Acute Promyelocytic Leukemia with unusual presentation- A case report and review of literature
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BACKGROUND

• Acute Promyelocytic Leukemia (APL) is a subset of acute myeloid leukemia which is curable in >90% of non-high risk patients. However, APL is associated with early death due to bleeding diathesis. Therefore, early diagnosis and treatment of patients is of high importance.
• Low or absent CD34 expression and absent HLA-DR expression are considered typical features of Acute Promyelocytic Leukemia (APL) immunophenotypic profile.
• Treatment with Neupogen can alter the cell population in the bone marrow and peripheral blood and therefore make diagnosis of acute leukemia more challenging.

CLINICAL COURSE

We report a 51 years old woman with history of colon cancer treated with surgery and chemotherapy two years prior to presentation. She initially presented with V2V meningitis and was under treatment with IV Acyclovir. She was found to be pancytopenic with absolute neutrophil count of 600 and was started on Neupogen treatment. A bone marrow study 2 months prior to presentation showed no evidence of myelodysplasia or neoplasms. To assess the patient's pancytopenia, peripheral blood and bone marrow study was done. Additional material was sent for flow cytometry, karyotype analysis and fluorescence in situ hybridization (FISH).

RESULTS

The patient’s CBC showed WBC 2.2 x 10^3/mm, RBC 2.53 M/cmm, Hgb 7.3 g/dl, Hct 20.2%, MCV 79.7 fl and Plt 18000/cmm with differentials of 34% Neutrophils, 19% Lymphocytes and 46% Monocytes. Peripheral blood demonstrated normocytic normochromic anemia with blasts, promonocytes, and atypical cells suspicious for abnormal promyelocytes. Flow cytometry on peripheral blood in gate of granulocytes with low side scatter showed approximately 40% of cells positive for CD4, CD56, CD34 (partial), CD13, CD33, CD117 and CD38. Approximately 55% of these cells aberrantly expressed CD2. These findings were suggestive of acute leukemia, however the effect of Neupogen treatment couldn’t be ruled out because the patient had received her last dose of Neupogen 3 days prior to these studies. Bone marrow aspirate was aparticulate and hemodiluted rendering the accurate differential impossible. However, blasts, promonocytes and rare cells with Auer rods and one “faggot cell” were seen, constituting more than 20% of bone marrow cells. Bone marrow biopsy was suboptimal for assessment, however some focal areas showed 100% cellularity. Bone marrow clot section was also aparticulate and did not help in diagnosis. The flow cytometric analysis of the bone marrow aspirate in the same gate showed 20% of the cells positive for CD4, CD 34 (partial), HLA-DR (partial), CD 13, CD 33, CD 117, CD 64 and CD 38 with partial expression of CD 2. Flow cytometry and morphologic features in our case were not typical for APL. APL typically shows absent or low expression of CD34 and HLA-DR which was not so in this case and positivity of monotypic markers (CD4, CD64) could lead to diagnostic dilemma. However, FISH analysis demonstrated t(15;17) which is the hallmark of APL.

CONCLUSIONS

• APL is associated with high incidence of early death due to associated disseminated intravascular coagulation (DIC) syndrome mostly seen in high risk patients. Therefore early diagnosis and treatment is of great importance for saving patients.
• APL with the t(15,17) is characterized by low expression or absence of HLA-DR, CD 34.
• One of the unique genetic features of APL is the chromosomal translocation t (15,17) causing chimeric PML-RARA oncprotein. This unique genetic feature cause exquisite sensitivity of APL blasts to treatment with retinoic acid (ATRA).
• Combination therapy ATRA with arsenic trioxide (ATO) has resulted in potential cure in >90% of cases of non-high risk APL.
• High risk patients are defined as those exhibiting >10 x 10^9/L WBC at presentation, CD34, CD 56 and CD 3 expression, short PML/RARA isofom and FLT3-internal tandem duplication (ITD) mutation.

REFERENCES