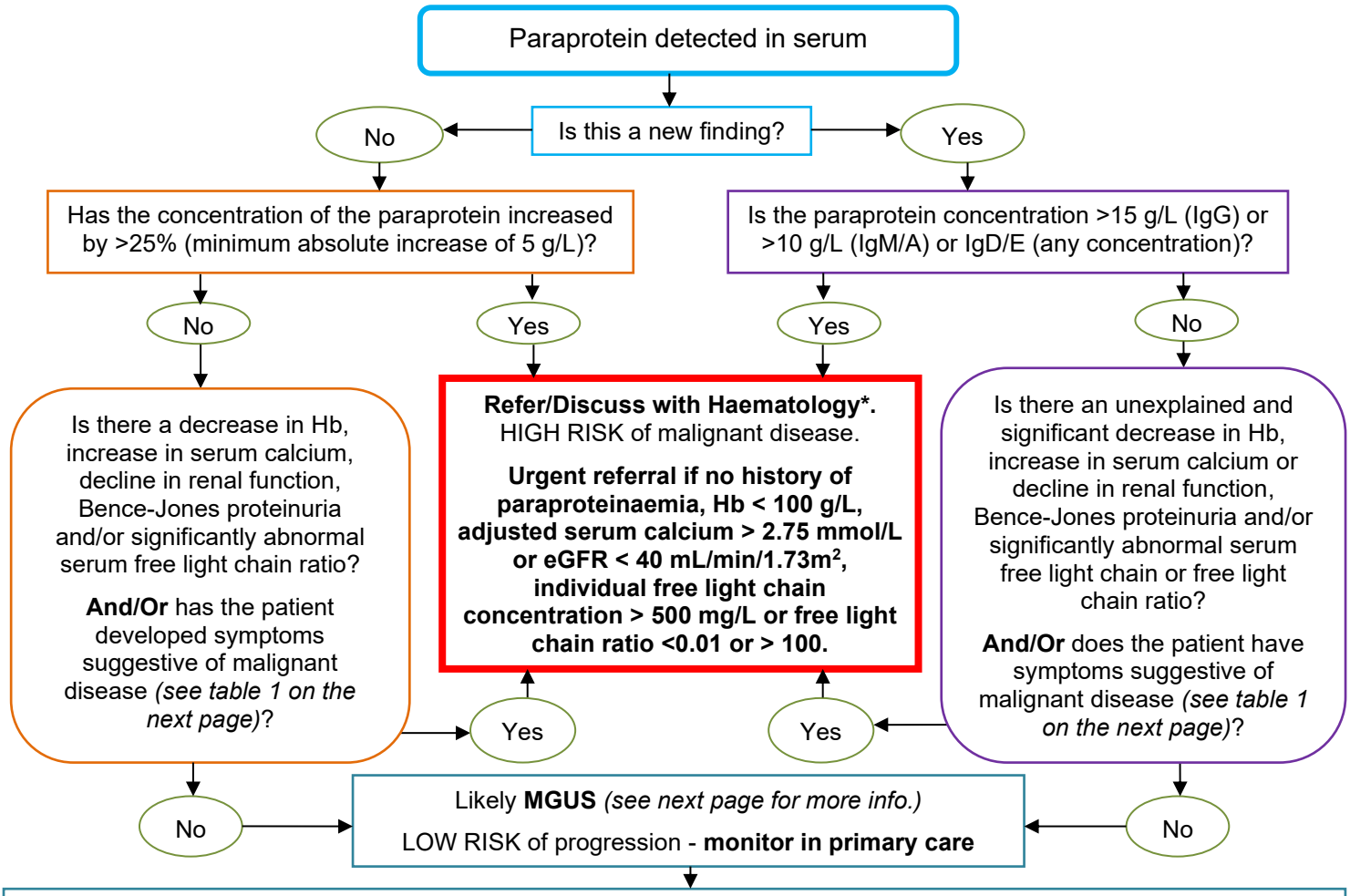
Scarborough, Hull and York Pathology Service

Management of Patients with Paraproteins And a Guide to Serum Free Light Chains



Box 1: Management of Patients with MGUS

Regular monitoring (every 3-6 months) should include a clinical review and blood tests for the following:

- Full blood count
- Urea and electrolytes, including creatinine (renal function)
- Adjusted calcium
- Serum protein electrophoresis

If no change in the patient's condition is seen, the frequency of follow-up can be reduced to 6-12 monthly.

Box 2: When to refer a patient with MGUS to the haematology clinic

- It is normal for the paraprotein concentration to slowly increase, but a sudden increase (>25%, and >5 g/L) or rise to over 15 g/L (IgG) or 10 g/L (IgM/IgA) should trigger referral to the haematology clinic.
- If there are unexplained abnormalities in their blood test results, such as renal impairment (eGFR <40 mL/min/1.73m^2), anaemia (Hb < 100 g/L) and hypercalcaemia (Adjusted calcium > 2.75 mmol/L) (N.B. the patient may remain asymptomatic).
- If the patient develops symptoms or physical signs suggestive of multiple myeloma, lymphoproliferative disorder or AL amyloidosis *(see table 1 on the next page)*.
- The identification of any lytic lesions or osteoporosis on X-rays.

