

Waldenstrom's macroglobulinaemia – A case report

Ng Soo Chin, MBBS (Mal), MRCP (UK), MPath (Mal)

Haematologist and Lecturer

Haematology Division

Department of Pathology

Alan Teh, MBBS (Mal), MRCP (UK)

Lecturer

M.K. Lee, MBBS (Mal), MRCP (UK)

Lecturer

Department of Medicine

Medical Faculty

University of Malaya,

Kuala Lumpur.

Summary

A case of Waldenstrom's macroglobulinemia with classical findings of IgM paraproteinaemia and a typical lymphoplasmacytic marrow infiltrate is reported and the treatment of this patient outlined.

Key words: Waldenstrom's macroglobulinemia, IgM paraproteinaemia, bone marrow histology.

Introduction

The condition known as macroglobulinaemia was first described by Jan Waldenstrom in 1944.¹ It is an interesting condition in being relatively uncommon, accounting for 5% of all malignant B cell disorders associated with a monoclonal protein spike in the serum or urine.² To our knowledge, no case has been described in Malaysia. We report the first case seen in our institution.

Case report

O.B.M. a 55 year old Malay labourer was first seen at the University Hospital in February 1988 with a two month history of lethargy and exertional dyspnoea which interfered with his work. Although his appetite was unchanged, he has lost about five kilograms in weight. He had no bone pain, bleeding diathesis or ankle swellings. He had been a smoker for the past 20 years. Clinical examination revealed a thin and fairly well patient who was markedly pale but not jaundiced. He had mild hepatomegaly without splenomegaly or lymphadenopathy. His fundi showed old exudates but no haemorrhages.

Blood counts showed severe anaemia with haemoglobin concentration of 5.5 g/dl, white cell count of $4.5 \times 10^9/l$ and platelet count of $42 \times 10^9/l$. The reticulocyte count was 1.5% while the peripheral blood film showed a leucoerythroblastic picture and marked rouleaux formation.

Direct Coomb's test was negative. Bone marrow aspirate was a "dry tap". Trephine biopsy showed a hypercellular marrow with replacement of the normal marrow architecture by a lymphoplasmacytic infiltrate (Fig. 1). Both the lymphocytes and plasma cells were mature-looking. There was also some background fibroblastic reaction with a diffuse increase in reticulin which accounted for the difficulty in aspirating the marrow. Serum electrophoresis revealed a distinct band in the mid-Gamma zone region and immunoelectrophoresis confirmed the presence of IgM lambda paraprotein (Fig. 2). The immunoglobulins quantitations were as follows: IgG 1.38 g/l (normal, 6.4–13.5g/l), IgM 10.7 g/l (normal, 0.5–3.5g/l). IgA 0.295 g/l (normal, 0.7–3.3g/l). Urine immunoelectrophoresis was negative for Bence Jones protein. The diagnosis of Waldenstrom's macroglobulinaemia was made on the basis of IgM lambda paraproteinemia with presence of typical marrow findings. The renal and liver function were normal. Radiographs of the skull and pelvis showed no lytic lesions.

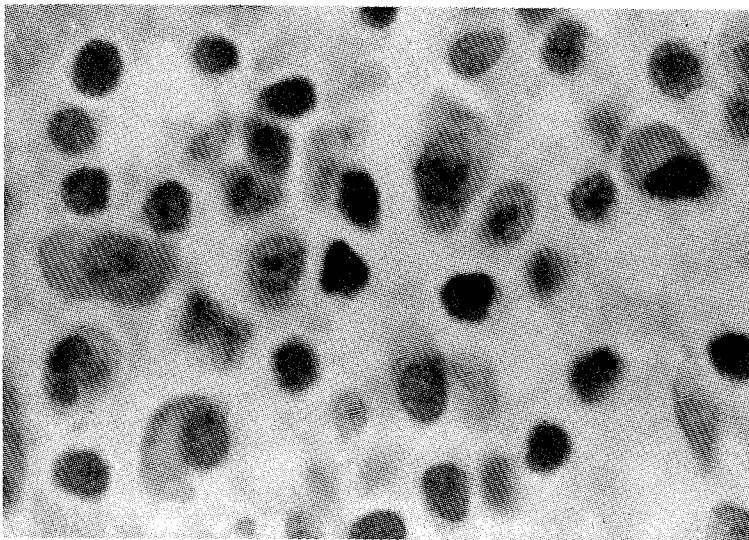
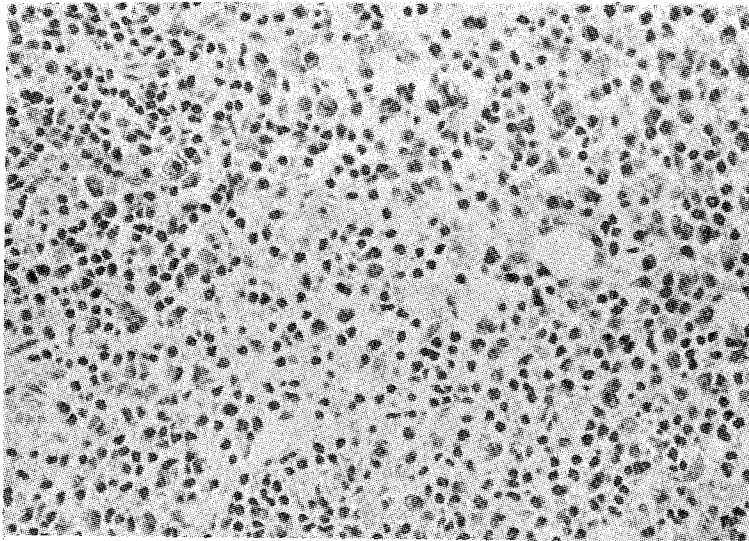


Fig. 1 Trephine biopsy showing a hypercellular marrow with replacement of normal marrow by lymphoplasmacytic infiltrate. H&E x 200 and H&E x 800.

