A Case of a De Novo JAK2 V617F Myeloproliferative Neoplasm Presenting After Treatment of Core Binding Factor Acute Myeloid Leukemia

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PATIENT BACKGROUND

- 45-year-old woman without significant prior medical history presented to her PCP with night sweats and spontaneous bruising
- Labs at diagnosis showed anemia, thrombocytopenia, leukocytosis, and 32% circulating myeloid blasts
- Expedited work-up returned consistent with Acute Myeloid Leukemia with CBFB/inv(16)(q22): Core Binding Factor AML, ELN 2022 favorable risk

INITIAL DIAGNOSIS: BONE MARROW BIOPSY

Morphology

- Hypercellular bone marrow with involvement by acute myeloid leukemia (blasts 69% of cells by aspirate smear differential)

Cytogenetics

- CBFB/inv(16)(q22) rearrangement DETECTED
- Extra copy of RUNX1T1/8q22 locus DETECTED (low level clone)

Molecular

- KIT (NM_000222.3) VAF: 30.30%
- RUNX1 (NM_001754.5) VAF: 3.90%

TREATMENT COURSE

- Induction
  - Daunorubicin 60 mg/m2 + cytarabine 100 mg/m2 + gemtuzumab ozogamicin 4.5 mg (one dose), achieving a complete remission
- Consolidation
  - HiDAC 3000 mg/m2/dose x 6 doses for three total cycles
  - MRD negative for Inv16 after end of cycle one of HIDAC in bone marrow
- Relapse
  - MRD detectable by peripheral blood six months after completion of consolidation
  - Azacitidine and venetoclax x 4 cycles
- Transplant
  - Myeloablative regimen with fludarabine and busulfan conditioning (FluBu4) with post transplant cyclophosphamide, mycophenolate, and tacrolimus GVHD prophylaxis

TREATMENT COMPLICATIONS

- Consolidation complicated by:
  - Appendicitis
  - Axillary adenopathy concerning for infection
  - Post-consolidation work-up notable for MRD negativity of Inv16, but new finding of JAK2^{V617F} without sufficient morphological evidence of a myeloproliferative neoplasm

TIME COURSE OF MOLECULAR AND MORPHOLOGICAL RESPONSES

	Inv16	JAK2	Morphology
Diagnosis	+	−	Diagnosed with AML with CBFB::MYH11 fusion
Post Induction	+	+	Megakaryocytes are suggestive of underlying chronic myeloproliferative process
Post Consolidation (2 mo)	−	+	Current and prior bone marrow (7/2025) show a JAK2 V617F mutation by NGS in addition to megakaryocytic atypia and peripheral thrombocytosis, suggestive of involvement by a JAK2 positive myeloproliferative neoplasm. NGS from the patients diagnostic AML sample (5/16/25) was reviewed and no evidence of a JAK2 V617F variant is seen at this time-point.
Post Consolidation (6 mo)	+	+	Frank morphologic relapse isn't appreciated, blasts appear borderline increased by CD34 stain with rare loose groups
Post Salvage	−	+	Most compatible with essential thrombocythemia
Post HSCT	−	−	No morphologic evidence of AML. Megakaryocytes are slightly increased with few larger forms.

Figure 1: Molecular and morphologic data over the treatment course.

JAK2 TREND OVER TIME

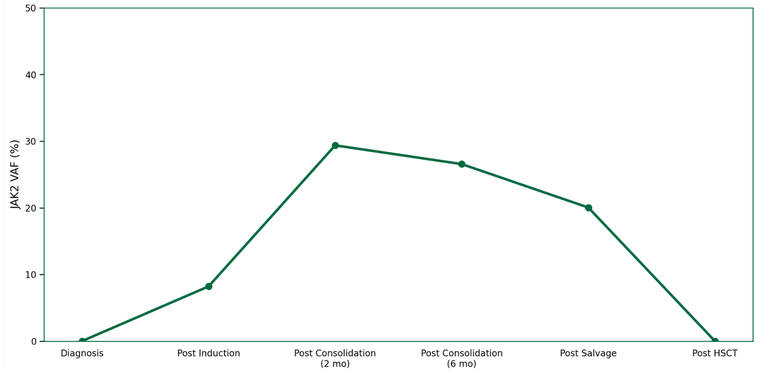


Figure 2: Variant allele measurements over the treatment course.

DISCUSSION

- Retrospective molecular sequencing of this patient's diagnostic marrow demonstrated a single cell positive for JAK2 variant, well below the threshold of reportability for this assay
- MPN arising after treatment for AML is rare; only three reported cases in the preceding decade[2–4]
- MPN driver mutations may be present decades before clinical disease emerges; somatic JAK2^{V617F} mutations have been found acquired *in utero*[1]
- This case raises the possibility that chemotherapy for an unrelated malignancy, or a myeloid malignancy itself, may create selective pressure that contributes to the development of a pre-existing mutant clone and the subsequent clinical manifestation of an overt MPN
- Opportunity for further research to understand the mechanisms and risks factors for development of a MPN after chemotherapy

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