Some Common Haematological Problems in General Practice

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Some Common Haematological Problems in General Practice

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Learning Objectives – an overview of:

- Leucocytosis & Lymphocytosis
- Neutropenia
- Anaemia
- Thrombocytopenia
- Paraprotein
Leucocytosis

- Most patients with a leucocytosis do not have a haematological malignancy
- Careful history taking is important - fevers, diarrhoea, drugs (e.g. lithium), smoking
- Examine skin, liver, spleen, lymph nodes
- Ask for a blood film - what is the white cell differential, what do the white cells look like, and is the rest of the FBC normal?
- Consider repeating the blood count 2-4 weeks later before referring to haematology. The white cell count may have settled in this time.
Case - lymphocytosis

- Mr B 68 yr old
- Feels tired
- FBC - lymphocytosis 5 x 10^9/L

What do you do?
- Consider infection
- ? Palpable lymph nodes ? Palpable spleen
- Check if the rest of the FBC is normal.
- Repeat FBC in 3 - 6 months and request a blood film
Asymptomatic Lymphocytosis
Asymptomatic Lymphocytosis

<table>
<thead>
<tr>
<th>Lymphocyte count</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 x 10⁹/L</td>
<td>Refer to haematology for investigation</td>
</tr>
<tr>
<td>&gt;3.5 and &lt;10 x 10⁹/L</td>
<td>Repeat FBC and Blood film in 3 - 6 months:</td>
</tr>
<tr>
<td>Rest of blood count normal.</td>
<td>- If lymphocytes are lower or the same level:</td>
</tr>
<tr>
<td>No lymphadenopathy or splenomegaly</td>
<td>- no further investigation or monitoring required but repeat blood count in 1 year</td>
</tr>
<tr>
<td>&gt;3.5 and &lt;10 x 10⁹/L</td>
<td>- If lymphocytes are &gt; 10 x10⁹/L: refer to haematology for investigation</td>
</tr>
<tr>
<td>and anaemia or thrombocytopenia or lymphadenopathy or splenomegaly</td>
<td>Refer to haematology for investigation</td>
</tr>
</tbody>
</table>

See CLL advice sheet
Asymptomatic lymphocytosis

- Early CLL - Stage A
  - Normal Hb, neutrophils, platelets
  - Does not require treatment (usually)

- Immunosuppressed
  - Treat shingles with anti-viral drugs
  - May increase risk of bacterial infection
  - Annual ‘flu vaccination and consider for Pneumovax

- May be associated with increased risk of other malignancies

- Should be monitored with blood count and clinical assessment every few months initially
Case - neutropenia

- Mr B  60 year old African
  - Incidental finding of neutrophils $1.0 \times 10^9/L$
Isolated neutropenia

- The severity of neutropenia is categorised as:

  - Mild: neutrophils 1.0 - 1.5 \( \times 10^9/L \)
  - Moderate: neutrophils 0.5 – 1.0 \( \times 10^9/L \)
  - Severe: neutrophils <0.5 \( \times 10^9/L \)
Causes of Neutropenia

- Transient
- Persistent
Transient Neutropenia

- Viral infections - neutropenia usually only lasts \( \leq 2 \) weeks and there are seldom any clinical problems.

- Occasionally, the neutropenia may persist for months.
Persistent Neutropenia

- Benign ethnic neutropenia.
  - Neutrophil counts down to $1 \times 10^9/L$ are a relatively common finding in individuals of African-Caribbean or Middle Eastern descent.

- Viral infections
  - EBV, HIV, hepatitis viruses

- Autoimmune disorders
  - SLE, Rheumatoid Arthritis

- Drugs
  - A long list!

