A RARE PRESENTATION OF ACUTE MYELOID LEUKEMIA ASSOCIATED WITH PHILADELPHIA CHROMOSOME

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Introduction

- Philadelphia chromosome-positive AML (Ph+AML) is a rare subtype characterized by t(9;22)(q34;q11) translocation, resulting in the BCR-ABL1 fusion gene.
- While commonly linked to CML and ALL, its presence in AML indicates aggressive disease with poor prognosis. Treatment typically involves tyrosine kinase inhibitors (TKIs) with chemotherapy.
- Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the preferred curative approach. Median overall survival for patients who forgo allo-HSCT is approximately 7.1 months.

Case Presentation

- A 70-year-old male with cardiovascular disease and oxygen-dependent COPD presented with leukocytosis (94.4cells/μL), hemoglobin 11.2g/dL, platelets 76cells/μL.
- Labs showed creatinine 1.6mg/dL (baseline 1.2mg/dL), uric acid 11.3 mg/dL, LDH 392 units/L.
- Hemodynamically stable, he reported night sweats, fatigue, dyspnea and chest pain.
- CT scans showed terminal ileum thickening and emphysematous lungs.
- Rasburicase was administered for tumor lysis syndrome and hematology-oncology recommended leukapheresis and hydroxyurea for cytoreduction.
- Bone marrow showed 68 percent blasts/promyelocytes. Core biopsy revealed hypercellular marrow with predominant blasts without Auer rods.
- He started azacitidine/venetoclax induction, however, failed to achieve response with increasing peripheral blasts.
- Cytogenetic analysis revealed t(9;22) in all metaphases. Review of prior peripheral blood counts and differentials was not indicative of prior CML, confirming de novo Ph+AML.
- He started cladribine, low-dose cytarabine (LDAC) and dasitinib. Bone marrow biopsy after one cycle revealed no leukemic blasts. After two additional cycles of LDAC+dasatinib, LDAC was discontinued due to intolerance.
- He continued dasitinib with excellent disease control for over two years before switching to asciminib due to edema. He remains stable and BCR-ABL fusion quantitative level is at 0.0902%.

Discussion

- Tyrosine kinase inhibitors have demonstrated efficacy inducing remission in Philly Chromosome+AML.
- Typically combined with chemotherapy, their role as monotherapy, particularly in HSCT-ineligible patients, remains unclear.
- Our case highlights prolonged remission with TKI-monotherapy after LDAC induction, suggesting patients may achieve sustained disease control without transplantation.
- Further research is needed to evaluate TKI-monotherapy outcomes and identify factors predicting durable response in Ph+ AML.

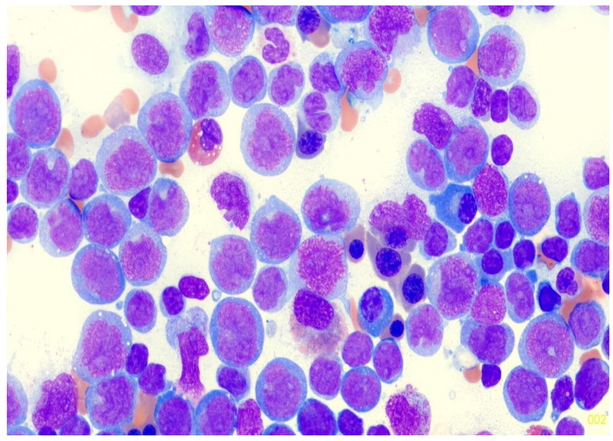


Figure 1: A bone marrow biopsy revealing a marked increase in blasts/promyelocytes is noted comprising 68%. The blasts are large and irregular nuclei, 1-2 prominent nucleoli and moderate amount of basophilic cytoplasm, some with cytoplasmic granules. In all 20 metaphases, the classic (9;22) translocation with its characteristic Philadelphia chromosome was identified. Furthermore, in all twenty metaphases an apparently balanced translocation between the short arm of chromosome 15 at band p11.2 and the long arm of chromosome 18 at band q21 was detected. The BCR/ABL p190 fusion transcript was identified in 44.9% of unique RNA reads.

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