CD34 Negative HLA-DR Negative Non-acute Promyelocytic Leukemia Acute Myeloid Leukemia

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Background: CD34 and HLA-DR negativity is a well-known characteristic of abnormal promyelocytes in acute promyelocytic leukemia (APL), however, is not specific for APL and can be seen in non-APL acute myeloid leukemia cases. The purpose of this study was to investigate characteristics of CD34 & HLA-DR negative non-APL cases. A retrospective study was conducted in total 648 newly diagnosed case of AML. Diagnosis of AML was made based on the results of morphology, cytochemistry, immunophenotype, cytogenetics, and/or molecular studies as per the World Health Organization 2016 guidelines. Peripheral blood and bone marrow aspiration smears were stained by Zenner-Giemsa stain and examined by two hematopathologist independently. Immunophenotyping was done on 3 laser, 10 colour Gallios flow cytometer from Beckman and Coulter, La Brea, CA. Reverse transcription polymerase chain reaction (RT-PCR) qualitative analysis was done for AML-ETO t(8;21), CBFB-MYH11 t(16;16)/inv(16), PML-RARA t(15;17), NPM1-A mutation, FLT3-ITD mutation and FLT3-TKD(D835Y) mutation.

Materials and Method: Among 648 newly diagnosed cases of AML, CD34 and HLA-DR antigens were negative in 110 patients (17%). Out of these 110 CD34negativeHLADR negative cases, 49 were APL (44.5%) and 61 were non-APL (55.5%). In CD34negativeHLADR negative non-APL, median age was 35 years (range 10 months to 71 years) with male:female ratio of 1:1. Other FAB sub-types included M1 (18 patients), M2 (29 patients), M4 (4 patients), M5 (5 patient), M6 (1 patient) and M7 (4 patients). Most of them showed a raised LDH levels (88.5%) with a mean LDH of 733 U/L (range 182-2681 U/L). Around 80% and 35% patients showed raised fibrinogen and D-dimer levels, respectively. More than 90% patients had raised PT/INR values. The mean hemoglobin was 78 g/L (range 3.2-13.8g/L), total leucocyte counts 66.5x109/L (0.52-308.4x109/L) and platelet count 53x109/L (7-258x109/L). Approximately 25% showed hyperleucocytosis (>1 lac/cmm). More than 90% were presented with thrombocytopenia including 25% with marked thrombocytopenia (<20x109/L).

Results: On morphological examination, the percentage of blasts ranged for 0 to 98% (mean 68.5%) and 20 to 98% (mean 80.2%) on peripheral blood and bone marrow, respectively. On cytochemistry 45 (73.8%) showed Auer rod/MPO positivity. On flowcytometric immunophenotyping expression of stem cell and myeloid markers were as cMPO in 49 (80.3%), CD117 in 52(85.2%), CD13 in 52(85.2%), CD33 in 58(95.1%), CD123 in 28(45.9%), CD64 in 19(31.1%), CD14 in 5(8.2%), CD11b in 31(50.8%), CD38 in 57(93.4%), CD36 in 12(19.7%) cases. Aberrant immunophenotypic marker expression were seen in 28 cases (45.9%), CD56 being the most common aberrancy in 16 (26.2%) followed by CD4 in 13 (21.3%) and CD7 in 8 (13.1%) cases. None of these cases showed an expression of CD19, CD79a or CD2. Molecular analysis was done in 52 cases, out of which 32 (61.5%) were NPM1 positive, 20 cases (38.5%) were FLT3-ITD positive and 1 case (1.9%) was FLT3-TKD positive.

Conclusion: CD34negativeHLADR negative AML accounts for 17% of newly diagnosed AML which includes approximately 55% non-APL cases. Most patients were presented with raised LDH, PT/INR and fibrinogen levels. CD34negativeHLADR negative non-APL AML is commonly seen in AML-M2 followed by AML-M1 subtypes. Each approximately 25% patients presented with hyperleucocytosis and marked thrombocytopenia. CD56 expression was the most common aberrancy seen in more than 25% cases. CD34negativeHLADR negative is highly associated with NPM1 mutation.

Keywords: CD34negative HLA-DR negative AML, NPM1, FLT3-ITD, PML-RARA, Hyper leucocytosis