- Splenomegaly (including due to liver disease)

- Haematological diseases
  - Myelodysplasia, leukaemia, lymphoma, myeloma, B12/folate deficiency etc.)
Evaluation of a patient with neutropenia

History:
- Symptoms of recurrent infection?
- History of recurrent infections
- Drug history
- Family history of infections
- Records of past FBCs to establish the chronicity of the neutropenia
- Risk factors for HIV, TB

Examination: look for
- Signs of infection: oral mucosa, skin rashes, abscesses, lung infections, perianal/genital area
- Splenomegaly
- Other signs of causative medical problems (SLE, malignancy)
Evaluation of a patient with neutropenia

**Investigations:**
- *Repeat FBC with differential (what is the rest of the count like?)*
- *Blood film (do the cells look normal?)*
- Paul Bunnell (IMST)
- B12, folate
- Autoantibody screen & rheumatoid factor
- HIV testing if clinical risk factors are present
- Blood cultures if the patient is pyrexial (in which case send to hospital)
Neutropenia
When should I seek further advice or refer to haematology?

First check:
- How severe is the neutropenia?
- Are there any other abnormalities of the blood count?
- Does the patient have any symptoms relating to the neutropenia?
- How long has the neutropenia persisted for?

Consider referral if:
- Persistent neutropenia $<1.3 \times 10^9$/L over 6-8 weeks in Caucasian patients with no obvious cause as outlined above
- Neutropenia associated with severe and/or recurrent infection
- Neutropenia associated with other full blood count abnormalities
- Neutropenia associated with splenomegaly (NOT due to liver disease – fulfils 2 week wait criteria)
- Suspected underlying haematological disease: i.e. clinical symptoms or on blood film
## Pragmatic Classification of Anaemias based on the MCV

<table>
<thead>
<tr>
<th>Microcytic Anaemia</th>
<th>Macrocytic Anaemia</th>
<th>Normocytic Anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV &lt; 80 fl</td>
<td>MCV &gt; 100 fl</td>
<td>MCV 80 – 100 fl</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>B12 or folate deficiency</td>
<td>Myelodysplasia</td>
</tr>
<tr>
<td>Thalassaemia (α, β)</td>
<td>Hydroxycarbamide Rx</td>
<td>Recent bleed</td>
</tr>
<tr>
<td>Chronic disease (e.g. R.A.)</td>
<td>Myelodysplastic syndromes</td>
<td>Chronic diseases</td>
</tr>
<tr>
<td></td>
<td>Excess alcohol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver disease</td>
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</tbody>
</table>
54 year old woman - tired all the time

Known to have rheumatoid arthritis

Hb 108 g/L, MCV 77 fL, ESR 48 mm/hr

Serum Fe 5 µmol/l (low)

Commenced on oral iron

After 6 weeks - no improvement in symptoms or Hb

Question - is this iron deficiency?
Case - Anaemia (2)

- 67 year old man
- Pale and breathless on exertion
- Losing weight
- Liver edge palpable
- Hb 66 g/L, MCV 72 fL, MCH 23 pg
- Serum Fe 5 µmol/l, TIBC 80 µmol/l
- Ferritin 10 µg/l
- ? Refer to Haematology? (No!)
Ferritin, serum iron and TIBC

Ferritin

Serum ferritin microgram/L

U=unsaturated
### Causes of Iron-deficiency Anaemia

<table>
<thead>
<tr>
<th>Cause</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menstrual bleeding</td>
<td>Most frequent cause in young women</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Diversion of iron to the fetus and placenta</td>
</tr>
<tr>
<td>Children</td>
<td>Increased demand for Fe during growth</td>
</tr>
<tr>
<td>Upper GI Bleeding</td>
<td>Cancer, varices, hiatus hernia, gastritis, HHT</td>
</tr>
<tr>
<td>Lower GI Bleeding</td>
<td>Colon Cancer, angiodysplasia</td>
</tr>
<tr>
<td>Intestinal malabsorption</td>
<td>Crohn’s, coeliac sprue, intestinal surgery, hookworm</td>
</tr>
<tr>
<td>Urogenital</td>
<td>Bladder cancer, prostate pathology, schistosomiasis</td>
</tr>
<tr>
<td>Factitious bleeding</td>
<td></td>
</tr>
</tbody>
</table>
Iron deficiency anaemia

- Iron deficiency anaemia is almost never due to a primary haematological pathology.
- In adults consider occult bleeding as the first differential diagnosis if menstrual bleeding +/- multiple pregnancies are not the obvious causes.
- Refer to gastroenterology / gynaecology
- Cut out the middle-man - the haematologist (who will just refer to gastro or gynae)!
Thrombocytopenia

<table>
<thead>
<tr>
<th>Normal Plt count ($x10^{9}/$)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>150-400</td>
<td>100-150</td>
<td>30-100</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>

- Consider
  - Is the low plt count acute or chronic?
  - Is it associated with other abnormalities of the blood count?
  - Has the FBC been repeated?

