Myeloid neoplasm with $PCM1$-$JAK2$ presenting with hepatosplenomegaly

Case 376

Magdalena Czader, MD, PhD
Indiana University
Indianapolis, IN
Clinical history

- 13-year-old Caucasian male with a history of ulcerative colitis
- Presented with progressive hepatosplenomegaly and underwent liver biopsy as a work-up for possible primary sclerosing cholangitis or autoimmune hepatitis
- CBC:
  - WBC 13x10^9/L with eosinophilia (3.3x10^9/L)
  - Hemoglobin 11.2 g/dL
  - MCV 77 fL
  - RDW 17.3%
  - Platelet count of 187x10^9/L
Prominent eosinophilia
46,XY,t(8;9)(p22;p24)[21]/Nonclonal[2]/46,XY[2]
Proposed diagnosis

Myeloid neoplasm with *PCM1-JAK2*

2016 WHO classification:

Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of *PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2*

Provisional entity: Myeloid/lymphoid neoplasms with *PCM1-JAK2*
**PCM1-JAK2 rearrangement**

**Pericentriolar Material 1 (PCM1)**
- Localized in cytoplasmic granules-centriolar satellites
- Recruits proteins necessary for centrosome replication
- Microtubule organization
- Blocking with antibodies or siRNA leads to disorderly centrosome organization

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*PCM1*
- Coiled-coil domains

*PCM1-JAK2*
- SH2
- JH2
- PTK domain

*JAK2*
- SH2
- JH2
- PTK domain

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Dammermann et al. Dev Cell 2004
Bousquet et al. Oncogene 2005
Murati et al. Leukemia 2005
**Protrated**

- **JAK2 mutations**
  - Decreased autoregulation
  - Hypersensitivity to growth factor

  **STAT5**

  - PV, PMF, ET

**Aggressive**

- **PCM1-JAK2**
  - Increased oligo/dimerization
  - Growth factor independent

  **STAT5**

  - CEL, aCML, MDS/MPN-U, AML, ALL

Other partner genes: ETV6, BCR, SSBP2, PAX5, SEC31A

Adopted from Smith & Fan Human Pathol 2008
Diverse presentations of myeloid and lymphoid neoplasms with \textit{PCM1-JAK2}

MPN
PMF, PMF in transformation, CEL

MDS/MPN
aCML, MDS/MPN-U

Acute Leukemias
AML including erythroleukemia, myeloid sarcoma, B and T-ALL/LBL

Reiter et al. Cancer Res 2005
Murati et al. Leukemia 2005
Patterer et al. Ann Hematol 2013
Bain and Ahmad Br J Haematol 2014
Song et al. Ann Lab Med 2016

*Rare case of T cell lymphoma
Diverse presentations of myeloid and lymphoid neoplasms with *PCM1-JAK2*

- 35 cases
- 30 males
- Median age 47 (range 12-75 years)

- CBC:
  - Variable leukocytosis: 11.8-435x10⁹/L
  - Left shift
  - Frequent eosinophilia

Reiter et al. Cancer Res 2005
Murati et al. Leukemia 2005
Patterer et al. Ann Hematol 2013
Bain and Ahmad Br J Haematol 2014
Song et al. Ann Lab Med 2016
Common features of myeloid neoplasms with PCM1-JAK2

- Male predominance
- Hepatosplenomegaly
- Hypercellular bone marrow
- Bone marrow fibrosis
- Eosinophilia
- Prominent erythropoiesis with left shift
- Frequent transformation to acute leukemia

- Complete and partial responses to ruxolitinib (rare cases reported)

Reiter et al. Cancer Res 2005
Murati et al. Leukemia 2005
Patterer et al. Ann Hematol 2013

Bain and Ahmad Br J Haematol 2014
Lierman et al. Blood 2012
Rumi et al. JCO 2013
Schwaab et al. Ann Hematol 2015
Panel diagnosis

Myeloid/lymphoid neoplasm with $PCM1$-$JAK2$