Indy Hematology Review® 2024
TOWNHALL CASE PRESENTATION

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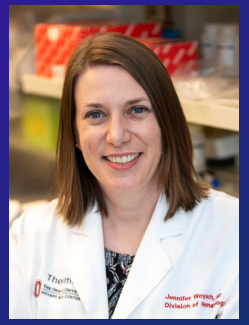
Hematologic Malignancies Town Hall

- Michael Wiemann, MD, FACP – Co-Chair
- Richard Childs, MD, Hematopoietic Stem Cell Transplantation
- Morie Gertz, MD, MACP – Plasma Cell Disorders and Amyloidosis
- Jennifer Woyach, MD – Chronic Lymphocytic Leukemia
- Rami Komrokji, MD – Acute Leukemias and Myelodysplastic Syndromes
- Matthew Lunning DO, FACP – Lymphomas
- Tycel Phillips, MD – Lymphomas
- Saad Z. Usmani, MD, MBA, FACP, FRCP – Multiple Myeloma
- Ayalew Tefferi, MD – Myeloproliferative Neoplasms





Bilateral submandibular Gland Marginal Zone lymphoma

- 41 year-old female with a history of Sjogren's disease diagnosed in 2012 and being with treated with steroids and methotrexate.
- Presents with progressive bilateral submandibular gland enlargement
- ENT consultation and surgical excision of the right submandibular gland
- Pathology: Low-grade B cell lymphoma, CD19/CD20 positive, kappa restricted, FMC7, CD5, CD23, CD10, MYD88 negative with plasmacytic differentiation and amyloid deposition
- PET and Bone marrow biopsy negative for disseminated disease.
- Left sided submandibular gland resection consistent with “low grade lymphoma”
- DIAGNOSIS: Sjogren's syndrome associated bilateral submandibular gland marginal zone lymphoma

High-risk Multiple Myeloma

- 56-year-old PMH of systemic lupus erythematosus and fibromyalgia presents to ED with intractable vomiting and acute on chronic back pain.
- LABS: Hemoglobin of 10.0, a platelet 24K, creatinine of 3.02, total bilirubin of 5.1, and an ionized calcium of 1.85, sodium 129, uric acid of 16.1, LDH 1606, total protein of 13.4 with an albumin of 4.5, beta2microglobulin; 9.05 and free kappa was 8.3 with a free lambda of 427.2, kappa/lambda ratio of 0.02, IgA was elevated at 2588, IgG was low at 525, and IgM was low at 24.
- SPEIP: IgA lambda monoclonal gammopathy and CT scan of the chest, abdomen, and pelvis revealed innumerable lytic lesions throughout the axial and appendicular skeleton.
- Bone marrow biopsy: Extensive plasma cell neoplasm with 95% involvement with sheets of plasma cells and dysplastic plasma cells present with 99% cytoplasmic lambda expression by CISH and flow cytometry revealed the presence of a CD38 positive, CD56 negative, CD11 and 7 positive/negative plasma cells consistent with plasma cell neoplasm.
- Genetics: abnormal karyotype with complex cytogenetics: IGH/MAF rearrangement, amplification of 1q, loss of TP53, other IGH, rearrangement, and gains of chromosome 11, 14, 6q, and 13q with amplification of the longarm of chromosome 1, a longarm of chromosome 13, as well as triploidy of TP53.
- DIAGNOSIS: ISS stage III I IgA lambda Multiple Myeloma.

High-risk Multiple Myeloma --- Continued

- Initial therapy in hospital: CyBorD x 1 cycle with pamidronate and rasburicase for hyperuricemia.
- Subsequent therapy: Carfilzomib, lenalidomide, dexamethasone, and daratumumab x 3 cycles.
- Restage: Normal creatinine, calcium, total protein and albumin. SPEIP: IgG kappa monoclonal protein most likely secondary to ongoing therapy with daratumumab with an M-protein of 0.1 g/dL with an IgG of 579, IgA of 80, and IgM of 80. Free kappa and lambda light chains were normal with a normal kappa/lambda ratio of 0.29. BM biopsy
- BM BIOPSY: Normocellular marrow with trilineage hematopoiesis without evidence of significant dysplasia or increased blasts, and no atypical plasma cell infiltrates were identified. No monoclonal residual plasma cells were noted, and cytogenetics were normal with13 chromosomes identified.
- ASCT planned
- I month later: Patient presents with a skin nodule:
- Skin biopsy: atypical plasma cell infiltrate of lambda origin consistent with extramedullary plasmacytoma.

