Case # 238

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Clinical History

- 54 year-old woman with routinely discovered thrombocytosis of $774 \times 10^9/l$.
- WBC: $7.4 \times 10^9/l$ (N 74%; L 23%; other 3%).
- Hb: 13.6 g/dl (MCV 92 fl).
- Treated with HU. Six years later, she developed secondary AML and is currently in remission post induction chemotherapy.
Six years later pt. developed secondary AML
Flow cytometry: blasts pos. with CD34, CD117, CD13, CD33, MPO +/-
No histiocytic or lymphoid antigens. Cytogenetics not available.
MDS/MPD associated with 5q- and JAK2 mutation

Thrombocytosis plus granulocytic proliferation in the bone marrow
• An unusual variant of MDS/MPD characterized by isolated 5q- abnormality in association with a JAK2-V617F mutation

• Frequency of JAK2 mutations is higher than that seen in the non-MPD-like 5q-syndrome

• Molecular analysis Bcr-Abl negative


Ingram et al: The JAK2 V617F mutation identifies a subgroup of MDS patients with isolated deletion 5q and a proliferative bone marrow. *Leukemia* 2006;20:1319-1321
Pathophysiology

- JAK2-V617F-negative 5q- positive ancestor represents a possible mechanism
- JAK2 as a secondary genetic event in the background of preexisting clonal hematopoiesis

Dr. Alan List, personal communication


- Erythropoietin independent colony formation (EEC): all colonies were JAK2 mutant
- All were negative for 5q-
- Argues for discordant clones
A candidate for provisional entity status within the MDS/MPD, WHO group because:

- True overlapping MDS/MPD
- Specific treatment (Lenalidomide)
- Can be reproducibly diagnosed (?)

Other member(s)
- RARS-T
- i(17)q syndrome ?
- CMML with thrombocytosis ?
- Other rare cases
Semi-molecular Classification

**JAK2 positive**
- Classical MPDs
- RARS-T
- 5q- myeloproliferative

**JAK2 negative**
- MDS/MPD
  - CMML
  - aCML
  - JMML
  - [i17q]