Question 35
A 65-year-old man with a history of osteoarthritis and mild chronic obstructive pulmonary disease presents with several days of nausea and vomiting and is now confused, febrile and icteric. He has extensive bruising and some oral mucosal bleeding. His medications are intermittent piroxicam and a salbutamol inhaler.

His full blood count shows:

- haemoglobin: 85 g/L [120-155]
- mean corpuscular volume (MCV): 101 fL [80-95]
- white cell count: 10.2 x 10^9/L [3.5-9.5]
- differential:
  - neutrophils: 8.5 x 10^9/L [1.5-6.0]
  - lymphocytes: 1.2 x 10^9/L [0.7-3.2]
  - monocytes: 0.4 x 10^9/L [0.2-0.6]
  - eosinophils: 0.1 x 10^9/L [0-0.4]
- platelet count: 14 x 10^9/L [130-330]
- reticulocyte count: 125 x 10^9/L [8-104]

Blood film as shown in the photograph below.

Direct Coombs' test: negative

Coagulation studies:
- prothrombin time-international normalised ratio (PT-INR): normal
- activated partial thromboplastin time (APTT): normal
- fibrinogen: normal
- D-dimers: normal
Biochemistry:

creatinine 0.29 mmol/L [0.07-0.13]
urea 30.0 mmol/L [2.0-8.5]
bilirubin 56 μmol/L [<21]
lactate dehydrogenase (LDH) 950 U/L [<250]

The most likely diagnosis is:
A. gram-negative sepsis.
B. leptospirosis.
C. disseminated intravascular coagulation.
D. thrombotic thrombocytopenic purpura.
E. piroxicam toxicity.

Answer: D

Key points from the investigation findings:

1. Anemia with reticulocytosis
   - Hb 85
2. Hemolysis
   - LDH ↑ 950
   - Bili ↑ 56
   - Reticulocytes ↑ 125
3. Unlikely to be autoimmune
   - Direct Coombs negative
4. Likely to be microvascular traumatic hemolysis
   - Blood film shows red cell fragmentation
5. No coagulation abnormalities
   - Can’t be DIC
6. Associated thrombocytopenia

Note:
- Hemolysis due to bacteremia (eg gram neg sepsis) is usually mild and transient
THROMBOTIC THROMBOCYTOPENIC PURPURA

- Fulminant often lethal disorder
- May be initiated by endothelial injury and subsequent release of vWF and other procoagulants from endothelial wall
- Severe Coombs negative haemolytic anemia with schistocytes, thrombocytopenia and minimal activation of the coagulation system

**Causes:**
1. pregnancy
2. Metastatic cancer
3. Mitomycin C
4. High dose chemo
5. HIV
6. Certain drugs eg ticlodipine

**Clinical features:**
- Classic pentad
  1. haemolytic anaemia with schistocytes (fragmented RBCs) and intravascular hemolysis
  2. Thrombocytopenia
  3. Diffuse and non-focal neurological findings
  4. Impaired renal function
  5. fever
- minimal activation of coagulation – abnormalities in coags suggests other diagnosis
- neurological and renal impairment only occur with plt counts <20-30
- neurological symptoms develop in >90% whose disease ends in death
- commences with change in mental state can include seizure, hemiparesis, aphasia, coma
- severity can be estimated by severity of anaemia and thrombocytopenia and LDH

**Pathogenesis**
- due to deficiency in activity of ADAMTS 13 (metalloproteinase)
- normal plasma constituent
- cleaves ultra high molecular weight forms of vWF
- usually get an inhibitory antibody

**Treatment**
- exchange transfusion or plasmapheresis
HEMOLYTIC UREMIC SYNDROME
- disease of infancy and early childhood
- resembles TTP

Clinical features:
1. Fever
2. Thrombocytopenia
3. Microangiopathic haemolytic anaemia
4. Hypertension
5. Acute renal failure

- Sometimes preceded by febrile or viral illness
- As in TTP there is no DIC
- In contrast to TTP isolated to kidneys – thrombi in afferent arterioles and glomerular capillaries
- Neuro symptoms are rare

Treatment
- No treatment except for dialysis for renal failure
- Mortality 5%
- 10-50% have chronic renal impairment