Thorax 1986;41:409–410

Bronchoalveolar lavage in Waldenström's macroglobulinaemia with pulmonary infiltrates

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In 1944 Waldenström first described a lymphoproliferative disorder comprising anaemia, lymphocytic infiltrates, and raised serum concentrations of high molecular weight globulins.[1] Waldenström's macroglobulinaemia usually occurs in the elderly and the serum globulin is now recognised as IgM. Some patients have radiographic evidence of manifestations of Waldenström's macroglobulinaemia in the lungs in the form of masses, nodules, infiltrates, and pleural effusions.[2 3] These features have been confirmed by necropsy or by examination of material gathered by percutaneous, bronchoscopic, or open lung biopsy. We describe a patient in whom the presenting manifestations of Waldenström's macroglobulinaemia were solely pulmonary. The patient presented with the problem of pulmonary infiltrates and examination of serum proteins showed a high concentration of IgM paraproteins. Computed tomography showed enlargement of abdominal lymph nodes. Analysis of bronchoalveolar fluid confirmed that the lung was affected by the disease.

Case report

A 44 year old man presented in late April 1982 with a one year history of frequent episodes of cough and phlegm with increasing shortness of breath. He had recently felt tired and had lost 2 kilograms in weight over three months. He had smoked cigarettes (10 pack years) but stopped in 1967. He had no clubbing or purpura. Examination of his chest showed no abnormality. There was one lymph node palpable in the left axilla.

A chest radiograph showed diffuse homogeneous infiltrates in the lower lung zones and a confluent area in the right middle lobe. Lung function tests showed normal lung volumes and expiratory flow, reduced carbon monoxide transfer factor, and a normal cardiorespiratory response to a progressive exercise test (196 watts) with no arterial oxygen desaturation.

Examination of the serum showed the presence of a large quantity of monoclonal paraproteins, which proved to be an IgM kappa immunoglobulin. The concentration of IgM was 47 g/l while concentrations of IgG and IgA were normal.

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Accepted 29 October 1985

Further investigations were undertaken in June when the IgM was still very high. The haemoglobin concentration was 136 g/l and the white blood count 7.9 × 10^9/l with 15% lymphocytes (of which most were B cells bearing surface IgM). Bone marrow examination showed a hypercellular marrow but no excess lymphocytosis. The blood had increased viscosity and clotting was prolonged, a lupus type inhibitor being present. The urine contained free kappa light chains but no Bence-Jones protein. Computed tomography showed the spleen to be slightly enlarged and lymphadenopathy was detected in the abdomen. A biopsy specimen of the palpable left axillary node showed no specific changes on histological examination.

The clinical picture, the enlarged spleen and abdominal nodes, the serum IgM paraprotein, blood B cells bearing IgM, and the clotting abnormalities led to a diagnosis of Waldenström's macroglobulinaemia. Our concern was the nature of the lung infiltrate. Open lung biopsy was considered but his clotting abnormalities were thought to add some risk to the procedure. We therefore chose to perform bronchoalveolar lavage (under local anaesthesia). About 150 ml of fluid was recovered, which contained 35.5 × 10^5 cells/mm^3—60% lymphocytes, 25% macrophages, 10% plasma cells, and 4% neutrophils. Most of the lymphocytes and plasma cells bore IgM, demonstrated by immunofluorescence. The myeloma protein identified by electrophoresis was identical to that of the serum. The lavage fluid IgM:albumin ratio was 30 times the serum IgM:albumin ratio. There was no evidence of pulmonary infection. The lavage confirmed that the lung infiltration was due to Waldenström's macroglobulinaemia rather than to complications of it.

Treatment with 6 mg chlorambucil and 50 mg of prednisone daily was started. Shortly afterwards he had a haematemesis; gastroscopy showed gastritis with enlarged rugae, biopsy of which showed infiltration with plasma cells consistent with Waldenström's macroglobulinaemia. His symptoms settled, his serum IgM concentration fell to normal, his chest radiograph cleared, and his lung function returned to normal. By June 1983 he was judged to be in remission and treatment was stopped. In September 1983, although his lung function and radiograph were normal a repeat bronchoalveolar lavage was performed for reevaluation. The 250 ml of lavage fluid contained 3.75 × 10^4 cells/mm^3—79% macrophages, 4.5% lymphocytes, 7% neutrophils, 10% epithelial cells. No IgM could be detected by electrophoresis. Serum and lavage fluid IgM:albumin ratios were the same—namely, 1.14.

In 1984 the patient's symptoms recurred, a mass devel-

oped in the right middle lobe, and his serum IgM concentration was 11.08 g/l. He was admitted to another hospital, where bronchoscopy but not bronchioalveolar lavage was done. A thoracotomy was performed (the clotting abnormalities had resolved) and his right lung was found to contain multiple nodules. Histological examination of the lung showed with lymphocytes and plasma cells, which stained strongly for IgM, on immunofluorescence. Treatment with chlorambucil was restarted. Again his chest radiograph has cleared, with amelioration of his symptoms and return of the serum IgM concentration to normal.

Discussion

Pulmonary complications of Waldenström's macroglobulinaemia are common and are usually due to concomitant infection,[4] although primary pulmonary disease does occur.[2 3] In the patient described here pulmonary symptoms due to pulmonary infiltration were the presenting feature of his Waldenström's macroglobulinaemia. The disease was diagnosed on the basis of the clinical and blood findings; the bone marrow and lymph node biopsy failed to confirm the diagnosis.

The bronchoalveolar lavage was helpful in identifying that the pulmonary infiltrate was due to Waldenström's macroglobulinaemia in the lung. The presence of IgM in the lavage fluid, and particularly the fact that the IgM:albumin ratio was higher in the lavage fluid than in serum, suggests local production in the lung. Usually there is little IgM in the lavage fluid from normal subjects[5] and those with benign or malignant disease.[6] Moreover, the lavage fluid contained a large number of lymphocytes, and plasma cells bearing surface IgM. In remission repeat bronchoalveolar lavage showed no evidence of Waldenström's macroglobulinaemia in the lungs.

Since its introduction[7] bronchoalveolar lavage has added to our knowledge of the interstitial disease.[8] Although not often specifically diagnostic it has aided the clinical investigation of several interstitial diseases; we believe it will be useful for identifying and monitoring pulmonary infiltrates in Waldenström's macroglobulinaemia.

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