Indy Hematology Review 2021

Challenging Cases Presentation

Michael C. Wiemann, MD, FACP

Program Co-Chair and Vice President

Indy Hematology Education Inc.

President, Clinical
St. John Providence Physician Network,

Detroit, Michigan.

CLINICAL PROFESSOR OF MEDICINE, MICHIGAN STATE SCOOL OF MEDICINE, East Lansing, MI

POST CLL CHEMOTHERAPY MDS: CMML

- 65 yr old female diagnosed with Rai Stage 0 Chronic lymphocytic leukemia diagnosed in December of 2000 watched and waited until December 2004. Treatment with rituximab and fludarabine for progressive disease achieving a CR.
- **June 2005**
- Generalized squamous cell carcinomas of the skin. Conservative management with excisions and Moh's surgery with progressive disease.
- **January 2018**
- Progressive anemia. No hemolysis, diagnosed for progressive CLL:
- PB CLL FISH: 13q deletion, del 17p/p53 negative, mutated IgVH status. Ibrutinib initiated in February 2018 with improvement.
- **August of 2018**
- Obinutuzumab added with minimal clinical response.
- **November 2018**
- Progressive persistent transfusion dependent anemia,
- Bone marrow biopsy: Pure red aplasia. PARVO virus B19 negative, no hemolysis. Normal cytogenetics.
- ESA initiated without response, transfusion dependence.

POST CLL CHEMOTHERAPY MDS: MDS/CMML

- **December 2018**
- Cyclosporine and prednisone initiated: Progressive cutaneous squamous cell carcinoma of the skin
- **January 2019:**
- IV IgG therapy with transfusion independence and improved cytopenias.
- **May 2020**
- Progressive anemia: Repeat BM biopsy: Markedly hypercellular marrow, left shifted, with granulocytic and erythroid hyperplasia, monocytosis, dysmegakaryopoiesis with dyserythropoiesis, 3% blasts, normal cytogenetics. NGS testing reveals
  mutations of TET2, ASL1, U2AF1, DNMT3A, ETV6, and NRAS2.
- DIAGNOSIS: CMML type 0
- **July 2020:**
- Decitabine initiated.
- **November 2020**
- Restaging BM biopsy: Hypercellular, with multilineage dyspoiesis, 10% blasts
- PB monocytosis and 12% circulating dysplastic blasts.
- NGS: Mutations of TET2, ASL1, U2AF1, DNMT3A, ETV6, and NRAS2
- Cytogenetics: Trisomy 13 and complex chromosome abnormalities consistent with a poor prognosis.
- **DIAGNOSIS**: Residual high risk myelodysplastic syndrome/CMML.

39 YEAR OLD WITH LOW RISK MDS

- 34-year-old presents with leukopenia and mild splenomegaly:
- **May 2017**
- WBC 3.4, hemoglobin 13.9, platelets 272, ANC 800
- PB flow cytometry: Polyclonal without any immunophenotypical evidence of lymphoma, leukemia.
- **August 2017:** Progressive neutropenia. Peripheral blood: Rare giant cells.
- **Bone Marrow Biopsy**: Hypocellular marrow with granulocytic hypoplasia with frequent hypogranular neutrophils and megablastic erythropoiesis and dysmegakaryopoiesis. No morphologic evidence of marrow involvement by lymphoma or leukemia.
- Cytogenetics normal and MDS FISH MDS panel: Negative. NGS: ASXL, ATRX except for a mutation of DNMT3A mutation.
- Diagnosis: Myelodysplastic syndrome (MDS) with multilineage dysplasia and DNMT3A mutation; Observation recommended.
- **February 2021**: WBC 2.5, Hemoglobin 13 13.6, Platelets 246, ANC 520
- July 2021: WBC 4.5, Hemoglobin 13.5, Platelets 245, ANC 3420
- **Bone Marrow Biopsy:** Hypocellular (~30%) bone marrow with trilineage hematopoiesis, hypoplastic granulopoiesis, and features of dysgranulopoiesis and dysmegakaryopoiesis. Mildly increased CD34(+) blasts, ~4% -5% of cellularity. No morphologic evidence of a lymphoproliferative neoplasm. A minute monoclonal B-cell population (0.2%) noted by flow cytometry, uncertain significance.
- BM FISH: Negative for Deletion of 5q/Monosomy 5, Deletion of 7q/Monosomy 7, Trisomy 8, Deletion of 20q, and KMT2A (MLL) rearrangement. BM cytogenetics: Normal, 46,XY[20]
- BM NGS: No evidence of mutation in: JAK2, MPL, CALR, FLT3, NPM1, IDH1 and IDH2
- IPPS –R SCORE: 2 (LOW RISK) and Age Adjusted IPSS-RA SCORE: 0.76 (VERY LOW RISK)

POST MYELOFIBROSIS
ACUTE MYELOID LEUKEMIA

- 63-year-old diagnosed of essential thrombocytosis in 2011 associated with mild bone marrow myelofibrosis, initially treated with anagrelide/aspirin, then erythropoietin.
- In October 2014 secondary to progressive anemia, Ruxolitinib initiated with responsive disease.
- **March 2021**
- Progressive anemia and sweet's syndrome.
- **Bone marrow biopsy**:
- Acute myeloid leukemia arising from the chronic myeloid neoplasm with 40% blasts positive for CD45, CD34, CD117, and CD33.
- Cytogenetics/FISH: Normal karyotype with absence of deletions of chromosome 5, 7, 8, and absence of CBFB rearrangement and 8;21 translocation
- NGS: FLT3 ITD mutation and IDH2 mutation in addition to mutations of ASL1, RUNX1, and NRAS.

Primary Myelofibrosis with progressive anemia

- 57-year-old presents with Stage III CKD, anemia in 2015
- **2017**: Portal vein thrombosis in 2017 without an obvious etiology.
- **January 2019**: Progressive anemia: No splenomegaly. No constitutional symptoms.
- BM Biopsy: Hypocellular, with moderate to focally severe myelofibrosis, and megakaryocytic hyperplasia/atypia. Blasts not increased.
- Flow cytometry and cytogenetics/FISH: normal. Hemoglobin 11, Plts
- JAK2 V617F mutation positive.
- Diagnosis: Primary myelofibrosis (IPSS-0)
- **November 2019**: Progressive anemia, 1% circulating blasts (IPSS-1): Ruxolitunib initiated.
- **March 2021**: Progressive transfusion dependent anemia.
- BM Biopsy: Myeloproliferative neoplasm with myelofibrosis without increased blasts or plasma cells. Hypercellular and a cluster of atypical large megakaryocytes and no increase in blasts with grade 3 reticulin fibrosis and adequate storage iron
- Cytogenetics/FISH and NGS: Normal/Negative

46-YEAR-OLD WITH SYSTEMIC MASTOCYTOSIS

- 46-year-old presents with a history of severe allergies and near anaphylaxis and a new hyperpigmented maculopapular rash.
- Elevated Serum tryptase: 16.4.
- Normal CBC/diff, CMP, TSH, SPEP, Vitamin D, and IgE levels.
- Skin biopsy: Increased CD117 and tryptase positive mast cells consistent with urticaria pigmentosa.
- Bone Marrow Biopsy: Normocellular ~(50%), c-kit, CD25, tryptase positive,10% atypical mast cell lesions with a with patchy mild increase in marrow reticulin fibers and adequate storage iron. No evidence of dysplasia. Cytogenetics/FISH negative.
- DIAGNOSIS: Systemic Mastocytosis