Wegener’s granulomatosis simulated by a T cell lymphoma of the lung

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Abstract
A case of primary T cell lymphoma of the lung associated with antineutrophil cytoplasmic antibody simulated Wegener’s granulomatosis, the patient having features compatible with but not diagnostic of Wegener’s granulomatosis.

Case report
A 44 year old man presented in April 1989 with a two month history of cough, wheeze, and shortness of breath. Proliferative glomerulonephritis had been diagnosed by renal biopsy 18 years previously through investigation of asymptomatic proteinuria. Renal function had remained normal and he has received no treatment.

A chest radiograph at presentation showed a left hilar mass (fig 1). A full blood count and the results of renal and liver function tests were normal; the urine contained a trace of protein, and microscopic examination of the urine showed nothing abnormal. At bronchoscopy a yellow tumour was seen to be obstructing the left main bronchus. Biopsy showed bronchial mucosa with a heavy lymphoid and mononuclear cell infiltrate centred around blood vessels with areas of necrosis. Granulomas were not seen (fig 2). The appearances were considered to be compatible with Wegener’s granulomatosis, though not diagnostic. Computed tomography of the chest showed the mass but no mediastinal abnormalites. Examination of the ear nose and throat showed nothing abnormal. Antineutrophil cytoplasmic antibody was detected in the serum at a titre of 1/80 and a coarse, granular cytoplasmic pattern was seen by indirect immunofluorescence. The test is performed on cytocentrifuge preparations of healthy donor peripheral blood neutrophils. Serum samples are screened at 1:10 dilution on ethanol fixed slides by indirect immunofluorescence with an Fc piece specific anti-human IgG antibody (Atlantic Antibodies Cat No 012-04 from Incstar Ltd). When results are positive serial dilutions are made and the staining pattern reported. Serum showing perinuclear staining is also tested on formalin fixed slides. Slides are viewed on a Leitz Dialux 20 EB fluorescence microscope.

A diagnosis of limited Wegener’s granulomatosis was made on the basis of the lung mass, compatible histological appearances, and the presence of antineutrophil cytoplasmic antibody. The patient was started on cyclophosphamide 2 mg/kg daily and prednisolone 1 mg/kg daily initially. Three months later the chest radiograph showed complete resolution of the mass. Five months after presentation, however, while having treatment he relapsed, with recurrence of the left hilar lesion. Repeat bronchoscopic biopsy showed extensive infiltration of the bronchial mucosa by large atypical mononuclear cells with open chromatin, several nucleoli, and scanty cytoplasm. These neoplastic cells showed strongly positive staining with UCHL1 (Dako), and MT1 (Eurodiagnostics), but were negative for B cell, epithelial cell, and other markers, thus indicating that they were T cell lymphoma
cells, possibly related to lymphomatoid granulomatosis.

Computed tomography of the abdomen and bone marrow examination showed no extra-thoracic spread. The patient is now in remission after chemotherapy consisting of hydroxydaunorubicin (Adriamycin), vincristine, prednisolone, and etoposide. A repeat measurement of antineutrophil cytoplasmic antibody was negative.

**Discussion**

In 1985 Van der Woude et al first reported a new antineutrophil cytoplasmic antibody in Wegener's granulomatosis,\(^1\) a finding subsequently confirmed in prospective studies.\(^2,3\) A positive result, consisting of a bright granular centrally accentuated cytoplasmic fluorescence, with a titre of at least 1/16, is reported as 93% sensitive and 97% specific for active Wegener’s granulomatosis.\(^4\) Antineutrophil cytoplasmic antibody has also been found in other conditions, including microscopic polyarteritis, mixed connective tissue disease, the Churg-Strauss syndrome, Paget’s disease, and carcinoma of the lung,\(^5\) but usually with a weak granular or diffuse immunofluorescence pattern.

Classically, Wegener’s granulomatosis is defined as a necrotising granulomatous vasculitis of the upper and lower respiratory tract, with focal necrosing and segmental glomerulonephritis. A limited form exists in which only the lung is affected. A firm histological diagnosis is often not possible, particularly with mucosal biopsy, and this may lead to delayed treatment and irreversible organ damage. In one series only two of 11 patients had diagnostic histological appearances, despite fulfilling typical clinical criteria.\(^6\) In our patient the initial histological appearance was compatible with but not diagnostic of Wegener’s granulomatosis, but with the antineutrophil cytoplasmic antibody persuaded us to treat him as having it. Review of this biopsy specimen showed scanty atypical cells.

T cell lymphomas often cause difficulty in interpretation owing to migration of large numbers of non-neoplastic reactive cells into the tumour.\(^6\) Primary lymphomas of the lung, particularly those of T cell origin, are rare, and may have many features in common with lymphomatoid granulomatosis.\(^7\) In one series only one patient out of eight with lymphomatoid granulomatosis had antineutrophil cytoplasmic antibody, and this was in low titre.\(^8\) We suggest that the antineutrophil cytoplasmic antibody in our patient was due to the T cell lymphoma, and after satisfactory treatment the serum antineutrophil cytoplasmic antibody is no longer detectable.

This case shows that care should be taken in interpreting the finding of antineutrophil cytoplasmic antibody in the presence of histological appearances that are not diagnostic of Wegener’s granulomatosis. We suggest that if relapse occurs despite treatment a careful search should be made for other conditions, in particular lymphoproliferative conditions affecting the lung.

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