86-YEAR-OLD WITH NEWLY DIAGNOSED AML

- 86-yr old with a history of stage pT1bpN2a breast cancer, status post adjuvant radiation therapy and hormonal therapy with anastrozole.
- ECOG: PS 1
- Presents with a WBC: 86K, with 30% PB blasts, Hg: 7.6, Plts: 21K
- BM: 90% cellularity, 90% myeloblasts, myeloperoxidase positive: CD45(+)/CD34(+)/CD13(+)/CD33(-)/HLADR(+)
- Cytogenetics: 46XX,t(4:12)(q11.2;p13)(13)
- NGS: Alterations of NRAS, DNMT3A, TET, BCOR and PHF6

MYELOFIBROSIS

- 74-year-old with a PMH of prostatic carcinoma, status post DaVinci radical prostatectomy presents with cytopenia's.
- WBC: 7200, hemoglobin; 12.5, MCV; 88.3, platelet count; 298,000 with 58% neutrophils, 13% lymphocytes, 8% monocytes, 3% eosinophils, and 6% basophils.
- Peripheral smear revealed moderate anisocytosis or polychromasia with rare nucleated red blood cells and blasts, and peripheral blood flow cytometry was performed which revealed 1% myeloblasts with myelocytes and metamyelocytes.
- Bone marrow biopsy: Primary myelofibrosis, fibrotic stage, with 50% cellularity and ME ratio of 3:1 with increased trilineage hematopoiesis with markedly dysplastic megakaryocytes seen and no stainable reticuloendothelial iron stores. Reticulin stain revealed increased reticulin fibrosis.
- Cytogenetics: Unbalanced rearrangement involving the long arm of chromosome 1 and 4 resulting in loss of the distal 14q with a partial gain of 1q, der (14), t(1:14) and interstitial deletion pf the long arm of chromosome13
- CT scan of the abdomen: Marked splenomegaly.
- Observation initiated.

MYELOFIBROSIS …… CONTINUED

- 6 months later: WBC; 6.9, hemoglobin; 11.9, and a platelet count of 318 with 53% segmented neutrophils, 14% lymphocytes, 11% banded neutrophils, 1% metamyelocytes, 3% myelocytes, 2% promyelocytes, and 4% blasts.
- Diagnosis: Intermediate 2 (high-risk) myelofibrosis, ruxolitinib therapy was instituted.
- 4 years later progressive severe anemia resulting in the institution of erythropoietin stimulating agent therapy without adequate response and with the subsequently the addition of luspatercept but with persistent anemia and as a result in October 2023, ruxolitinib was discontinued and momelotinib was instituted.
- Current status: Resolved anemia.

Myeloma/Amyloidosis

- 51-year-old presented with acute on chronic mixed systolic and diastolic congestive heart failure resulting in an echocardiogram which revealed Stage 3 diastolic dysfunction with a strain pattern suggestive of an infiltrative process like amyloidosis with an ejection fraction of 4045% and as a result was placed on carvedilol and referred to the Cardiology service.
- WBC; 6.4, hemoglobin; 13.8, platelet count; 209,000, EKG: Poor R-wave progression,
- Echocardiography; moderate concentric left ventricular hypertrophy with LVEF of 4045% without reginal wall abnormalities and a global longitudinal strain, and an apical sparing pattern consistent with amyloidosis.
- SPEIP: normal pattern without monoclonal gammopathy identified.
- sFLC: free lambda; 652.9, free kappa of 10.1 with an abnormal kappa/lambda ratio of 0.02 and a free lambda monoclonal protein and an NTproBNP of 2890.
- Endomyocardial biopsy: Amyloidosis with amyloid protein identification ordered.
- Bone marrow biopsy: 30% lambda restricted plasma cells compatible with plasma cell neoplasm, negative for amyloid deposition, with 50% trilineage hematopoiesis with normal cytogenetics and normal karyotype (46,XY).
- Myeloma FISH: Negative for loss of TP53 consistent, rearrangement of IGH suggesting a gain of the long arm of chromosome 1.
- NGS: IGH/CCND1 rearrangement

