Local Guidance for managing MGUS for primary care Nov 2021

New finding of paraprotein (M-protein)

IgG or IgA paraprotein <15g/l
No myeloma-defining features
(see 2ww box)

Rpt bloods at 3m, 6m,12m, then annually
(FBC, U&Es, creatinine, eGFR, s-protein electrophoresis, FLC & immunoglobulins, bone profile)

If no progression

If suspicion of myeloma: add LDH and beta-2-microglobulin, which can assist with prognosis (not necessary for annual monitoring in low risk patients)

Annual monitoring in primary care

- IgG or IgA paraprotein (non-IgM MGUS) <15g/l
- Serum Free light chain kappa:lambda ratio 0.125-8
- No other concerns (see 2ww criteria)

Monitoring should include: FBC, U&Es, creatinine, eGFR, s-protein electrophoresis, FLC & immunoglobulins, bone profile

Routine referral / Haem A&G

- IgG/IgA paraprotein >15g/l = higher risk: routine referral to haematology (may revert to community monitoring if appropriate and both patient and GP are happy with plan)
- FLC (kappa:lambda) ratio <0.125 or >8 (with increased level of appropriate involved light chain)

2ww referral

Suspected Myeloma
- Paraprotein >30 g/l
- Serum free light chain ratio ≥100 or ≤ 0.01 (provided the involved light chain is >100mg/l)
- Bony pain or lytic lesions on imaging
- Hypercalcaemia: (>2·75 mmol/l or >0·25 mmol/l higher than upper limit of normal)
- Renal insufficiency: serum creatinine >177 µmol/l or eGFR <40 ml/min
- Anaemia: Hb <100 g/l or 20 g/l below lower limit of normal

Suspected Lymphoma / Lymphoproliferative disorder
- IgM paraprotein (IgM MGUS)
- Lymphadenoathy, hepatosplenomegaly
- Pancytopaenia
- Night sweats, weight loss, fevers

MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE (MGUS)

- **Definition:** MGUS is defined by a monoclonal immunoglobulin (also known as M-protein or paraprotein of up to 30 g/L in the absence of lytic bone lesions, anaemia, hypercalcaemia and renal insufficiency that is related to the underlying monoclonal plasma cell proliferation and <10% plasma cells in the bone marrow. It is a potential precursor to multiple myeloma (MM) or related disorders and so needs long term clinical follow-up once detected.
- **Prevalence/associations:** The prevalence is 3% of people > 70 years, but is higher in African/Caribbean persons. The commonest type of M-protein is IgG (isotope), followed by IgM and then IgA. IgM M-proteins are associated with lymphoproliferative conditions such as Waldenstrom Macroglobulinaemia (WM), B cell non-Hodgkin's lymphoma (B-NHL) or chronic lymphocytic leukaemia (CLL), rather than myeloma.
- **Risk of progression:** Progression to MM or related disorders is around 1% per year. The single most discriminatory parameter that is predictive of progression is the level of the M-protein (paraprotein). The level in grams/litre is roughly equivalent to the risk of progression for that patient at 10 years following detection. So a patient with an M-protein of 5g/L has a 5% chance of progression to MM compared to a 20% chance for a patient with an M-protein of 20 g/L. The other important parameter is the M-protein isotype: IgA and IgM MGUS are more likely to progress than IgG. Factors such as the presence of BJP in the urine, suppression of involved immunoglobulins, age and sex are not predictors for progression.
- **Bence-Jones proteins (BJP)** Note that urinary Bence-Jones proteins (BJP) are no longer being used, and this has been replaced by the free light chain ratio (kappa-lambda ratio)
- **Amyloidosis:** As well as malignant transformation, there is also a risk of AL amyloidosis, which warrant referral if any suggestive features, such as macroglossia, unexplained heart failure, peripheral neuropathy, carpal tunnel syndrome or nephrotic syndrome.
- **Haematology Advice and Guidance:** can be sought by emailing: huh-tr.haem@nhs.net

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