Myelodysplastic Syndrome

Case 158

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Clinical History

- 86 year old man
- Persistent borderline anemia and thrombocytopenia.
- His past medical history was significant for coronary artery disease, stroke and epilepsy.
- A bone marrow study was performed to evaluate his hematological status.
Hematology Lab Results

• **CBC:**
  - Hgb: 13.0 g/dL
  - Hct: 38.1%
  - MCV: 88.3 fL
  - RDW: 15.7%
  - WBC: 7.7 x10^9/L
  - PLT: 102 x10^9/L

• **WBC Differential (%):**
  - Neutrophils 63
  - Lymphocytes 21
  - Monocytes 13
  - Eosinophils 2
  - Basophils 1
  - NRBC: 0
  - Blast: 0
Bone Marrow Aspirate and Biopsy

Bone Marrow Smear
600X
45,X,-Y,add(21)(q22) [16]/46,XY [4]
Image indicates 3 signals for AML1
Possible t(1;21)(p35-36;q22)
The Proposed Diagnosis

• Slightly hypercellular bone marrow (40%) with no morphologic or immunohistochemical features of myelodysplasia.

• Clonal cytogenetic abnormality of uncertain clinical significance.
Follow Up

Four years later, this patient developed high grade MDS or AML and died.

Bone Marrow Biopsy

Myelobasts in Peripheral Blood (10-15%)
The Unique Features

- Unexplained persistent cytopenia.
- No clear morphologic evidence of MDS.
- Definitive clonal cytogenetic abnormalities.
- Unclassifiable by either WHO or FAB classification system.
- Progression to overt MDS/AML.
Pertinent Questions

• Prevalence ?
• Clinical outcome ?
• Explanations ?
• What to do ?
Recurrent Chromosomal Abnormalities in Patients with Morphologically Unremarkable Bone Marrows

1994-2000

7514 BMs with Cytogenetic Studies

55 Patients

- Del(20q) or monosomy 20: 18%
- Monosomy 7, der(1;7), del(7q): 15%
- Trisomy 8: 9%
- Del(13q): 4%
- Del(13q) or a translocation involving 5q: 7%
- Del(5q) or a translocation involving 5q: 7%
- Complex: 20%
- Other (including +15): 27%

The Clinical Outcome

Patients (55)

Dead (22)  20 months F/U  Alive (32)

Possible Explanations

- The chromosomal abnormalities precede the detectable bone marrow abnormalities.
- Amount of disease in the bone marrow is minimal.
- Inadequate bone marrow sampling for morphologic component.
Cytogenetic Abnormality ≠ Malignancy

• A fleeting abnormality.
• May not associate with hematological malignancy, e.g. -Y, +15.

A **BM cytogenetic analysis is necessary** in the diagnostic evaluation of patients with persistent unexplained cytopenias even if the bone marrow appears morphologically unremarkable.

An abnormal cytogenetic result **should not** be automatically equated to a malignant process.

**Continued follow-up** is critical.
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Identical fusion transcript associated with different breakpoints in the AML1 gene in simple and variant t(8;21) acute myeloid leukemia. de Greef GE, et. al. Leukemia. 1995, 9(2):282-7


WHO Pathology and Genetics : Tumors of Haematopoietic and Lymphoid Tissue. 2001