Acute Promyelocytic Leukemia

Although acute promyelocytic leukemia (APL) is relatively rare, it is a medical emergency that is important for the intensivist to recognize. APL is a variant of acute myeloid leukemia (AML) that is highly curable (80-90%) but carries a significant early mortality risk due to bleeding and thrombotic complications. Outcomes can be improved through early recognition, prompt initiation of definitive treatment, and aggressive management of coagulopathy.

Pathologic Diagnosis

Definitive diagnosis = Presence of PML-RARA fusion gene and/or the t(15;17) translocation.

While awaiting molecular confirmation, a presumptive diagnosis of APL can often be made based on the presence of atypical promyelocytes on the peripheral smear.

- Hypergranular variant: Granular cytoplasm visible on light microscopy, auer rods may be present
- Microgranular variant: Granules not visible on light microscopy

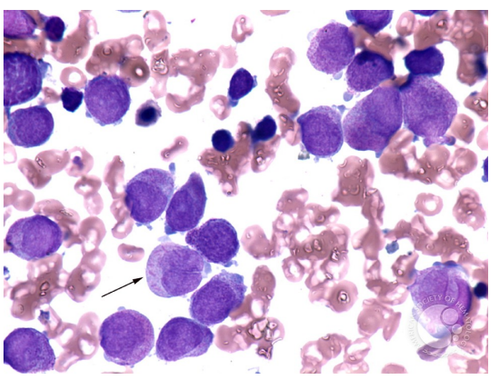

Image credit: American Society of Hematology Image Bank

Clinical Presentation

Presenting Symptoms:

May be variable depending on the extent of cytopenia and include the following:

- Systemic symptoms: Fever, generalized malaise, fatigue, weakness
- Bleeding complications: Easy bruising, petechiae, epistaxis, gingival bleeding, menorrhagia

WBC Count:

Patients frequently present with a low WBC with few promyelocytes in the peripheral circulation. If presenting WBC is > 10 x 10^9/L, patients are at a higher risk of complications and early death.

Key Features:

Patients often present with evidence of hyperfibrinolysis and DIC:

- Thrombocytopenia and schistocytes
- Elevated INR and PTT
- Low fibrinogen

Life-threatening bleeding complications including intracranial or pulmonary hemorrhage may occur.

Thrombosis may also be observed

Management

1

Start Treatment Immediately:

Therapy should be started ASAP, even if a definitive diagnosis has not been made. Your local Hematologist as well as the closest cancer center with a leukemia program should be contacted urgently.

Treatment = all-trans retinoic acid (ATRA) plus either arsenic trioxide (ATO) or anthracycline-based chemotherapy.

2

Coagulopathy is a life-threatening emergency:

Patients must be closely monitored:

- Check CBC, INR/PTT, fibrinogen Q6H

Administer blood products as needed to meet the following targets:

- Fibrinogen > 1.5g/L , INR < 1.5, and platelets > 20 to 30 x 10^9/L (> 50 x 10^9/L in bleeding patients).

3

Recognize differentiation syndrome:

After treatment is started, promyelocytes rapidly mature leading to a systemic inflammatory response characterized by the following:

- Onset is usually within 2 weeks of chemotherapy
- Fever, hypotension, hypoxemia, lung infiltrates, pleural/pericardial effusions, ascites, elevated bilirubin, and acute kidney injury

Differentiation syndrome may occur in up to 25% of patients. When suspected, treatment with steroids should be initiated:

- Dexamethasone 10mg BID
- Low-dose prophylactic dexamethasone (2.5mg BID) may be considered for patients with starting WBC > 5 x 10^9 in consultation with the treating Oncologist

COIN