

renal function at the time of diagnosis.<sup>4</sup> Severe renal failure may develop in some patients, but others improve and no renal dysfunction occurs during follow up.

The reason why some patients are more susceptible to lung than to renal disease is not clear. Inhaled agents may play a part, among them insecticides and herbicides.<sup>5</sup> The fungicides inhaled by our patient have not been reported to induce anti-basement membrane antibody disease, but cigarette smoking is associated with pulmonary manifestations of the disease.<sup>6</sup> In animals inhalation of petrol induces lesions in the alveolar basement membrane, allowing circulating anti-basement membrane antibodies to gain access.<sup>7</sup> Thus increased capillary permeability may be essential for damage to occur. Our patient was a cigarette smoker and was exposed to fumes of fungicides, both of which might have been contributory factors. The unusual susceptibility of a few individuals to widely used exogenous agents suggests a genetically determined background for the development of anti-basement membrane antibody disease. This is supported by the association of the HLA antigen DR2, which our patient possessed, with the disease.<sup>3,8</sup>

Treatment regimens consist of immunosuppression with or without plasmapheresis. The outcome in patients treated with plasmapheresis is slightly better; but the initial degree of the renal disease is more important for the prognosis than the type of treatment received.<sup>9</sup> Combined cytotoxic drugs and plasmapheresis also shorten the time needed for clearance of antibodies and improve the

outcome in patients with lung haemorrhage and in those not dependent on dialysis.<sup>10</sup>

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## 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 multi-system disorder thought to be related to the systemic necrotising vasculitides,<sup>1</sup> is characterised by hypereosinophilia, systemic vasculitis, asthma, and allergic rhinitis.<sup>1,2</sup> Extravascular granulomas are frequently found but are absent in many cases.<sup>2</sup>

Antineutrophil cytoplasmic autoantibodies

(ANCA or ACPA) have been described recently in patients with Wegener's granulomatosis and microscopic polyarteritis.<sup>3,4</sup> These antibodies are directed against a 29 kD glycoprotein with serine protease activity derived from the azurophilic granules of the neutrophil,<sup>5-8</sup> probably proteinase-3.<sup>8-10</sup> 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.<sup>11-13</sup> In this report we describe the occurrence of myeloperoxidase ANCA in three consecutive patients with the Churg-Strauss syndrome.

### 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-

plex. Peripheral blood eosinophilia ( $2.0 \times 10^9/l$ ) and increased serum IgE (1695 IU/ml) were found. Visceral angiography disclosed no abnormalities but a muscle biopsy showed necrotising arteritis with many giant cells. Treatment with high dose corticosteroids was started and cyclophosphamide was added after four weeks because of progression of the disease. Remission was obtained.

#### PATIENT 2

A 58 year old man presented in 1986 with asthma. In 1988 he was admitted to hospital because of dyspnoea, rhinitis, sinusitis, and episcleritis. He was treated with corticosteroids and while the dose was being reduced he developed myalgia, weight loss, fever, pulmonary infiltrates, pericarditis, and mono-neuritis multiplex. Peripheral blood eosinophilia ( $12.7 \times 10^9/l$ ) and increased serum IgE (822 IU/ml) were detected. Muscle biopsy showed necrotising arteritis with many eosinophils. He was treated with high dose corticosteroids and plasmapheresis and went into remission.

#### PATIENT 3

A 39 year old man presented in 1988 with asthma and rhinitis. Subsequently he developed weight loss, fever, and mono-neuritis multiplex. He had peripheral blood eosinophilia ( $9.1 \times 10^9/l$ ) and increased serum IgE (1620 IU/ml). A muscle biopsy specimen was normal. In 1989 treatment with high dose corticosteroids was started. One month later paralytic ileus developed and bowel perforation was found at laparotomy. Histological examination disclosed necrotising arteritis with many eosinophils and extravascular granulomas. Remission was obtained after the start of cyclophosphamide treatment.

#### Methods

Anticytoplasmic antibodies were detected by indirect immunofluorescence.<sup>3</sup> Antibodies to myeloperoxidase were detected by an enzyme linked immunosorbent assay (ELISA), in which a mouse monoclonal antibody to myeloperoxidase was the capture antibody and an extract of azurophilic granules from normal human granulocytes the antigen.<sup>13</sup> Autoantibodies to the 29 kD ANCA antigen or to elastase were detected by an assay identical to the ELISA method used for antimyeloperoxidase antibodies except that monoclonal antibodies either to the 29 kD ANCA antigen or to elastase were used.<sup>13</sup>

#### Results

Serum from all three patients, obtained at the time of diagnosis, produced a perinuclear staining pattern with indirect immunofluorescence. In all three cases antimyeloperoxidase antibodies were found in the serum;

antibodies to elastase or to the 29 kD ANCA antigen were not detected.

#### Discussion

Recently c-ANCA were found in one patient with the Churg-Strauss syndrome.<sup>14</sup> All our three patients had antimyeloperoxidase antibodies. These have been reported in patients with crescentic glomerulonephritis, either idiopathic or associated with vasculitis,<sup>12 13 15</sup> and in limited Wegener's granulomatosis,<sup>16</sup> but not in other forms of glomerulonephritis, systemic lupus erythematosus, tuberculosis, or sarcoidosis,<sup>12 13</sup> though one patient with this last disorder was weakly positive for antimyeloperoxidase antibodies. The finding of either antimyeloperoxidase antibodies or c-ANCA in patients with the Churg-Strauss syndrome places this disorder within the group of vasculitides, in which microscopic polyarteritis and Wegener's granulomatosis also occur.

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