Haematology Update

Arvind Arumainathan
Consultant Haematologist
Royal Liverpool University Hospital

Outline

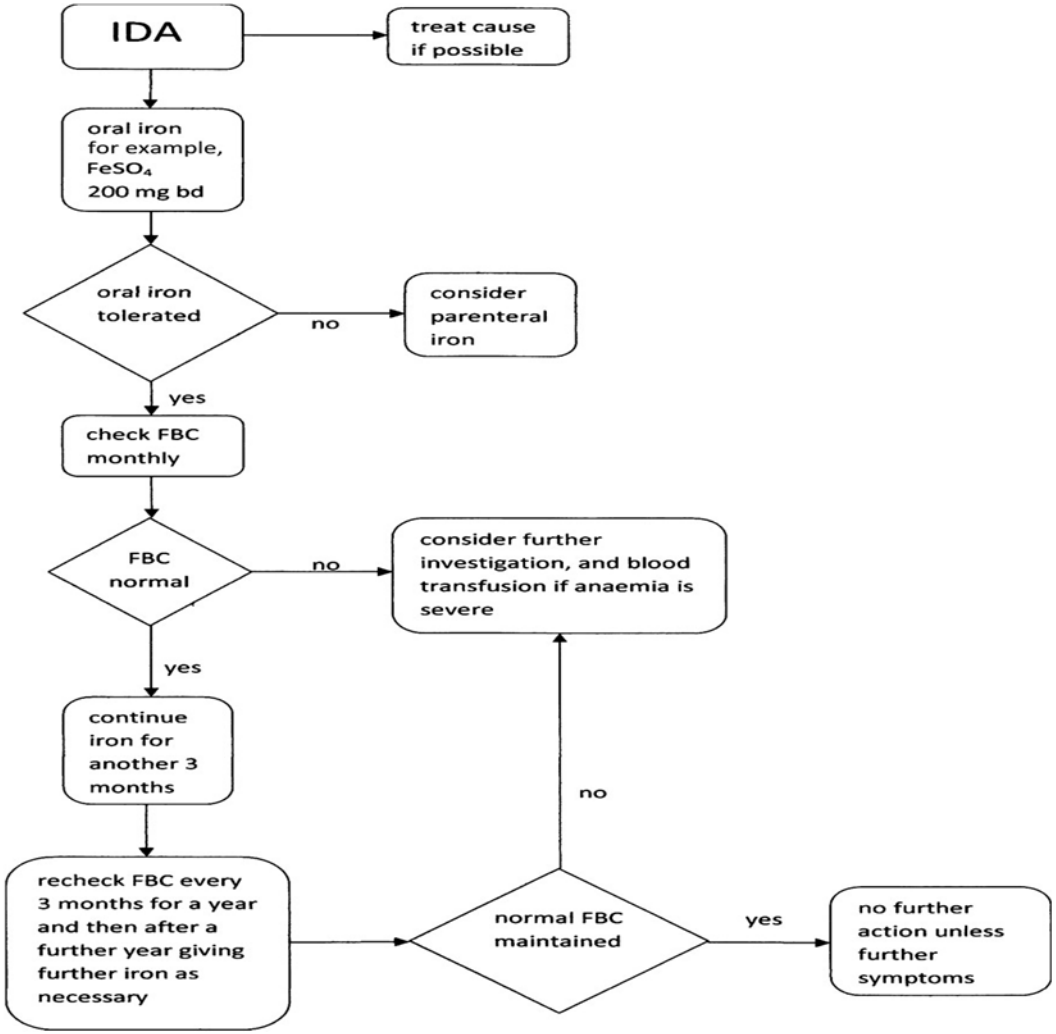
- Common haematological presentations
  - Modes of presentation
  - What to look for
  - When to refer
- Case scenarios to illustrate each
  - Iron deficiency
  - B12 deficiency
  - Lymphocytosis
  - Paraproteins

Case 1

- A 34 year old woman attends complaining of lethargy. She is otherwise well.
- Baseline blood tests:
  - Hb 104 MCV 76.6 WCC 7.1 Platelets 514
  - U&E, LFT normal
- Probable diagnosis:
  - Iron deficiency
- Differential diagnoses:
  - Haemoglobinopathy
  - Anaemia of chronic disease
- Potential causes:
  - Menorraghia
  - GI bleeding
  - Malabsorption
  - Diet

