QUESTION 9 Bruising

A previously well 37-year-old man presents with lethargy and easy bruising over several weeks. Physical examination is unremarkable apart from occasional bruises.

His full blood examination shows:
- haemoglobin 125 g/L [128-175]
- mean cell volume (MCV) 82 fL [80-97]
- white cell count 8.8 x 10^9/L [3.9-12.7] (normal white cell differential)
- platelets 1060 x 10^9/L [150-396]

His blood film is shown below.

The most likely diagnosis is:
A. essential thrombocythaemia.
B. occult haemorrhage.
C. primary myelofibrosis.
D. occult carcinoma.
E. chronic myeloid leukaemia.

**Differentials for elevated platelet count**

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<thead>
<tr>
<th>Primary</th>
<th>Essential thrombocythaemia</th>
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<tbody>
<tr>
<td></td>
<td>Another myeloproliferative disorder –</td>
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<tr>
<td></td>
<td>a) Polycythæmia Rubra vera</td>
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<td>b) CML</td>
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<thead>
<tr>
<th>Reactive</th>
<th>Iron deficiency anaemia</th>
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<td>Haemorrhage</td>
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<td>Severe haemolysis</td>
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<td>Trauma</td>
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<td>Infection, inflammation</td>
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<td>Malignancy</td>
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Essential thrombocythaemia
Definition: persistent elevation of peripheral blood platelet count as a result of increased marrow production in the absence of a systemic cause of thrombocytosis

Clinical features
- Thrombosis - both arterial (peripheral vessels with gangrene of toes, coronary and mesenteric arteries) and venous (Budd-Chiari syndrome, DVT)
- Asymptomatic (20%)
- Excessive haemorrhage (spontaneously or traumatic)
- Splenomegaly (30%) and in other atrophied because of infarction but massive splenomegaly is more characteristic of other myeloproliferative disorders

No clonal marker for this disorder, clinical criteria have been proposed to distinguish it from other chronic myeloproliferative disorders which may also present with thrombocytosis

Laboratory features
- Platelets are >1000 X 10^9/L
- Raised red or WCC (30%)
- Blood film: platelet anisocytosis with circulating megakaryocyte fragments
- Autoinfarction of spleen causes changes in red cells – target, Howell/Jolly bodies
- JAK2 mutation present in 30 – 50%
- Serum uric acid raised
- Serum LDH raised
- Bone marrow: hypercellular with increased number of megakaryocytes

Treatment
1. Chemotherapy
2. Hydroxyurea to maintain platelet count below 600 X 10^9/L
3. Alpha interferon and oral anagrelide
   - Effective but more S.E
4. Aspirin (75mg) daily
   - Except those with haemorrhage

Prognosis
- Median survival more than 20 years
- Main cause of morbidity and mortality: thrombosis and haemorrhage
- Transformation to AML may occur
Chronic myeloid leukaemia

Lab findings

- Raised WCC (50 X 10^9/L) – mainly neutrophils and myelocytes
- Basophils prominent
- Platelet count may be raised
- Raised serum uric acid
- Bone marrow aspirate: hypercellular with raised myeloid/erythroid ratio
- Cytogenetic analysis of bone marrow cells:
  a) Philadelphia chromosome in > 95% of metaphases
  b) BCR – ABL fusion gene is detectable by FISH and its RNA product by PCR.

Myelofibrosis

Lab findings

- Normocytic anemia
- Leucocytosis and thrombocytosis with circulating megakaryocyte fragments occur early
  - Leucopenia and thrombocytopenia occur later
- Blood film: red cell poikilocytosis with teardrop forms and circulating red cell and white cell precursors

1 Haematology at a Glance Mehta and Hoffbrand CML
• Serum LDH is raised
• Bone marrow aspirate is usually unsuccessful (‘dry tap’)
  - Trephine biopsy shows increased cellularity, increased megakaryocytes and fibrosis

Answer: A Essential