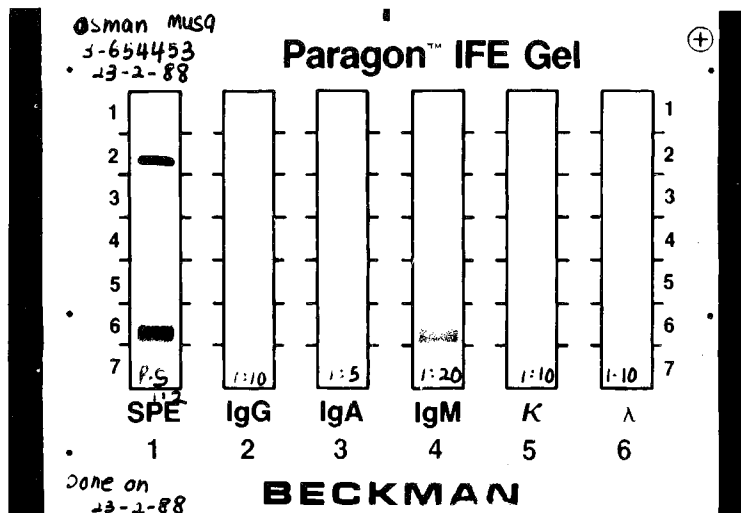


Fig. 2 Serum electrophoresis showing a monoclonal band in mid Gamma region while immunoelectrophoresis confirmed IgM lambda paraprotein.

Because the patient was symptomatic and had rather high IgM level, he was started on low dose chlorambucil. He had good response with complete normalisation of blood counts one month later. He was last seen six months after diagnosis and was keeping well.

Discussion

The mean age of presentation of Waldenstrom's macroglobulinaemia is about 65 years and approximately 60% of patients are men.³ Our patient presented with anaemia, fatigue and weight loss as the main clinical features. In a series of 45 patients described by Krajny M et al,⁴ fatigue weakness and/or weight loss was the commonest manifestation occurring in about 89% of patients. Anaemia in Waldenstrom's macroglobulinaemia is multifactorial. It is partly dilutional due to the increase in plasma volume caused by high IgM level as well as a hypoproliferative anaemia due to bone marrow infiltration with abnormal lymphocytes and plasma cells.

The diverse clinical manifestations of the disease is linked to the presence of IgM paraprotein, a high molecular protein, which is capable of binding other components of blood and different tissues.⁵ The main features of hyperviscosity syndrome include ocular changes, mucous membrane bleeding, neuropsychiatric manifestations and congestive heart failure are generally seen in patients when their IgM level exceeded 30g/l.⁶ Though hyperviscosity syndrome is a well known clinical problem in Waldenstrom's macroglobulinemia, it is not a common main presenting manifestation. Krajny M et al⁷ reported only five out of 45 patients had hyperviscosity syndrome as the presenting problem. Our patient did not have features of hyperviscosity syndrome at presentation. The diagnosis of Waldenstrom's macroglobulinaemia is usually made based on overall assessment of the clinical features, presence of a monoclonal IgM protein in the serum and bone marrow finding of typical lymphoplasmacytic infiltrate.⁸

Treatment of Waldenstrom's macroglobulinaemia is generally reserved for symptomatic patients as the condition is considered a relatively low grade neoplasm. Chemotherapy is a useful form of therapy in symptomatic patients. However some patients are sensitive to chemotherapy so this

must be initiated cautiously, looking out for neutropenia and thrombocytopenia. An alkylating agent usually chlorambucil is given either in continuous low dose or intermittent fashion with or without prednisolone. Cyclophosphamide and melphalan have also been used as well as various other combination chemotherapy protocols. In general however, less toxic chemotherapy should be tried first and treatment intensified only if justified by the patients symptoms and clinical course.⁹ Our patient appears to have done reasonably well on low dose chlorambucil thus far. Long term prognosis is however guarded as the median survival is said to be about 50 months.¹⁰

References

1. Waldenstrom JG. Incipient myelomatosis or 'essential hyperglobulinemia with fibrinogenopenia – a new syndrome. *Acta Med Scand* 1944; 117: 216–47.
- 2,3,6,9. Reis CA. Waldenstrom's macroglobulinemia (Medical Staff Conference). *West J Med* 1988 Mar; 148: 320–32.
- 4,7,10. Krajny M, Pruzanski W. Waldenstrom's macroglobulinemia: Review of 45 cases. *Can Med Assoc J* 1976, 114: 899–905.
5. Anonymous. Waldenstrom's macroglobulinemia. *Lancet* 1985; Aug 10: 311–2.
8. Barh R, Frisch B, Mahl G et al. Bone marrow histology in Waldenstrom's macroglobulinemia. *Scand J Haematol* 1983; 31: 359–75.