.A.T. 1 : 512, family history). This may have no connexion with pulmonary hæmosiderosis but those who believe in the auto-immune mechanism of both diseases may find the association significant.

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