Nottingham University Hospitals NHS
NHS Trust

Guideline for the investigation of newly detected serum paraproteins

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Explicit definition of patient group to which it applies *(e.g. inclusion and exclusion criteria, diagnosis):*	Adult patients
Changes from previous version *(not applicable if this is a new guideline, enter below if extensive):*	Parameters necessitating urgent and routine referral have been revised and updated Reference to the new guideline regarding interpretation of serum free light chains has been included
Summary of evidence base this guideline has been created from:	British Standards in Haematology guidelines and local best practice
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.	

Guideline for the investigation of newly detected serum paraproteins

Purpose

To provide clear guidance for the effective investigation of patients with newly detected serum paraproteins.
The guidance may not be appropriate to all patients and individual patient circumstances should be assessed and may dictate an alternative approach.
This guideline should be read in conjunction with the guideline for the interpretation of serum free light chains.

Background

Monoclonal paraproteins can be detected in the serum of approximately 1% of the population aged under 50yrs, rising to 5% in those over 70 yrs.
Causes of paraproteins include:

- Plasma cell dyscrasias
  - such as myeloma, plasmacytomas and AL amyloidosis
- Lymphoproliferative disorders (LPDs)
  - such as Waldenstrom's macroglobulinaemia, low grade B-cell non-Hodgkin's lymphoma and CLL
- Monoclonal gammopathy of undetermined significance (MGUS)
  - Over 50% of patients with a newly detected paraproteins have MGUS (Kyle, 2006).

Investigations

Each patient found to have a serum paraprotein should be evaluated. In particular, the type of paraprotein should be identified by immunofixation, a careful history taken, and clinical examination and further investigations performed.

a) The type of paraprotein
   - Myeloma is typically associated with IgG and IgA paraproteins, and less commonly: IgD, IgE and free light chain paraproteins

- IgM paraproteins are more commonly associated with LPDs

b) History and examination
Symptoms and clinical signs suggestive of myeloma, AL amyloid and LPDs are listed in Table 1.

Table 1: Symptoms and signs suggestive of myeloma, AL amyloid and LPDs
• B symptoms such as drenching night sweats, unexplained fever, significant weight loss • Bone pain and/or cord compression • Symptoms of anaemia • Symptoms of hyperviscosity • Unexplained peripheral neuropathy • Lymphadenopathy and/or hepatosplenomegaly • Peripheral oedema and/or signs of CCF • Macroglossia

c) Further investigations:
- FBC
- U+E
- Calcium
- Serum free light chains
- Xray if patient has bone pain

For interpretation of serum free light chains (SFLC), please see the separate SFLC guideline.

Referral guidelines

2 week wait referral pathway

Patients should be referred to Clinical Haematology for further evaluation on a 2 week wait referral if they meet the criteria outlined in **Table 2.**

Table 2: Parameters that should prompt 2 week wait referral

- Serum paraprotein ≥ 30g/l
- A serum paraprotein of any level with **ANY** of the following features:
  - Significant anaemia (Hb < 100 g/l in absence of haematinic deficiency, or fall in Hb by 20 g/l)
  - Unexplained acute renal impairment
  - Hypercalcaemia (adjusted calcium > 2.65)
  - Lytic lesion
  - Symptoms described in table 1

Routine referrals

Patients should be referred to Clinical Haematology for further evaluation on a routine basis if they meet the criteria outlined in **Table 3.**

Table 3: Parameters that should prompt routine referral
• Serum IgG paraprotein ≥ 15g/l • Serum IgA or IgM paraprotein ≥ 10g/l • IgD or IgE or free light chain paraprotein of any level

Primary care monitoring

- Patients with low-level IgG, IgA and IgM paraproteins without any of the features detailed in Table 1 are suitable for monitoring in primary care

- These patients should have their FBC, U+E, calcium and serum immunoglobulins and SFLC levels checked after 3 months. If these tests are stable, they should be repeated every 6 months. Patients should be referred to Clinical Haematology if they meet the criteria outlined in table 2 or table 3.

NOTES

- Polyclonal rises in immunoglobulins without a paraprotein are usually associated with infection (including HIV); inflammation; autoimmune conditions and/or liver dysfunction. These patients do not need to be referred to Haematology.

References

- BCSH guidelines for the investigations of newly detected M-proteins and the management of MGUS. *Br J Haem* 2009; **147**: 22 - 42
- Kyle *et al*. Prevalence of MGUS. *N Engl J Med* 2006; **354**: 1362 - 1369

Algorithm for the investigation of a patient with a newly detected serum paraprotein