- Subsequent investigations:
  - Ferritin 8µg/L (30-400)
  - Serum iron 2.4µmmol/L (13-32)
  - TIBC 74 µmol/L
  - Iron saturation 5%
  - B12 and serum folate normal
- On further questioning, it emerges that she has been suffering with heavy periods
- Action:
  - Iron replacement (e.g. ferrous sulphate 200mg BD)
  - Coeliac screen
  - Management of menstrual symptoms

An abbreviated flow chart of the treatment of iron deficiency anaemia



Andrew F Goddard et al. Gut doi:10.1136/gut.2010.228874

Iron deficiency – important considerations

- Serum ferritin is the best test for iron deficiency (but can be elevated in inflammation)
- Other markers of iron deficiency include low ferritin, low transferrin saturation, low iron, raised total iron-binding capacity, and increased serum transferrin receptor
- A higher ferritin cut-off should be used in patients with co-existent inflammatory disease
- All patients should be tested for coeliac disease
- GI investigation should be considered in all patients >50, and all male patients
- Iron therapy should be continued for 3 months after the FBC normalises

Case 2

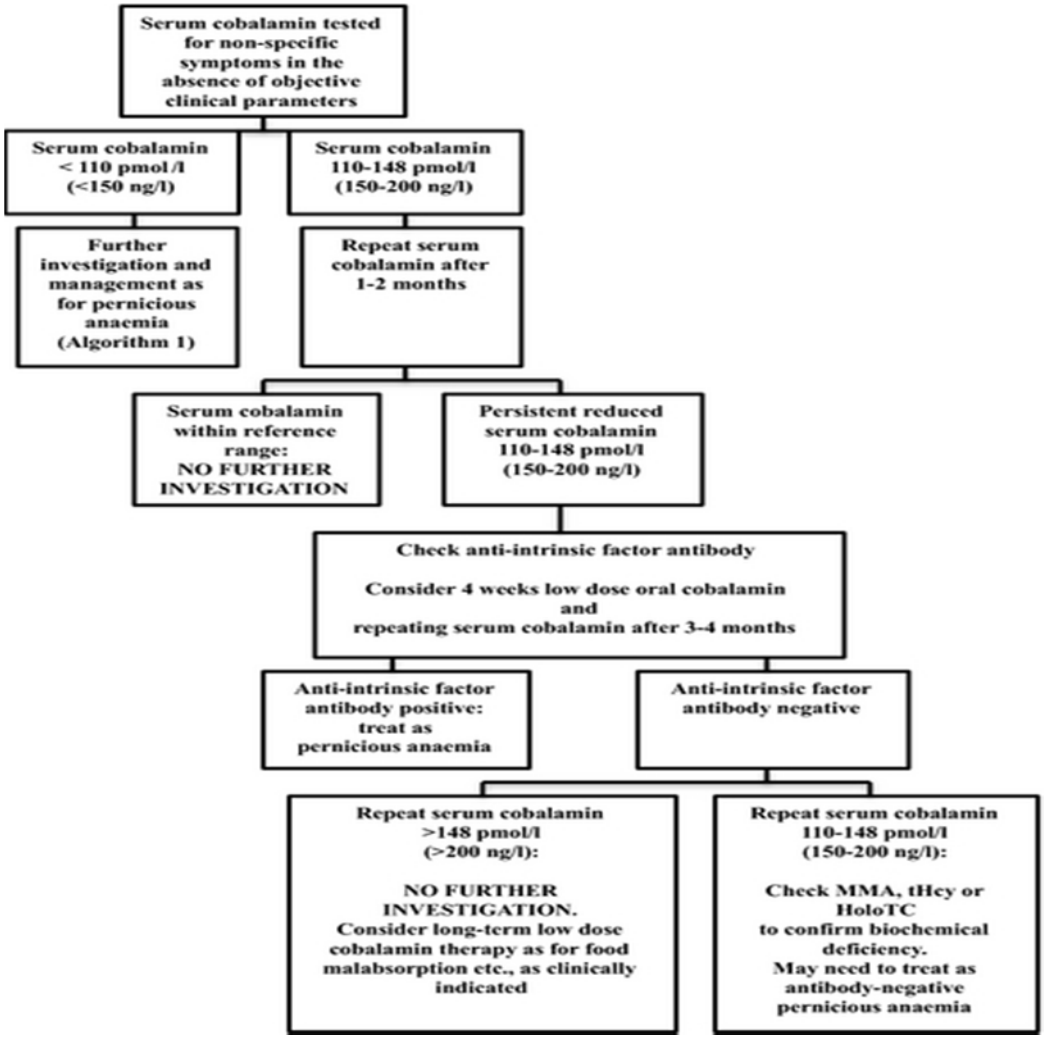
- A 56 year old man has a routine blood test as part of his diabetes monitoring. The FBC shows:
  - Hb 121 WCC 6.9 Platelets 235 MCV 95
  - eGFR 57 (longstanding)
- Additional tests:
  - Ferritin 124
  - Serum B12 166ng/L (200-770)
  - Serum folate normal
- Differential diagnosis:
  - Pernicious anaemia
  - Metformin
  - Other causes of malabsorption
  - Artefactual

