GI Bleed with Pancytopenia - A Rare Case of AML Subtype Acute Panmyelosis with Mylefibrosis (APMF)

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Background

- Pancytopenia is defined by a reduction in the counts of RBC, WBC and platelets with etiologies ranging broadly from infectious, malignant to many others.
- Given the decline, presentation can vary from anemia, infection to bleeding diathesis.
- In cases of AML, as in this case, presentation with such form becomes important to distinguish between Acute Megakaryoblastic Leukemia (AML-M7), AML with Myelodysplasia (AML-MRC) and the rare form APFM, given the standard treatment assigned to the former two.

Case Presentation

- A 63-year-old obese Caucasian male with no significant past history except for uncontrolled Type 2 DM and OSA was brought to the ER by his daughter with a chief complaint of subjective fevers, rigors and episodic dyspnea over few days.
- He denied any recent infectious exposure or malignant history, but complained of constant fatigue, lethargy, unintentional 14 pound weight loss over 3 months and lightheadedness.
- Upon ER presentation, he was found to be febrile at 103.2F with admission diagnostic labs reflecting pancytopenia with hemoglobin of 6.7, white count of 2.7 and platelets of 45,000. Physical exam was impressive for gross heme positive stools and orthostatic hypotension.
- Pan-scanning was non-diagnostic and an upper and lower GI scope didn't establish a clear source of bleeding except for mild gastritis with superficial antral and body erosions besides superficial ascending colonic ulcer.
- Despite a broad array of testing from an infectious, gastrointestinal and rheumatologic standpoint, no etiology was identified, but a subsequent bone marrow biopsy illustrated acute panmyelosis with extensive fibrosis with a dry tap and negative JAK2, V617F and CALR mutation.
- Numerous left shift myeloid and erythroid precursors were identified and mixed T and B-lymphocytes with CD34 positive T infiltrate cells were noted.
- Thereafter, patient was being evaluated for potential allogenic stem cell transplant, when he declined precipitously and transformed into acute myelogenous leukemia (AML) with blast crisis, requiring immediate induction therapy with various complications leading to his salvage chemotherapy and ultimately demise from septic shock.

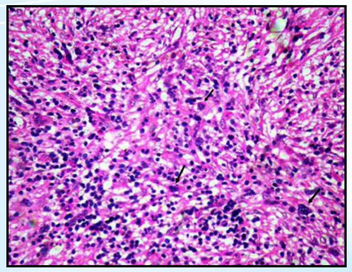

Figure 1: A pictorial representation of APFM: Classic hypercellular bone marrow with panmyeloid proliferation along-with dyspoietic megakaryocytes, immature myeloid precursors and erythroid precursors. No atypical localization of immature precursors seen with small megakaryocytes noted with hypolobated and nonlobated nuclei and dispersed chromatin. Blasts were seen dispersed as well as in clusters.

Discussion

- Pancytopenia, as defined by a reduction in number of red and white blood cells along-with declined platelet count can present as a challenge to clinicians given the broad differential it encompasses. In our patient, the combination of high-grade fever along-with hemodynamic instability and heme positive stool raised strong suspicion for infectious and/or gastrointestinal etiologies.
- Initial diagnostic studies for blood and urine cultures were negative with pan-scanning unimpressive for a focal infectious source. Given culture negativity, infectious profiles were run – including Lyme disease profile, Ehrlicia, Histolpasma, Fungal Antibodies, CMV, EBV, HIV, Parovirus, Viral Hepatitis and Babeosis – which resulted negative. Biopsies of gastric and colonic ulcers were non-malignant and negative for Whipple's bacillus.
- After these etiologies were deemed negative, toxic insults and malignant sources were considered, for which the former was negative. Given pan-scanning didn't showed any focal malignant sources or osseous metastatic lesions, a bone marrow biopsy was performed, which showed APMF with immunohistochemical stain for CD20, CD3, CD34, CD117, CD 71, CD138 and cytokeratin showing mixed T and B lymphocytes favoring T infiltrate CD34 but negative for CD34 blasts. CD117 and CD71 showed early erythroid precursors and reticulin showed extensive reticular fibrosis with negative trichrome stain besides iron staining, which was positive, affirming the diagnosis.
- The World Health Organization (WHO) classification of tumors of the hematopoetic tissue defines APMF as a rare subtype of AML; with APMF profiled as a hematological malignancy associated with fibrosis of the bone marrow, with little or no splenomegaly, and peripheral blood counts indicative of pancytopenia, few myeloblasts (< 5%) and shift to the left with immature neutrophils and rare normoblasts.
- Given the distinct nature of this classification, it becomes imperative to distinguish it from acute megakaryoblastic leukemia (AML-M7), Primary Myelofibrosis (PMF) and AML with myelodysplasia – as the classification of these latter three allows for honed in treatment and prognosis.
- Given the rarity of this pathology, no standard therapy has been established and the disease has been reported to have poor response to chemotherapy with strong probability of transition to AML with blast crises on occasion with median survival of 9 months.
- In our patient, he was initiated on the standard 7+3 induction therapy (Cytarabine plus Daunorubcin) and post-induction bone marrow biopsy showed minimal residual disease with 5% blast.
- Later, in a span of five months, he was placed on salvage chemotherapy with azacitadine, but with recurrent neutropenic fevers and transfusion dependent anemia, he succumbed to septic shock – reflecting a protracted course of this rare AML subtype.

Tumor Classification

AML-M7
- Blasts > 20% of all nucleated cells in peripheral blood and/or bone marrow and at least 50% are megakaryoblasts (CD41/CD61 positive)

AML with Myelodysplasia
- Blasts >20% of all nucleated cells in peripheral blood without a history of prior cytotoxic drug therapy with 1 of the following:
  - MDS diagnosis
  - MDS-related cytogenetic abnormalities, such as monosomy 5 or del(5q) monosomy 7 or del(7q), isochromosome 17p
  - Morphologically identified multilineage dysplasia, defined as dysplasia present in >50 percent of cells in two or more hematopoietic lineages

Primary Myelofibrosis
- Proliferation of an abnormal clone of hematopoietic stem cells that results in fibrosis with bone marrow showing leukoerythroblastosis with clonal marker – JAK2 or MPL

References:

1 Chatterjee, Tathagata et al. "Acute Panmyelosis with Myelofibrosis - A Rare Subtype of Acute Myeloid Leukemia." *Mediterranean Journal of Hematology and Infectious Diseases* 5.1 (2013): e2013042. PMC. Web. 06 July 2015.

2 Thiele J, Kvasnicka HM, Zerhusen G, Vardiman J, Diehl V, Luebbert M, Schmitt-Graeff A. "Acute panmyelosis with myelofibrosis: a clinicopathological study on 46 patients including histochemistry of bone marrow biopsies and follow-up." *Ann Hematol.* 2004 Aug; 83(8):513-21. Epub 2004 Jun 2.

3 Orazi, A. "Histoopathology in the diagnosis and classification of acute myeloid leukemia, myelodysplastic syndromes, and myelodysplastic/ myeloproliferative diseases." *Pathobiology.* 2007;74(2):97-114.