

Pulmonary paraprotein production in Waldenström's macroglobulinaemia

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Summary

A case of Waldenström's macroglobulinaemia is presented where marrow examination was normal and production of the abnormal protein was centred on the lungs. Symptomatic and biochemical improvement was achieved with chlorambucil and prednisone. Lung manifestations in the disease are briefly reviewed.

Introduction

Waldenström's macroglobulinaemia (Waldenström, 1944) is a rare disease characterized by the excess production of a monoclonal paraprotein of the IgM class. Pulmonary manifestations are uncommon. A case is reported in which there was predominantly pulmonary paraprotein production.

Case report

A retired farmer presented in 1973, aged 62 years, with a productive cough which had lasted for a number of weeks for several successive winters. Physical examination was normal apart from expiratory rhonchi. A chest X-ray was normal. Investigations showed an ESR of 10 mm/hr, WBC $6.8 \times 10^9/l$, 8% eosinophils; the sputum also showed some eosinophils.

He presented again 4 years later with increasing dyspnoea which had not responded to inhaled bronchodilators and steroids. He could only walk 30 yards at a brisk pace. His productive cough had persisted.

Examination of his chest revealed bilateral basal crepitations. There was no hepatosplenomegaly or lymphadenopathy. A chest X-ray showed mottled shadowing in both lung fields with confluent areas in the left lower lobe consistent with pulmonary fibrosis.

Laboratory investigations showed the following results: Hb 17.3 g/dl; WBC $9.7 \times 10^9/l$; neutrophils 76%; lymphocytes 19%; monocytes 2%, eosinophils 3%, plasma viscosity 3.65 mNs/m², RA latex negative, sputum cytology negative, sputum culture for tuberculosis negative. *Micropolyspora faeni*, *Thermoactinomyces vulgaris*, and *Aspergillus fumi-*

gatus precipitins negative. Sodium 135 mmol/l, potassium 4.5 mmol/l, urea 3.7 mmol/l, total protein 90 g/l, albumin 35 g/l, alkaline phosphatase 70 i.u./l, bilirubin 6 μ mol/l, total globulin 55 g/l, α_1 -globulin 4 g/l, α_2 -globulin 9 g/l, β -globulin 36 g/l, γ -globulin 6 g/l, IgG 8.2 g/l, IgA 3.2 g/l, IgM 56 g/l, Bence-Jones protein negative and cold agglutinins negative.

Bronchoscopy showed slight narrowing of the left lower lobe bronchus. A biopsy from this area was normal. Multiple transbronchial lung biopsies were taken and showed interstitial infiltration by close packed masses of lympho-plasmacytoid cells. Bone marrow examination showed a moderate increase of cytologically normal plasma cells.

He was treated initially with prednisone but his IgM continued to rise reaching a maximum of 89.6 g/l. He was started on chlorambucil with a good response, his IgM falling to 44 g/l and his plasma viscosity from 4.0 mNs/m² to 3.06 mNs/m². He had two plasmaphereses which reduced his IgM to 32 g/l and his viscosity to 2.37 mNs/m².

Three years following diagnosis he was asymptomatic. There was no lymphadenopathy, splenomegaly, hepatomegaly or retinal vein distension. His Hb was 14.7 g/dl, WBC $6.5 \times 10^9/l$, platelets $264 \times 10^9/l$, urea and electrolytes normal. A repeat bone marrow showed some increase in plasma cells although they were still considered to be within the limits of normal. Immunofluorescence showed IgA, IgG and IgM in plasma cells and no excess of monoclonal IgM was demonstrated. His chest X-ray had returned to normal.

Discussion

Waldenström's macroglobulinaemia is a rare lymphoproliferative disease first described in 1944 (Waldenström, 1944), which usually presents in later life, and has a relatively benign prognosis. It commonly presents with fatigue and weight loss, bleeding phenomena, anaemia and painless lymphadenopathy, or symptoms of the hyper-viscosity syndrome. There is excessive production of a monoclonal macroglobulin, usually of the IgM class, and

infiltration of bone marrow, lymph nodes or liver and spleen with lymphoplasmacytoid cells. Very occasional infiltration into non-lymphoid tissue has been observed. Lamm (1961) reported a case of macroglobulinaemia in which there were lymphocytic foci in lung, gastrointestinal tract, liver, gall-bladder, kidneys, skeletal muscle and fibro-adipose tissue at post-mortem examination.

Bolinelli *et al.* (1970) differentiated pulmonary involvement in macroglobulinaemia into 3 broad groups: infections; specific infiltrates, including effusions and parenchymal infiltrates varying from basal infiltration as in this case to a disseminated miliary picture; and thirdly, associated lung disease such as tuberculosis. Winterbauer, Riggins and Bauermeister (1974) reported 20 cases of which 5 had pulmonary manifestations; 4 had histological infiltration with lymphocytes and plasmacytoid cells of the lungs, pleura or hilar nodes; 3 of the 4 cases also had histological evidence of the disease in lymph nodes or bone marrow. All 4 had abnormal chest X-rays.

Nieman, Wolson and Berenson (1973) described a case with lymphoplasmacytic infiltration of both lungs producing diffuse reticular shadowing radiologically. There was also lymphadenopathy and

hepatosplenomegaly. The lung changes also responded to chlorambucil and prednisone.

The present patient at the time of diagnosis had histological evidence of diffuse involvement of the lung parenchyma with a normal bone marrow aspirate and no clinical evidence of disease elsewhere. This infiltration resolved radiologically with chlorambucil and prednisone so that he is at present asymptomatic.

Acknowledgment

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