Case Presentation No. 075
Session 4. Myelodysplastic Syndrome

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Clinical Summary

- 64 year-old male with untreated diabetes
- Presented with new-onset decreased exercise tolerance of two months duration
- Past Medical History:
  - Negative previous hematologic disorder
- Physical Examination:
  - No splenomegaly
Complete Blood Count

- Pancytopenia

- Peripheral Smear:
  - RBC:
    - Mild anisocytosis and macrocytosis
    - No poikilocytosis
  - WBC:
    - Predominantly mature neutrophils and lymphocytes
    - No dyspoiesis
    - No blasts

- WBC $2 \times 10^3/\mu\text{L}$
- RBC $1.84 \times 10^6/\mu\text{L}$
- Hgb $6.8 \text{ g/dL}$
- Hct $19.5 \%$
- MCV $106 \text{ fL}$
- Platelet $22,000/\mu\text{L}$

*Differential:*
- 55% PMN, 32% Lymph, 12% Mono, 1% Eos
• No aspirate smear

• Hemodilute flow sample

• **Touch Prep:**
  – Dyserythropoiesis
  – Two possible megakaryoblasts
  – No other blast-like cells identified

• **Iron Stain:** Increased stores without ringed sideroblasts
Immunohistochemistry
Myeloperoxidase
Cytogenetics

- Multiple Complex Abnormalities:
  - Monosomy 2, 5, 7 and 15
  - Trisomy 8
  - Unbalanced translocation b/t 17p and 2q
  - Additional chromosomal material of unknown origin replacing 7q (of the remaining 7) and on 17q and 12p
  - Two to five marker chromosomes of unknown origin
Differential Diagnosis of Myeloid Disorders with fibrosis

- Chronic Myeloproliferative Disorders
- Acute Megakaryoblastic Leukemia (M7)
- Myelodysplastic Syndrome
- Acute Panmyelosis with Myelofibrosis
Differential Diagnosis

- Chronic Myeloproliferative Disorders
  - No splenomegaly, no leukoerythroblastic smear

- Acute Megakaryoblastic Leukemia (M7)
  - Blasts >20% could not be established

- Myelodysplastic Syndrome

- Acute Panmyelosis with Myelofibrosis
Myelodysplastic Syndromes

• Group of clonal disorders characterized by peripheral cytopenias and dysplasia
  – Elderly patient without organomegaly
  – Slow onset, with chronic progressive course to BM failure

• MDS “with fibrosis”
  – Fibrosis is not a typical feature of MDS
  – Is it a distinct clinico-pathological entity?

W.H.O. Classification of Tumors. IARC Press. 2001
Acute Panmyelosis with Myelofibrosis

• A rare *acute myeloid disorder* with an unfavorable prognosis

• Definition:
  – “An acute pan-myeloid proliferation with accompanying fibrosis of the marrow”

• Clinical Features:
  – Marked pancytopenia without splenomegaly
  – *Abrupt onset, rapidly progressive*

W.H.O. Classification of Tumors.
IARC Press. 2001
Morphologic Overlap

• Hypercellular marrow with variable degrees of myeloid hyperplasia

• Dysplasia
  – MDS:
    • Dyserythropoiesis in virtually all
    • Dysmegakaryopoiesis common
  – APMF:
    • Granulocyte dysplasia common
    • Dysmegakaryopoiesis characteristically prominent

• Moderate-marked increased in reticulin fibrosis
Acute Panmyelosis with Myelofibrosis: an entity distinct from acute megakaryoblastic leukemia

- The true nature of APMF is not completely understood

- Some believe it is a variant of AML, others an equivalent to AMKL and yet others an acute variant of MDS
Acute Panmyelosis with Myelofibrosis: an entity distinct from acute megakaryoblastic leukemia

• Comparison of 11 cases of AMKL and 4 cases of APMF
  
  – Higher frequency of BM blasts in AMKL than in APMF
    • Mean of 63% vs. 21%

  – The blasts in all cases of AMKL stained strongly for CD42b and negative for MPO, a finding consistent with their megakaryoblastic nature
    • Paralleled flow cytometric results, i.e. Positivity of CD61 and CD41 in the majority of the blasts

  – In APMF, the blasts did not express significant megakaryocytic reactivity, but were identifiable by CD34
    • In the biopsy, blasts were less numerous overall and the background was more cellular and polymorphic
Myelofibrosis in Primary Myelodysplastic Syndromes: A clinico-morphological study of 10 cases

• Important clinical differences exist between APMF and MDS-F, particularly the abrupt onset of APMF and its shorter survival

• It is prudent to maintain these two diagnostic entities separate and to consider APMF as a variant of AML as defined by the WHO
• It is important to recognize that APMF is an acute process and has sufficient number of blasts, ≥20%, to be considered an AML.

• APMF can be distinguished from the fibrotic form of MDS by its slow onset, chronic course, ≤20% blasts and a much less pronounced marrow fibrosis.

• The BM fibrosis in APMF is reactive, evoked by the megakaryocytic cell line which secretes transforming growth factor – β and thereby stimulating a fibroblast proliferation.
Acute Panmyelosis with Myelofibrosis: Clinical, Immunophenotypic and Cytogenetic Study of Twelve Cases
Suvajdzic, et. al. Leukemia and Lymphoma. 2004

- The cytogenetic analyses did not establish any characteristic chromosomal abnormalities.

- Clonal changes frequent (found in 8/10 patients analyzed)
  - Two had complex karyotypes with >5 chromosomes involved
  - Structural abnormalities were present in all, most frequently involving ch. 12
  - Del (5q) and del (12p), abnormalities commonly associated with MDS were each found in one patient
Summary

- 64 y/o male with 2-mo history of symptoms
  - In the absence of a prior CBC, whether this represent acute onset cannot definitely be ascertained
- No splenomegaly
- Pancytopenia with macrocytic anemia
- Hypercellular, fibrotic marrow with distinct megakaryocytic atypia and increased blasts
- Multiple complex abnormalities on CG

- In conclusion, this case highlights an interesting constellation of findings infrequently encountered in the marrow. It also demonstrates some of the diagnostic difficulties faced by hematopathologists in separating MDS with fibrosis and APMF, entities which share numerous clinico-pathologic features.