Examination of the blood film confirms the low platelet count and also shows the presence of spherocytes as indicated by the raised MCHC.

Presentation

Male (73 years old)
Multiple Instrument alarms (with WBCs in particular)

- WBC: 51.9* (10^3/mm3)
- RBC: 2.48 (10^6/mm3)
- HGB: 8.0 (g/dL)
- HCT: 20.9 (%)
- MCV: 84 (fL)
- MCH: 32.0 (pg)
- MCHC: 38.1 (g/dL)
- PLT: 18* (10^3/mm3)

Differential

- Neutrophils: 0.7%
- Lymphocytes: 7.1%
- Metamyelocytes: 1.4%
- Myelocytes: 0.7%
- Blasts: 90.1%

Diagnosis

Acute promyelocytic Leukemia (variant)
The patient presented as a haematology emergency – sepsis and haemorrhagic disease.
Acute Promyelocytic Leukaemia – In Brief
An overview of the clinical features, laboratory findings and treatment

Introduction
Acute Promyelocytic Leukaemia (APL) is a differentiated variant of Acute Myeloid Leukaemia (AML) that usually (>95%) carries a t(15:17) chromosomal translocation. It accounts for around 10% of AML cases and has a different treatment protocol from AML.

Clinical Presentation
The disease can be seen in either gender and at any age but is most common in middle-age. It frequently presents with a severe haemorrhagic syndrome.

• The following features may be seen:
  • Symptoms of anaemia- leading to fatigue, pallor, tachycardia, dyspnoea
  • Fever and infections due to neutropaenia
  • Symptoms relating to abnormal platelet function and or coagulopathy – severe bleeding and or ecchymosis
  • Non-specific such as pain, slow healing and unexplained weight loss

Laboratory Findings
Laboratory investigations, besides FBC/Differential and blood film morphology, include the following:
• Bone Marrow Aspirate and Trephine
• Immunophenotyping
• Cytogenetic and mutation analysis
• Biochemistry (LFTs, U+E, Calcium, LDH)
• Coagulation Screening/ D-Dimer

Haematological investigations normally show normochromic normocytic anaemia and thrombocytopenia on presentation. WBC is usually increased with a variable number of blast cells. The condition is morphologically identified as M3 by the FAB classification. The bone marrow is hypercellular, typically containing many leukaemic blasts. Morphology, immunophenotyping and genetic analysis confirm the diagnosis. Coagulopathy is often present in APL. Biochemistry tests are performed as a baseline prior to treatment. Raised Uric Acid and/or LDH may be present.
Acute Promyelocytic Leukaemia Continued

Genetics
The somatic mutation that causes acute promyelocytic leukemia involves two genes, the PML gene on chromosome 15 and the RARα gene on chromosome 17.

A rearrangement of genetic material (translocation) between chromosomes 15 and 17, written as \( t(15;17) \), fuses part of the PML gene with part of the RARα (retinoic acid receptor α) gene. The protein produced from this fused gene is known as PML-RARα.

The RARα gene controls the maturation of WBCs which is blocked in APL.

Treatment
Treatment consists of supportive therapy (maintaining haemoglobin and platelet count, treatment of infection and treatment of DIC (FFP)) and specific chemotherapy.

Treatment differs from that of other acute myeloid leukaemia with the addition of all-trans retinoic acid (ATRA), often combined with arsenic trioxide or anthracycline.

Prognosis
APL can be aggressive on presentation but cells are relatively sensitive to chemotherapy. The addition of ATRA and other targeted therapies gives a >90% prospect of remission.

This Month’s Q&A Morphology Tips
Quick tips for making manual blood films. Problems and answers

- Blood film extends right to the end of the slide
- Blood drop is too large or too small an angle between slide and spreader
- Blood film is too short
- Blood drop too small or too large an angle between slide and spreader
- The blood film is irregular with ridges and a long tail
- The edge of the spreader is dirty or chipped
- Holes appearing in the spread
- The slide is dirty/ greasy. Nb. Sometimes it can be lipaemia in the sample

Bibliography
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QSP April 2020
Acute promyelocytic leukaemia: from highly fatal to highly curable
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