79-year-old man with h/o MDS/MPN, treated with Epoetin, now concern for conversion to AML

CBC: WBC, 4.0; Hgb 8.6; platelet, 474.
Contributed by Dr. Frank Zhao
Bone Marrow (x100)

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Cytogenetic and Molecular Studies (Mayo)

• Normal male karyotype: 46,XY[20]. No clonal abnormality is apparent.
• No BCR/ABL fusion or JAK2 V617F mutation by RT-PCR.
• No CALR or MPL mutations by RT-PCR.
Next Generation Sequencing (NGS) (Mayo)

1. MPL: Chr1(GRCh37):g.43818291C>T; NM_005373.2(MPL):c.1756C>T; p.Gln586* (6%)

2. SRSF2: Chr17(GRCh37):g.74732959G>C; NM_003016.4(SRSF2):c.284C>G; p.Pro95Arg (40%)

3. TET2: Chr4(GRCh37):g.106156465G>T; NM_001127208.2(TET2):c.1366G>T; p.Glu456* (39%)
   Chr4(GRCh37):g.106197113_106197116del;
   NM_001127208.2(TET2):c.5446_5449del; p.Leu1816Thrfs*3 (39%)

Note: Alterations in genes with FDA-Approved Therapies for Acute Myeloid Leukemia
   FLT3: Not Detected; IDH1: Not Detected; IDH2: Not Detected.
Final Diagnosis

• Bone Marrow, Site unspecified, Aspirate, Clot Section and Biopsy:
  - MARKEDLY HYPERCELLULAR MARROW WITH PERSISTENT MDS/MPN AND MARROW FIBROSIS
Discussion

This case is interesting for its remarkable megakaryocytic proliferation with moderate reticulin fibrosis in the marrow, as the result of the patient’s long standing MDS/MPN.

Since the conventional molecular studies for JAK2, CALR, and MPL are negative, this may be considered a triple negative MDS/MPN with marrow fibrosis.

However, NGS revealed several pathogenic variants: 1) MPL: p.Gln586* (6%); 2) SRSF2: p.Pro95Arg (40%); and 3) TET2: p.Glu456* (39%), Leu1816Thrfs*3 (39%). These findings support the diagnosis of MDS/MPN with marrow fibrosis.

Unfortunately, none of the three (3) genetic alterations associated with FDA-Approved Therapies for Acute Myeloid Leukemia (FLT3, IDH1, and IDH2) were detected.