The Winding Road to Aplastic Anemia

Julie Tang, MD, William Lerner, MD FACP, Kimberly Odell, MD, Kenneth Kronhaus, MD
Department of Family Medicine. Hackensack Meridian Health Ocean Medical Center, Brick NJ

Hackensack Meridian *Health*

LEARNING OBJECTIVES

1. Develop differential diagnoses for an adult patient presenting with pancytopenia
2. Define and identify etiologies of Aplastic anemia

CASE PRESENTATION

- 44 year-old male presented shortness of breath, headache and palpitations
- CBC revealed severe pancytopenia, placed on neutropenia precautions
- No fever, chills or bleeding
- Stated he had a “rare blood disorder”
- Bone marrow biopsy years ago did not show specific diagnosis for mild thrombocytopenia
- Received PRBC and platelet transfusions as well as granix and folic acid with appropriate follow-up
- Presented again for left knee swelling and pain
- No clinical indication for aspiration at the time per Orthopedics; received transfusions and discharged
- Second opinion at Cornell University, knee pain improved after steroids but the pancytopenia remained the same
- Initial working diagnosis was TLGL leukemia with plan to start methotrexate, however T-cell studies including molecular genetic testing of STAT3 were negative
- PNH (-), HIV (-), hepatitis panel (-), Iron studies (-)
- CMV and EBV antibodies slightly elevated
- Started on Cyclosporine and Promacta (BM stimulant) as well as Bactrim for prophylaxis

PHYSICAL EXAMINATION

- Vital signs normal. No acute distress.
- Oxygen saturation 98% on room air

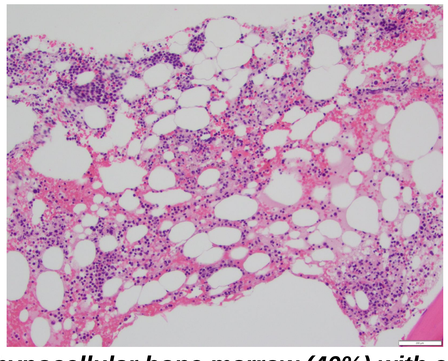
LABORATORY DATA

	12/25	1/2
WBC	2.1	2.4
Hgb	4.7	7.3
MCV	112.5	102.0
RDW	16.9	18.3
Platelet Count	9	9
Absolute neutrophil count	.4	.7
Pathologist review of peripheral blood smear	No blasts	

PANCYTOPENIA DIFFERENTIAL DIAGNOSIS

BM infiltration/ replacement	BM failure	Destruction/ sequestration/ redistribution
Malignant vs non-malignant	Immune destruction (AA/PNH)	Consumption (DIC)
Acute/Chronic leukemia	Suppression (HIV, hepatitis, EBV)	Splenomegaly (portal HTN, cirrhosis)
Myelodysplastic syndromes	Medications (cytotoxic)	
Multiple Myeloma	Nutrition (B12, folate), ETOH)	
Infectious/ Myelofibrosis	Autoimmune (SLE, RA)	

BONE MARROW BIOPSY #1

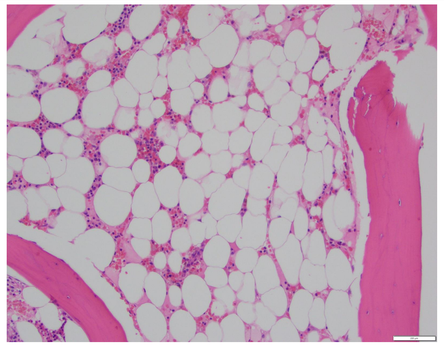


Mildly hypocellular bone marrow (40%) with erythroid predominant trilineage hematopoiesis. Flow cytometry immunophenotyping detected relatively increased number of T-lymphocytes with a slight expansion of T-cell large granular lymphocytes. No overt diagnostic evidence of high grade myeloid neoplasm/myelodysplastic syndrome

T-Large Granular Lymphocytic Leukemia (TLGL)

- Lymphoproliferative disorder that manifests as leukemia in absence of any lymphadenopathy, involves tissue invasion of marrow, spleen and liver
- Two types: T-cell and natural killer cell; chronic vs aggressive
- 1:10 million in U.S with median age of 60
- Associated with autoimmune disease (rheumatoid arthritis)
- Most present with symptoms related to neutropenia but approximately one-third asymptomatic
- Diagnosis: cytology (large cells containing azurophilic granules), immunophenotyping (express CD3+, CD8+, CD 57+), T cell receptor PCR analysis (clonally rearranged TCR genes), Molecular (mutations found in 30-40%)

BONE MARROW BIOPSY #2



Markedly hypocellular bone marrow with decreased granulopoiesis, virtually absent megakaryocytes and lymphocytosis. No immunophenotypic evidence of acute leukemia or non-hodgkin’s lymphoma.

APLASTIC ANEMIA

- BM failure characterized by pancytopenia and bone marrow hypocellularity in absence of abnormal infiltrate or fibrosis
- Misnomer; no required duration of cytopenias
- Often, no specific cause is identified
- Rare; 2 per million per year; half of cases occur in the first three decades of life
- Causes include: drugs, radiation, toxins, viruses
- Chloramphenicol, antiseizure medications – idiosyncratic reactions – cytopenias arise while taking the medication
- Dose-dependent radiation
- Insecticides, prolonged benzene exposure
- Hepatitis/ HIV - alter antigen on bone marrow cells
- Co-exist with or evolve into another disorder (PNH, MDS,AML)

SUMMARY

- The differential diagnoses for an adult presenting with pancytopenia can be divided into bone marrow infiltration/replacement vs. failure vs destruction/sequestration/redistribution
- Aplastic anemia is a type of bone marrow failure; the cause is often not identified
- Heterogeneity of bone marrow can be seen when biopsy done at one site may differ from another site – unclear if the first biopsy result was related to inflammation from knee
- Often times in medicine, we can be led to one diagnosis and have to shift our thinking to get from one point to another point when new studies/results arrive

REFERENCES
1. Killick SB, Bown N, Cavenagh J, et al. Guidelines for the diagnosis and management of adult aplastic anaemia. Br J Haematol 2016; 172:187.
2. Lamy T, Loughran TP Jr. Clinical features of large granular lymphocyte leukemia. Semin Hematol 2003; 40:185.