Association of idiopathic pulmonary haemosiderosis with IgA monoclonal gammopathy

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The typical features of pulmonary haemosiderosis include haemoptysis, reticulonodular shadows on chest radiographs, and in some cases iron deficiency anaemia.¹ The pathogenesis of idiopathic pulmonary haemosiderosis is obscure. Certain observations suggest that immune mechanisms may play a part; but there is at present no convincing evidence for an immune aetiology.² In this report we describe the association of idiopathic pulmonary haemosiderosis with the presence of an IgA monoclonal gammopathy.

Case report

A 43 year old woman who had developed papules and vesicles surrounded by erythema on the elbows and knees at the age of 20 years, and was diagnosed as having dermatitis herpetiformis on the basis of the histological appearances of skin biopsy specimens,³ had subsequently been treated with 4,4'-diaminodiphenyl sulfone (DDS). In March 1984 she was admitted because of massive haemoptysis and dyspnoea. Physical examination showed pallor, and papules and vesicles on the face and trunk. Crackles were heard in both lower lung fields, but cardiological examination showed no abnormality. There was no hepatosplenomegaly or lymphadenopathy. Laboratory data included: haemoglobin concentration 5.6 g/dl, platelet count $191 \times 10^9/l$, and white blood cell count $3.8 \times 10^9/l$ with a normal differential count. Serum immunoglobulin concentrations were: IgG 6.14 g/l (normal 7.5-18 g/l), IgA 11.77 g/l (normal 0.65-4.2 g/l), and IgM 0.14 g/l (normal 0.5-4.2 g/l). Serum immunoelectrophoresis showed the presence of monoclonal IgA λ . No Bence Jones protein was detected in the urine. Microscopic examination of bone marrow aspirate showed normal cellularity with 4.6% plasma cells, including flaming cells. The results of bleeding screening tests and uric acid and creatinine concentrations were normal. Proteinuria and haematuria were not found. The result of a test for circulating antiglomerular basement membrane antibodies was negative and levels of circulating immune complex were not increased. A tuberculin test gave a negative result. Arterial blood gas values were: oxygen tension 24.7 mm Hg (3.3 kPa), carbon dioxide tension 33.5 mm Hg (4.5 kPa), and pH

7.38 while the patient was breathing room air. A chest radiograph showed fine diffuse reticulonodular infiltrates throughout both lungs. Examination of the sputum showed no haemosiderin laden macrophages, tubercle bacilli, malignant cells. Upper and lower gastrointestinal barium studies gave normal results.

SPECIAL STUDIES

The histological examination of transbronchial lung biopsy specimens showed erythrocytes and macrophages containing haemosiderin within the alveolar spaces (fig 1). Prussian blue stains were intensely positive for iron. Direct immunofluorescence studies showed granular localisation of IgA and λ light chain along the alveolar basement membrane. Indirect immunofluorescence studies were performed as follows. The patient's serum (1:10 dilution) was allowed to react with normal lung sections and a second layer of reagent (FITC labelled anti-human IgA) was used to identify the localisation of IgA. This showed granular deposits of IgA along the alveolar basement membrane (fig 2). No deposits of non-IgA immunoglobulins or fibrinogen were observed. In the dermis round cell infiltration and fibrosis without microabscess and eosinophilic infiltrations were found. Deposits of IgA were not observed along the basement membrane of the skin by direct immunofluorescence studies.

Fig 1 Erythrocytes and macrophages containing haemosiderin in the alveolar space. (Haematoxylin and eosin.)

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Fig 2 Granular deposits of IgA along the alveolar basement membrane shown by immunofluorescence microscopy (indirect method).

Discussion

Twenty three years after the diagnosis of dermatitis herpetiformis the patient was diagnosed as having pulmonary haemosiderosis. In view of the absence of haematuria and circulating antiglomerular basement membrane antibodies, Goodpasture's syndrome could be eliminated.¹ This case of pulmonary haemosiderosis is considered to be idiopathic, as DDS is not reported to induce pulmonary haemosiderosis.

There have been no previous reports of deposition of immunoglobulins in lung tissue obtained from patients with pulmonary haemosiderosis.^{4,5} It is noteworthy that in this case the immunofluorescence studies showed antialveolar basement membrane antibodies, composed of monoclonal IgA, by the direct method and circulating IgA antialveolar basement membrane antibodies by the indirect method. The patient was also found to have an IgA monoclonal gammopathy. It seems likely therefore that IgA played an important part in the pathogenesis of idiopathic pulmonary haemosiderosis in our patient. The coincidence of idiopathic

pulmonary haemosiderosis and dermatitis herpetiformis is rare, but has been reported.^{6,7}

Although the patient's skin lesions had no IgA deposits characteristic of dermatitis herpetiformis,⁸ long term administration of DDS might conceivably have modified the clinicopathological picture, although there are no reports of this. Thus the abnormalities of IgA regulation and deposition could provide a link between the three disorders—idiopathic pulmonary haemosiderosis, IgA monoclonal gammopathy, and dermatitis herpetiformis—found in our patient.

Similar circumstances may be found in coeliac disease, where there may be abnormalities of IgA regulation and an association with dermatitis herpetiformis and idiopathic pulmonary haemosiderosis.⁵ Serum concentrations of IgG and IgM were reduced in our patient. Although this might suggest a malignant paraproteinaemia, subsequent follow up has produced no evidence of this.

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