- Additional tests:
  - Intrinsic factor antibody: negative
- Additional history:
  - No neuropathic symptoms
  - No family history of autoimmune disease
  - Not on PPI
  - No history to suggest malabsorption
- Probable diagnosis:
  - B12 deficiency secondary to Metformin
- Action:
  - B12 replacement (haematology referral is appropriate)

B12 deficiency

- Falsely normal B12 levels can occur – if there is a strong clinical suspicion of B12 deficiency, but with normal levels, consider empiric therapy and haematology review
- Low B12 level:
  - If FBC normal and otherwise asymptomatic, recheck in 1-2 months
    - If normal, no further investigation
    - If still low, proceed as below
  - If FBC abnormal or symptomatic, check Intrinsic factor antibody
    - If positive: Replace B12 as per regimen in BNF
    - If negative: Look for alternative causes e.g. metformin
      - If present, replace
      - Otherwise consider haematology referral

Guidelines for the diagnosis and treatment of cobalamin and folate disorders



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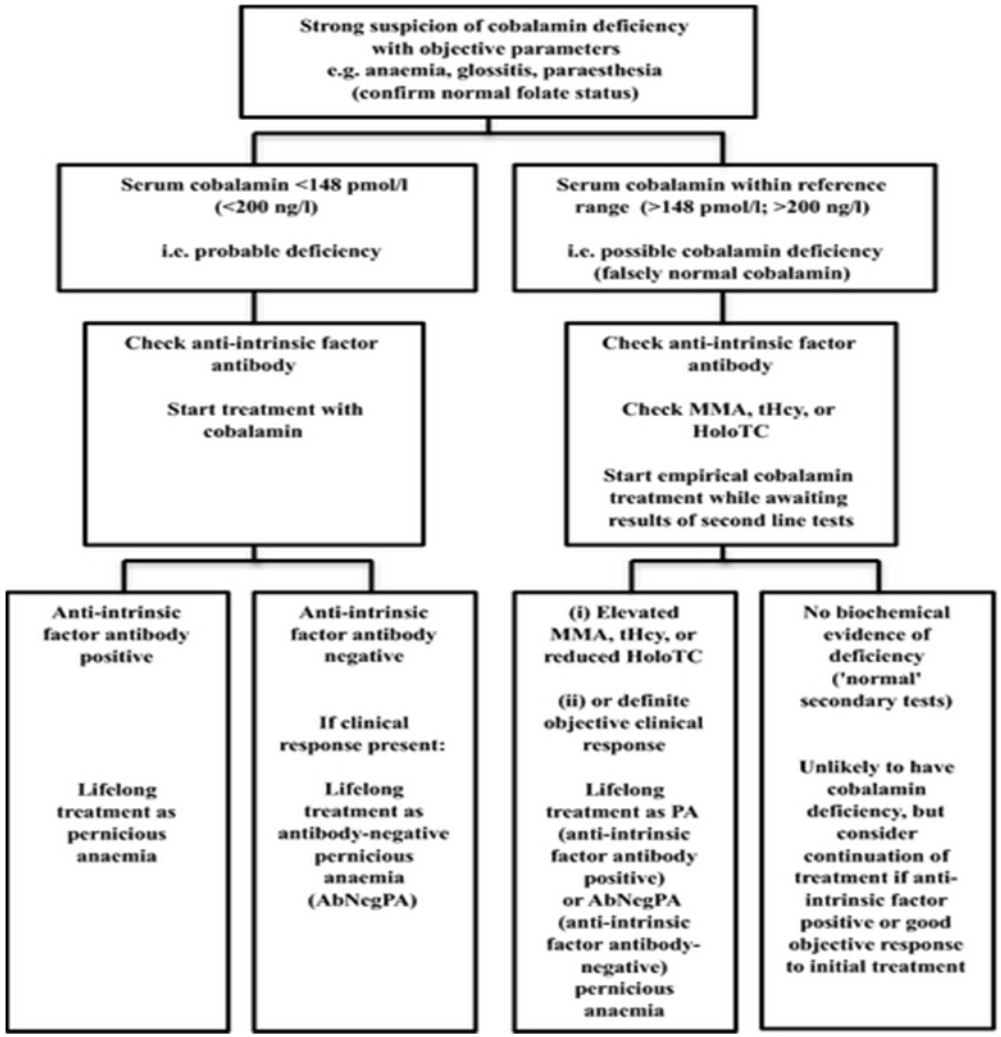

