Primary Care Management Guideline

Monoclonal Gammopathy

Monoclonal gammopathies are a group of disorders characterised by the proliferation of a clone of plasma cells or lymphoid cells that produce a monoclonal immunoglobulin protein, sometimes referred to as a paraprotein or M-band. These cells may also produce abnormal immunoglobulin light chains (excess of kappa or lambda light chains) as well as, or instead, of an M-protein. Polyclonal gammopathy signifies a non-specific immune reaction, does not indicate underlying haematological disorder and does not require haematology referral.

Clinical problem	Action	Implementation
Paraprotein detected in serum or urine (note 1)	• Clinical assessment for unexplained weight loss, bone pain, night sweats, lymphadenopathy or splenomegaly • CBC • Immunoglobulins (if not already done) • Serum free light chains • Creatinine • Calcium/albumin • Urine Bence Jones protein • Dipstick urine for protein	Discuss acute referral with haematology if any of the following • anaemia • bone pain/pathological # • non pre-existing or recently progressive renal impairment • significant proteinuria i.e. 3+ on dipstick • hypercalcaemia Refer haematology clinic if any of the following • Significant paraprotein on electrophoresis i.e. IgA>10g/l or IgG>15g/l or IgM>10g/l • Serum free light chain ratio >10 • Positive clinical findings • Bone marrow diagnostic of myeloma • Uncertain of diagnosis
Monoclonal Gammopathy of Undetermined Significance (MGUS) i.e. paraprotein with no concerning features (note 2)	Review at 3 months • Clinical assessment for unexplained weight loss, bone pain, night sweats, lymphadenopathy or splenomegaly • CBC • Immunoglobulins + electrophoresis • Serum free light chains • Creatinine • Calcium If stable review 6-12 monthly as above	Refer haematology clinic if any of the following • Development of positive clinical symptoms/signs • Anaemia • Renal impairment • Hypercalcaemia • Rise in monoclonal immunoglobulin by >5g/L or significant paraprotein IgA>10g/l or IgG>15g/l or IgM>10g/l • Serum free light chain ratio >10 If uncertain, phone haematologist for advice

Notes

1) Paraprotein is usually detected by serum or urine electrophoresis and is most often IgG, but can be of any immunoglobulin class. Disorders characterised by the production of paraprotein include monoclonal gammopathy of undetermined significance (MGUS, also referred to as benign monoclonal gammopathy or benign paraproteinaemia), multiple myeloma and Waldenstrom's macroglobulinaemia. Less commonly paraprotein may be associated with chronic lymphocytic leukaemia, non-Hodgkin's lymphoma and amyloidosis.

2) MGUS is a diagnosis of exclusion. It refers to the presence of a monoclonal paraprotein in serum or urine in the absence of any clinical-pathological evidence of multiple myeloma, Waldenstrom's macroglobulinaemia, chronic lymphocytic leukaemia, non-Hodgkin's lymphoma and amyloidosis. These patients are typically asymptomatic, with no related physical findings, and the paraprotein is an incidental finding. 3% of the population >50 years and 5% >70 years have a paraprotein. The term MGUS is preferable to benign monoclonal gammopathy or benign paraproteinaemia, as approximately 20% of these patients will progress to overtly malignant disease some years later.

   Of all patients with MGUS, 1% per annum will progress to myeloma. IgM paraproteins are rarely due to myeloma but occur in Waldenstrom's macroglobulinaemia and may be associated with lymphoma.

Risk stratification model for MGUS (Blood. 2005; 106: 812-817 *Rajkumar et al.*)

Risk group	**20 year risk of progression %**	**20 year risk accounting for death %**
Low risk (serum M-protein <15g/l, IgG subtype, normal FLC ratio)	5	2
Low-intermediate risk (any one factor abnormal)	21	10
High-intermediate risk (any two risk factors abnormal)	37	18
High risk (all three factors abnormal)	58	27