QUESTION 66

A 28yo man presents with a fractured ankle requiring surgical fixation.

Full blood examination shows:

- **Haemoglobin**: 115g/L [128-175]
- **Red cell count**: 5.6x10^{12}/L [4.0-5.7]
- **Mean cell volume**: 62fL [80-97]
- **White cell count**: 12.5x10^{9}/L [3.9-12.7] (mild neutrophilia)
- **Platelet count**: 390x10^{9}/L [150-396]
- **Serum ferritin**: 95ug/L [15-325]

Haemoglobin (Hb) studies show:

- **HbA2**: 5.2% [1.8-3.5]
- **HbF**: 1.2% [0-2.0]
- **HbH preparation**: no HbH bodies seen
- **Hb electrophoresis**: no abnormal Hb bands seen

The most likely explanation for his anaemia is:

A. B-thalassaemia trait
B. Chronic blood loss
C. Anaemia of chronic disease
D. Congenital sideroblastosis
E. Sickle cell trait

**THALASSAEMIA**

- Hereditary disorder, autosomal recessive
- Reduced or absent production of one or more globin chains
- Most pts with alpha or beta thalassaemia minor (trait) are asymptomatic
- More common in Mediterranean populations

**Beta Thalassaemia**

- Impaired production of beta globin chains → relative excess of alpha chains
- Excess alpha globin chains are unstable, incapable of forming soluble tetramers and precipitate within the cell → shortened RBC lifespan
- Degree of alpha globin chain excess determines the severity of clinical manifestations

**Major:**
- Two defective B-globin genes
- Severe, transfusion dependent anaemia
- Symptoms emerge late in 1st year of life when HbF levels decline
Signs/Symptoms:
- Chronic anaemia – pallor, irritability, growth retardation
- Stigmata of haemolysis
- Ineffective erythropoiesis – bony abnormalities, hepatosplenomegaly
- Fe overload – effects endocrine organs, heart
- Profound microcytic anaemia, bizarre red cell morphology
- Patients with higher levels of HbF have less severe disease
- Patients with co-inheritance of alpha thalassaemia also have milder disease due to less imbalance between alpha and beta chains
- Rx = transfusion for Hb 90-100, Fe chelation, allogenic haematopoietic transplantation

Minor:
- One normal beta globin allele and one beta thalassaemic allele
- Rarely symptomatic
- Hypochromic, microcytic RBCs
- Microcytosis usually much more profound and the anaemia milder than seen in Fe deficiency
- HCT >30%, MCV <75fL
- In Fe deficiency MCV rarely low without low HCT also
- RDW usually normal (increased in Fe deficiency)
- Splenomegaly in 15-20%
- Target cells on film
- Reticulocytes normal or slightly increased
- >90% haemoglobin will be HbA
- Elevated HbA2 diagnostic of thalassaemia (but normal HbA2 does not exclude thalassaemia trait)
- **HbA2 = alpha-delta tetramers, usually ~4-6% in thalassaemia trait**

<table>
<thead>
<tr>
<th>B-Thalassaemia Minor</th>
<th>Fe Deficiency</th>
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<tbody>
<tr>
<td>Microcytic MCV significantly reduced</td>
<td>Microcytic MCV mildly reduced</td>
</tr>
<tr>
<td>HCT &gt; 30%</td>
<td>HCT &lt; 30%</td>
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<tr>
<td>RDW normal</td>
<td>RDW increased</td>
</tr>
<tr>
<td>Ferritin normal</td>
<td>Ferritin reduced</td>
</tr>
<tr>
<td>Target cells</td>
<td>Microcytic, hypochromic only</td>
</tr>
<tr>
<td>Elevated HbA2</td>
<td>Normal HbA2</td>
</tr>
</tbody>
</table>

Sideroblastic Anaemia

- Hereditary or acquired
- Mitochondria inheritance (X-linked)
- Acquired due to toxins, drugs, nutritional deficiencies
- Ringed sideroblasts seen in bone marrow
- Ferritin increased, decreased TIBC, increased transferring saturation
- MCV normal or increased but can occasionally be low
HbH is for alpha thalassaemia when 3 of 4 alpha alleles are defective. Hb electrophoresis is used for diseases such as sickle cell.

Answer: A