Chronic Eosinophilic Leukemia Manifesting as Hypereosinophilia

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Introduction

- Chronic Eosinophilic Leukemia Not Otherwise Specified (CEL-NOS) is a myeloproliferative neoplasm caused by clonal proliferation of eosinophilic precursors and is a rare cause of hypereosinophilia.
- Hypereosinophilia is defined as an absolute eosinophil count greater than or equal to 1.5 x 10^3/uL on two occasions at least one month apart and/or eosinophilia greater than 20% in peripheral blood smear or bone marrow section.
- Hypereosinophilia most commonly causes damage to the skin, lungs, heart, gastrointestinal tract, and nervous system due to eosinophil granule overproduction and cytokine mediated damage.

Case

- A 64-year-old asymptomatic male underwent routine laboratory testing and was found to have a white blood cell count of 56.7 x 10^3/uL and an absolute eosinophil count of 54.4 x 10^3/uL. Physical exam was notable for splenomegaly.
- A peripheral blood smear was performed confirming marked eosinophilia (Figure 1A) with a manual differential cell count of 86% eosinophils (normal 0-7%), and showing morphologically mature eosinophils with occasional monolobation and/or hypogranulation (Figure 1B).
- A complete metabolic panel, serum immunoglobulins, serum tryptase, vitamin B12 levels, and stool PCR for parasites were within normal limits. EKG, echocardiography, troponin levels, and pulmonary function testing did not reveal evidence of end organ damage.
- Bone marrow biopsy was hypercellular for age (Figure 1C) with less than 20 percent blast cells and a marked increase in eosinophils and eosinophil precursors (Figure 1D). No PDGFRA, PDGFRB, FGFR1, ETV6-JAK2, BCR-ABL-1 mutations or T-cell or B-cell rearrangements were found. A genetic mutation of ASXL1 was identified with a variant allele frequency of 48 percent.
- A diagnosis of CEL-NOS was made. Treatment was initiated with hydroxyurea and the patient is preparing for an allogenic stem cell transplant.

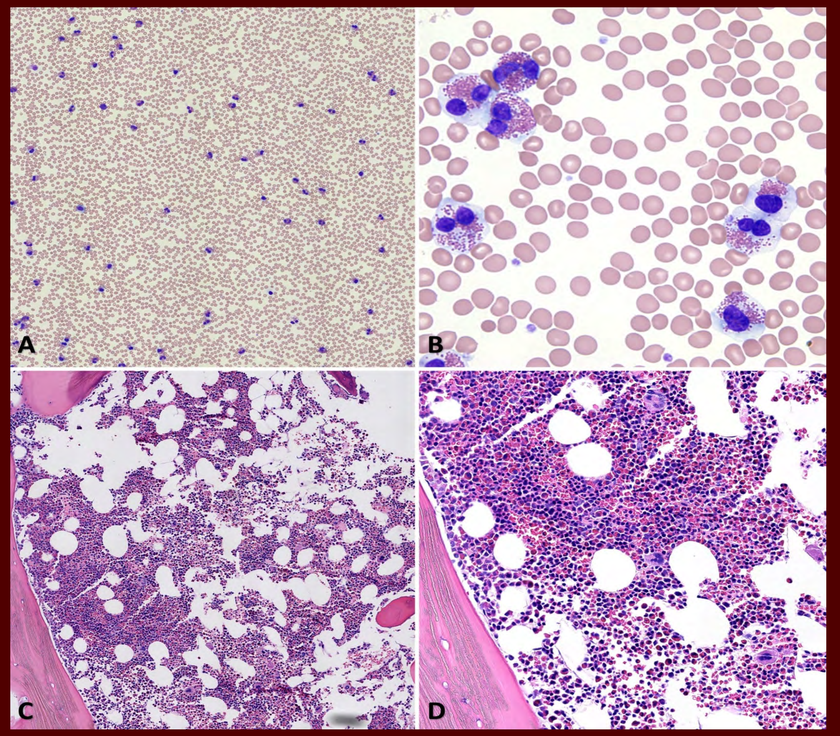

Figure 1: Peripheral blood smear and bone marrow core biopsy from the patient diagnosed with CEL-NOS.
A) Low-power view of peripheral blood smear showing marked hypereosinophilia (Wright-Giemsa stain).
B) High-power view of eosinophil morphology in peripheral blood with occasional monolobate and/or hypogranular eosinophils (Wright-Giemsa stain).
C) Low-power view showing hypercellular bone marrow for age (H&E stain).
D) High-powered view of bone marrow with marked increase in eosinophils and eosinophil precursors (H&E stain).

Discussion

- CEL-NOS is most commonly diagnosed in the 6th decade of life with an approximate incidence of 0.036 cases/100,000 person years and is found in a 1.5:1 rate of males to females.
- CEL–NOS as defined by the WHO criteria requires exclusion of CML, other myeloproliferative neoplasms, and secondary reactive causes including atopic disease, medication reactions, immune disorders, vascular-collagen disorders, and infectious etiologies.
- Diagnosis also requires eosinophilia > 1.5 x 10^3/uL for 6 months, an increase of myeloblasts in peripheral blood >2% or bone marrow myeloblasts < 20% of all nucleated cells, and the presence of a molecular clonal genetic abnormality.
- Management of CEL-NOS initially begins with corticosteroids and/or cytoreductive therapies such as hydroxyurea. Progression of disease is often treated with high dose chemotherapy and long term remission may be achieved through stem cell transplant.
- CEL-NOS is an aggressive disease with a high transformation rate to acute leukemia and poor response to chemotherapy, with mean survival in some studies showing ~22 months from time of diagnosis without stem cell transplant.
- Our case highlights a rare form of cancer that demonstrates the importance of a broad differential for hypereosinophilia with an urgent workup and treatment to avoid the end organ damage that can result from hypereosinophilia.

References

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