Anti-basement membrane antibody disease with severe pulmonary haemorrhage and normal renal function

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Abstract
A case of anti-basement membrane disease with severe pulmonary haemorrhage and normal renal function is reported.

The histological appearance of the lesion previously described as miliary pulmonary carcinoid tumour with amyloid is identical to that of metastatic medullary carcinoma of the thyroid. This tumour may present with symptoms of the carcinoid syndrome and pulmonary metastases are recognised in disseminated disease. Medullary carcinoma of the thyroid contains calcitonin but so may bronchial carcinoid, and both lesions may contain amyloid.

Medullary carcinoma accounts for about 10% of thyroid tumours and the course of disease is variable. About a quarter of cases are familial. Inherited as an autosomal dominant condition, it may form part of the multiple endocrine neoplasia syndrome type 2. A marfanoid habitus, myopathy, and colonic diverticulosis have been associated with the type 2b variant of this syndrome.

Even in cases that are apparently sporadic (probably because gene expression is variable) 10–15% of cases have the familial multiple endocrine neoplasia syndrome. Bilateral tumour and C cell hyperplasia in the thyroid gland may indicate familial disease and screening of relatives by means of stimulated calcitonin measurement may allow early detection and curative surgery. The relatives of our patient are currently undergoing screening. We believe that the patient reported by Skinner and Ewen may have had medullary carcinoma of the thyroid. Multi-focal bronchial carcinoid should not be accepted as a primary lung lesion without first excluding metastatic medullary carcinoma of the thyroid.

In 1919 Goodpasture described a syndrome of glomerulonephritis and pulmonary haemorrhage. Half a century later both manifestations were shown to be induced by circulating autoantibodies that reacted with alveolar and glomerular basement membranes. We present a case with severe pulmonary haemorrhage mediated by anti-basement membrane antibody in which renal function was normal.

Case report
A previously healthy 20 year old cigarette smoking farmer was referred complaining of dyspnoea and progressive haemoptysis of four days’ duration after accidental exposure to fumes of fungicides containing metalaxyl (8%) and mancozeb (64%). He was pale, weak, sweating, and febrile (38·5°C). His pulse rate was 104/min, blood pressure 110/50 mm Hg, and respiratory rate 26/min. A chest radiograph showed diffuse fluffy infiltrates predominantly in the lower lobes. The erythrocyte sedimentation rate was 80 mm in one
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hour, and he had normochromic, normocytic anaemia (haemoglobin 7·1 g/dl), a white blood cell count of 9·2 \times 10^9/l, and a normal platelet count. Clotting studies gave normal results. The urine sediment, results of urine electrophoresis, and creatinine clearance (113 ml/min/1·73 m²; normal 78–142) were all normal. A stained sputum smear showed no bacteria but contained abundant erythrocytes and haemosiderin laden macrophages. The arterial oxygen tension (Pao₂) while he was breathing air was 3·7 (normal 10·1–11·8) kPa, oxygen saturation 53%, carbon dioxide tension (Paco₂) 4·3 (normal 4·8–6·1) kPa, pH 7·47. Antibodies to cell nuclei, DNA, and neutrophil cytoplasm were not detectable. No antibodies to common viruses, Q fever agent, mycoplasmas, Chlamydia, or human immunodeficiency virus were detected. The indirect immunofluorescence test for antibodies to lung basement membrane showed a raised titre of 1:128. A titre 1:20 of anti-glomerular basement membrane antibody was measured by the enzyme linked immunosorbent assay and confirmed by immunoblotting (fig 1). HLA tissue typing showed the patient to be HLA-DR2.

Initial treatment included oxygen and daily intravenous methylprednisolone (1 g) for three days followed by oral prednisone 50 mg daily. On days 2, 3, and 4 plasmapheresis was performed. The patient recovered rapidly. On day 6 a chest radiograph showed minimal patchy opacities and the Pao₂ was 8·2 kPa in air. At that time a transbronchial lung biopsy and a renal biopsy were performed. The lung biopsy specimen showed extravasation of red blood cells and haemosiderin laden macrophages. The renal biopsy specimen issue was normal. Examination of the lung and kidney specimens by direct immunofluorescence showed linear deposits of IgG along basement membranes. The bars represent 50 µm.

Discussion

Goodpasture’s syndrome consists of pulmonary haemorrhage and glomerulonephritis. The discovery of antibodies deposited on alveolar and glomerular basement membranes allowed a more precise characterisation of this disorder. Our patient showed the rare combination of severe pulmonary haemorrhage mediated by anti-basement membrane antibodies and normal renal function. Renal failure did not occur in the year of follow up. Most patients with anti-basement membrane antibody disease develop glomerulonephritis that progresses rapidly to end stage renal failure. Up to 80% of these patients also have affected lungs. Cases in which the lung disease predominates are rare, with only a few reports of isolated anti-basement membrane antibody induced pulmonary haemorrhage and normal
Antimyeloperoxidase antibodies in the Churg-Strauss syndrome

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Abstract
Antibodies to myeloperoxidase were detected in the serum of three patients with the Churg-Strauss syndrome.

The Churg-Strauss syndrome, a rare multisystem disorder thought to be related to the systemic necrotising vasculitides, is characterised by hypereosinophilia, systemic vasculitis, asthma, and allergic rhinitis. Extravascular granulomas are frequently found but are absent in many cases. Antineutrophil cytoplasmic autoantibodies (ANCA or ACPA) have been described recently in patients with Wegener’s granulomatosis and microscopic polyarteritis. These antibodies are directed against a 29 kD glycoprotein with serine protease activity derived from the azurophil granules of the neutrophil, probably proteinase-3. A characteristic granular pattern of staining of the cytoplasm of ethanol fixed granulocytes occurs (c-ANCA). Other staining patterns, however, have also been recognised—in particular, a perinuclear pattern. It has been shown that a substantial number of serum samples producing a perinuclear pattern have antibodies to human leucocyte elastase and/or myeloperoxidase, both lysosomal enzymes.

Case reports

PATIENT 1
A 24 year old man presented in 1984 with asthma, rhinitis, and loss of weight. Treatment was started with corticosteroids. While the dose was being reduced severe dyspnoea developed followed by arthralgia, myalgia, episcleritis, fever, and mononeuritis multi-

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