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Case 3

- A 76 year old man is noted to have a persistently raised lymphocyte count on routine blood tests. He has multiple medical problems including COPD and smokes 10/day.
  - Hb 135g/l (130-160)
  - WCC 11.5 x 10^9/l (3.5-11.0)
  - Neut 4.5 x 10^9/l (2.0-7.5)
  - Lymphs 6.0 x 10^9/l (1.0-3.5)
  - Plts 230 x 10^9/l (150-400)
- He is referred to haematology

- There is no history of weight loss or drenching sweats
- Examination reveals no palpable lymphadenopathy or organomegaly.
- Cell markers: Mixed lymphocytosis
- Probable diagnosis: Polyclonal lymphocytosis associated with smoking
- Action: Discharge

Reactive lymphocytosis (commoner causes):

- Chronic smoking
- Acute hypoxia (transient)
- Acute asthma
- Pulmonary embolus
- Myocardial infarction
- Acute stress (transient)
- Chronic skin disorders
- Viral infections:
    - Most common—Epstein-Barr virus; cytomegalovirus
    - Less common—herpes simplex, influenza, mumps, HIV, hepatitis A or B
- Bacterial infections
- Drug hypersensitivity

If in doubt, consider referral (reasonable to repeat if thought to be related to infection/inflammation)

Case 4

- A 63 year old asymptomatic man presents for health assessment. He has no medical history and is not taking any drugs. Examination is normal
- FBC shows:

  Hb 136 g/l (130-160)

  platelets 160 x 10^9/l (150-400)

  WCC 13.1 x 10^9/l (3.5-11.0)

  neut 5.4 (2.0-7.5)

  lymphocytes 8.0 x 10^9/l (1.0-3.5)

- Next stage of tests:
  - Blood film: mature looking lymphocytes with many smears
  - Immunophenotyping: Consistent with CLL
- Action:
  - Non-urgent haematology referral

Lymphocytosis – when to refer

- Routine referral:
  - Persistently raised lymphocyte count (e.g. > 6 months)
  - No obvious reactive cause (e.g. non-smoker and otherwise well)

- Indications for urgent referral include:
  - Weight loss
  - Drenching sweats
  - Low blood counts (such as anaemia or falling platelet count)
  - Associated persistent lymphadenopathy

Case 5

- 76 yr old lady who is generally well, has routine bloods done for fatigue
  - FBC, LFT, Ca profile normal
  - eGFR 50 (longstanding and stable)
  - ESR raised
- Next stage of tests:
  - Serum immunoglobulins: IgG 12g/L, Small IgG PP 3g/L
- Probable diagnosis:
  - MGUS
- Action:
  - Non-urgent haematology referral

When to test for a paraprotein

- If results suggest the presence of a paraprotein
  - Raised ESR
  - Unexplained anaemia, hypercalcaemia or renal failure
  - Raised total protein or globulin

- Clinical suspicion of myeloma or related disease
  - people aged 60 and over with persistent bone pain, particularly back pain, or unexplained fracture (also do FBC, U&E, Ca)
  - Unexplained hypercalcaemia (also do urine BJP)
  - ‘B’ symptoms (unexplained weight loss, drenching sweats)

MGUS

- Monoclonal Gammopathy of Undetermined Significance
  - Paraprotein <30g/L
  - BM plasma cells <10% (If done)
  - No end-organ damage (CRAB)
- 5% of 70yr olds
- Ethnic variation
- Risk of progression to myeloma or other malignant lymphoproliferative disorder is approx. 1% per year
- Risk factors
  - Non-IgG type
  - Higher paraprotein level
- BJP NOT a risk factor

Paraproteins: Who should be referred urgently

- Symptoms/signs of myeloma or lymphoma
- Abnormal results-CRAB
- BJP pos
- Rarer forms-IgD or IgE paraproteins
- IgG PP>15g/L
- IgA or IgM PP>10g/L

Myeloma - Clinical features

- Anaemia
- Back ache
- Pathological fractures
- Renal failure
  - 25% at presentation
- Infection
- Hyperviscosity
- Incidental finding
  - Routine bloods
  - Renal screen
  - Osteoporosis

Thank you