17P-DELETED CHRONIC LYMPHOCYTIC LEUKEMIA

- 62-year-old with a history of Stage I hepatocellular carcinoma diagnosed in January 2020, resulting in a partial hepatectomy, and expectant monitoring.
- September 2021, routine CBC: WBC; 28,000 compared to 10.6 previously with a hemoglobin of 12.3, platelet count of 198 with 24,000 lymphocytes.
- Peripheral blood flow cytometry: Shows kappa-restricted CD5, CD19, CD20, CD23 and CD200 positive, CD10 and CD38 negative lymphocytes, consistent with Chronic Lymphocytic Leukemia.
- Cytogenetics: Abnormal female karyotype; Trisomy 12 and deletion of 17p, unbalanced translocation of the short arm of chromosome 17 and the long arm of chromosome 18, (47,XX,+12[3]/45,idem,X,der(17)t(17;18)(p11.2;q11.2),18[15]/46,XX[2])
- Molecular Studies; unmutated IgVH status.
- Diagnosis: Rai Stage 0 chronic lymphocytic leukemia
- " WATCH AND WAIT" or ?"ACTIVE SURVELLANCE"
- October of 2022.
- May 2023: Rapid progressive disease WBC of 148 with 90% lymphocytes, hemoglobin of 11.5, and a platelet count of 321,000, and fatigue.
- Treatment initiated: Venetoclax and Obinutuzumab.
- January 2024: WBC of 2.7 with ANC 1.66, hemoglobin 12.0, PLT 143,000, PB MRD: Undetectable

Aggressive DLBC Lymphoma

- 61-year-old presents with abdominal pain in June 2020.
- Diagnosis: Acute cholecystitis and subsequent cholecystectomy;
- July 2020: Persistent symptoms, CT scan of the abdomen shows a hypermetabolic large (11.5 x 6.9 x 7.7cm) soft tissue mass at the root of the mesentery, located along the inferior margin of the pancreatic head with mild mesenteric fat and small low-density lesion of right adrenal gland and a mildly enlarged prostate.
- CT guided core needle biopsy: Diffuse large B-cell lymphoma of germinal center origin with positivity for BCL6 and rare CD10 positivity associated with MUM-1 and c-Myc negativity, and positive Ki-67 stain in the large cells and negativity for cytokeratin AE1 and 3 and synaptophysin.
- July 2020: Progressive jaundice: Total bilirubin; 8.9 with elevated AST; 224 and ALT;467 and (direct bilirubin; 7.2) resulting in urgent biliary stenting.
- Chemotherapy initiated: Cyclophosphamide, rituximab and prednisone with pegfilgrastim support.
- Resolved jaundice: chemotherapy comprising of cyclophosphamide, doxorubicin, vincristine, and prednisone, with rituximab (RCHOP) x 6 and complete remission at completion of chemotherapy in November 2020.

Aggressive DLBC Lymphoma …Continued

- March 2021 with recurrent abdominal pain and PET/CT evidence of recurrent disease.
- Second line chemotherapy comprises of rituximab, ifosfamide, carboplatin, etoposide (RICE chemotherapy), with a follow up PET/CT scan showing achievement of a radiographic/PET/CT/endoscopic/ultrasonographically evaluated complete remission.
- Consolidation: High dose chemotherapy and autologous stem cell transplantation was recommended to be followed by consolidative radiation therapy to the root of the mesentery.
- November 2022: Restaging PET/CT scan consistent recurrent disease with
- Salvage chemotherapy comprising of gemcitabine, oxaliplatin, and rituximab (R-GEMOX chemotherapy) with partial remission with RGEMOX chemotherapy and in
- January 2023 CART with Axicabtagene Ciloleucel (axi-cel): Complete remission
- July 2023: Disease progression with new radiographically detected disease in the retroperitoneal region. This was not amenable to a biopsy.
- Therapy: Epcoritamab recommended and instituted in August 2023.
- December 2023, progressive abdominal symptomatology. PET/CT scan obtained prior to the hospitalization showed positive aggressive disease versus FLAIR effect of the upper abdomen because of which radiation therapy was instituted. In addition, lenalidomide was added to his regimen in December 2023.

Sickle Cell Disease

- 29-year-old man with a history of sickle cell anemia diagnosed prenatally treated with hydroxyurea and folic acid and has had intermittent and occasional sickle cell crisis episodes the last time being in 2002 and has been monitored expectantly.
- January 2021: Develops leg ulcers with left leg adenopathy associated secondary to hydroxyurea. Hydroxyurea discontinued.
- May of 2021: Hemoglobin; 6.1, hematocrit;17.4, platelet count; 277
- Lymph node biopsy negative.
- Lost to follow up until he reestablished hematologic care in due to recurrent bone pain crises in April 2023. At that time, the patient's wound had resolved.
- Recurrent bone pain crises off hydroxyurea ~ 3-4 times annually.
- Re-treatment with hydroxyurea 500 mg and folic acid.
- January 2024: Recurrent leg ulcers. Hydroxyurea permanently discontinued.
- February 2024: WBC; 8.7, Hg; 8.7, Plt; 556K
- Family History: One-half sibling with Sickle cell trait