- Does the patient have a history suggestive of infection, autoimmune disease, or malignancy?
Thrombocytopenia

- What drugs is the patient taking (the list is endless)?

- Examine for spleen, lymph nodes, skin rashes, musculoskeletal abnormalities.

- Ask for a blood film:
  - Platelet clumping
  - May-Hegglin
  - Hypersegmented neutrophils & macrocytosis (B12 / folate deficiency)
  - Lymphocytosis etc. - ? CLL
  - Macrocytosis and Pelgeroid neutrophils - MDS
Thrombocytopenia

- If thrombocytopenia is isolated and the blood film and physical examination are unremarkable then a bone marrow examination may not be necessary.

- If patient is asymptomatic then monitoring with serial blood counts may be all that is required.

- Most patients with isolated mild thrombocytopenia do not develop clinical disease but of those that do, the commonest group of diseases that develop is autoimmune in origin.

- Consider HIV and Hepatitis C as an underlying cause of a low platelet count without other explanation.
Case - Paraprotein

- 60 year old woman
- Presents with back pain following a recent fall
- FBC, U+E, LFT, CRP, calcium, SPEP
- XR spine
Serum protein electrophoresis
Results 60 year woman with back pain

- FBC - normal
- Renal function, calcium - normal
- IgG kappa paraprotein 8 g/L
- IgA and IgM normal

- Spinal XR - “osteopenia, crush fracture L4”
Assessment of Paraprotein

- Does the patient have symptoms?
- Does the patient have clinical signs (e.g. nodes)?
- How high is the paraprotein concentration?
- What sort of paraprotein is it?:
  - IgA / IgG ~ myeloma
  - IgM / IgG ~ lymphoma
- Are the other Igs suppressed?
- Is the blood count normal?
- Are the renal function and calcium normal?

Most paraproteins are discovered incidentally and do not mean that the patient has a malignancy (they usually represent MGUS)
## MYELOMA & MGUS - Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>MYELOMA</th>
<th>MGUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow plasma cells</td>
<td>&gt; 10% on aspirate</td>
<td>&lt;10% on aspirate</td>
</tr>
<tr>
<td>Serum paraprotein</td>
<td>Variable concentration</td>
<td>IgG usually &lt; 20 g/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IgA usually &lt; 10 g/l</td>
</tr>
<tr>
<td>BJP</td>
<td>&gt; 50% of cases</td>
<td>Rare</td>
</tr>
<tr>
<td>Immune paresis</td>
<td>&gt; 95% of cases</td>
<td>Rare</td>
</tr>
<tr>
<td>Lytic bone lesions</td>
<td>Often present</td>
<td>Absent</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Frequent</td>
<td>Absent</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Frequent</td>
<td>Absent</td>
</tr>
<tr>
<td>Hypercalcaemia</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>May be present</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Monoclonal Gammopathy of Undetermined Significance (MGUS)

- Monoclonal gammopathy found in:
  - 1% of people > 50 yrs
  - 10% of people > 80 yrs

- Clinical features of MGUS
  - No symptoms / signs
  - Incidental chance finding
  - ~10% will develop myeloma

- How to monitor?
  - 6 monthly FBC, U/E, calcium, protein electrophoresis and paraprotein quantitation.
  - Refer to haematology if Hb falling, urea or calcium rising, paraprotein rising, bone pain, lymphadenopathy
Polyclonal Hypergammaglobulinaemia

- The finding of raised globulins without a monoclonal band is **not** an indication of myeloma.

- Causes of polyclonal $\uparrow$ $\gamma$ globulins:
  - Chronic infection
  - Chronic liver disease
    - Cirrhosis
    - Autoimmune hepatitis
  - HIV infection
  - Connective tissue disease (Sjogren’s syndrome, SLE, RA)
  - Angioimmunoblastic lymphadenopathy
  - Tropical splenomegaly syndrome