*Please refer via A&G/ REI to haematology if you would like monitoring to take place via HMDS outreach

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Table 1. Symptoms and biochemical features of malignant disease associated with paraproteinaemia.

Myeloma	Lymphoma/ Lymphoproliferative disorder	AL amyloidosis
Hypercalcaemia	Lymphadenopathy	Macroglossia
Renal failure	Hepatosplenomegaly	Unexplained heart failure
Anaemia or other features of bone marrow failure	Hyperviscosity (especially if IgM)	Peripheral neuropathy
Bone/back pain (not usually joint pain) or bone lesions	Pancytopenia	Carpal tunnel syndrome
Hyperviscosity	Other symptoms e.g. night sweats, fever, weight loss, loss of appetite	Nephrotic syndrome

Patients with MGUS should be fully aware of these important symptoms and encouraged to report them outside appointment visits, should they occur in the meantime.

Monoclonal Gammopathy of Undetermined Significance (MGUS)

Definition

The presence of a monoclonal protein (also known as an M-protein or paraprotein) in the serum or urine of an individual with no evidence of multiple myeloma, AL amyloidosis, Waldenström macroglobulinaemia or other related disorder.

By definition, patients with MGUS have no symptoms related to this common precursor condition.

Risk Stratification for Disease Progression

Patients with MGUS have an increased risk of developing malignant disorders such as lymphoproliferative disorders (usually IgM) and multiple myeloma (IgG or IgA, rarely others). This risk is around 1% per year, making it more appropriate for these patients to be monitored in the community.

Risk factors for the malignant transformation of MGUS include:

- IgM and IgA paraproteins (more likely to progress than IgG)
- Higher initial concentration of the paraprotein.

It is recommended that all patients found to have a paraprotein are regularly reviewed in order to identify malignant transformation at an early stage. See Box 1 for more info.

References

Bird, J., Behrens, J., Westin, J. et al (2009) UK Myeloma Forum and Nordic Myeloma Study Group: guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS) *British Journal of Haematology,* 147(1), pp. 22-42.

Myeloma Diagnostic Tool: Guidance for Primary Care

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Serum Free Light Chains

What are serum free light chains (FLC)?

Multiple myeloma is a malignant disease of B-lymphocytes, leading to overproduction of immunoglobulin from a single clone, which is detected in the biochemistry laboratory as a paraprotein.

A paraprotein may be intact (both heavy and light chains of the immunoglobulin) or light chain only. Light chains are normally cleared from the circulation by glomerular filtration, before being reabsorbed and catabolised in the proximal tubules.

Where there is significant overproduction of free light chains, these may be detected as overflow in the urine (termed Bence - Jones protein (BJP)) or elevated free light chains in the serum.

Why have I received FLC results when I didn't request this test?

When a patient is found to have a new paraprotein in their serum by electrophoresis, the laboratory will add serum free light chains to their sample. This will allow prompt assessment of both intact and light chain components of their disease prior to referral or discussion with haematology if required.

In patients where no paraprotein is detected in their serum, it remains critical that a urine sample for Bence Jones protein analysis is provided. Myeloma cannot be excluded in patients where this is not completed.

What do the FLC results mean?

Three values are provided with results from serum free light chain analysis: kappa, lambda and a ratio of the two. Concentrations of the two individual light chains, and their ratio, remain stable in each individual during health, however do tend to increase slightly with age.

Elevations in the free kappa and free lambda, with a normal ratio, are unlikely to be of clinical significance and are most likely due to inflammatory responses.

Elevations in a single light chain, with an abnormal ratio, may indicate myeloma or related disease. The probability of a malignant disease increases with the degree of abnormality. Borderline high ratios may be seen in cases with renal impairment, polyclonal inflammatory responses (e.g. infection, inflammation, autoimmune). In patients on dialysis, the normal free light chain ratio is considered to be 0.37 – 3.10.

What Next?

Free light chain Ratio	Suggested Action
0.26 – 1.65 or 0.37 – 3.10 if on dialysis	Normal free light chain ratio. No action required.
<0.01 or >100	Significant abnormality in free light chain ratio. Suggest urgent referral to haematology.
0.01-0.125 or 8-100	Abnormal free light chain ratio. Suggest discuss with haematology by advice & guidance.
0.125 – 0.26 or 1.65 - 8	Slight abnormality in free light chain ratio may not be significant. Monitor paraprotein with serum electrophoresis in 3-6 months and consider discussion with haematology if this appears to be progressing.

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