Abstract

Background: There is little data on the immunophenotype (IP) of acute myeloid leukemia with myelodysplasia-related changes (AML-MDS). We therefore sought to systematically study the blast IPs in this heterogeneous subgroup by flow cytometry (FC), using comparisons to therapy-related AML (t-AML) and AML with normal cytogenetics (AML-nCG), with an emphasis on cytogenic (CG) correlations.

Design: AML-MDs and t-AMLs were defined according to 2008 WHO criteria; AML-nCGs had >20% blasts with a normal karyotype. Cases with t(15;17)/(16;16)/(8;21)/11q23 rearrangement by FISH were excluded. 4-color FC was performed on blood or bone marrow using the following antibodies: CD2, CD3, CD4, CD5, CD7, CD10, CD11b, CD13, CD14, CD15, CD16, CD19, CD20, CD22, CD33, CD34, CD8, CD45, CD117, HLA-DR, MPO and TdT. Blast aberrances were defined as a deviation from previously published normal IPs in myeloid blasts.

Results: 30 AML-MDs (17/31; F: 31-85 years), 27 AML-t-AMLs ($\times 3$; 20-73 years), and 8 AML-nCGs (50-72 years) were collected. The blast percentage from FC ranged from 0.2%-5.5% (median 2.4%) in AML-MDs, 5.2%-93% (55%) in AML-t-AMLs, and 1.7%-46% (19%) in AML-nCGs. Median number of blast aberrances was 7 in AML-MDs (1.1 cases) compared to 7 in AML-t-AMLs (1.8) and 8.5 in AML-nCGs (3.10). The most common aberrances observed in AML-MDs included aberrant expression of MPO (1316 cases, 81%), CD117 (2230, 73%), CD15 (1929, 68%), CD33 (1709, 59%), CD34 (1629 each, 56%), CD34 (1630; 53%), and CD7 (1303; 41%). The most common aberrances observed in AML-t-AMLs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. Positive antigen expression was defined based on a 20% threshold established with an isotype control tube. Relative antigen expression was defined relative to internal blast control populations when possible. Blast aberrances were defined as deviation from previously published normal IPs for myeloblast.

Materials and Methods

- 30 cases of AML-MDS, 8 t-AML, and 27 AML-nCG with available FC data were identified in the pathology archives. All cases were classified according to the 2008 WHO criteria; cases with recurrent cytogenetic aberrances were excluded.
- 4-color FC data obtained from blood or bone marrow was retrospectively analyzed using cluster analysis with the following antibodies: CD2, CD3, CD4, CD5, CD7, CD10, CD11b, CD13, CD14, CD15, CD16, CD19, CD22, CD33, CD34, CD36, CD38, CD45, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. The most common aberrances observed in AML-MDs included aberrant expression of MP0 (1316 cases, 81%), CD117 (2230, 73%), CD15 (1929, 68%), CD33 (1709, 59%), CD34 (1629 each, 56%), CD34 (1630; 53%), and CD7 (1303; 41%). The most common aberrances observed in AML-t-AMLs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. The most common aberrances observed in AML-nCGs included aberrant expression of MPO (1316 cases, 81%), CD117 (2230, 73%), CD15 (1929, 68%), CD33 (1709, 59%), CD34 (1629 each, 56%), CD34 (1630; 53%), and CD7 (1303; 41%). The most common aberrances observed in t-MDSs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. Upon antigen expression was defined based on a 20% threshold established with an isotype control tube. Relative antigen expression was defined relative to internal blast control populations when possible. Blast aberrances were defined as deviation from previously published normal IPs for myeloblast.

Results

- The AML-MDS cohort included 17M and 13 F, ages 31-85 years (median 65.5). The blast percentage by FC ranged from 0.2%-96% (median 22%) with a 1:1-98% blast to myeloid ratio. The AML-MDS cohort included 5M and 3F, age 50-72 (median 65), with 1.7%-46% blasts by FC (median 15%), and 3 and 10 aberrances/case (median 8.5). The AML-nCG cohort included 16M and 11F, ages 22-83 (median 54), with 5.2%-93% blasts by FC (median 55), and 11-18 aberrances/case (median 17). The most common aberrances observed in AML-MDs included aberrant expression of MPO (1316 cases, 81%), CD117 (2230, 73%), CD15 (1929, 68%), CD33 (1709, 59%), CD34 (1629 each, 56%), CD34 (1630; 53%), and CD7 (1303; 41%). The most common aberrances observed in AML-t-AMLs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. The most common aberrances observed in AML-nCGs included aberrant expression of MPO (1316 cases, 81%), CD117 (2230, 73%), CD15 (1929, 68%), CD33 (1709, 59%), CD34 (1629 each, 56%), CD34 (1630; 53%), and CD7 (1303; 41%). The most common aberrances observed in t-MDSs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT. The most common aberrances observed in t-MDSs included aberrant expression of TdT (45; 80%), CD117 (65; 75%), CD34 (41, 55%), CD34, CD36, CD45, CD56, CD64, CD117, HLA-DR, MPO, and TdT.

Conclusions

- When comparing AML-MDS, t-AML, and AML-nCG, the majority of antigens examined did not show statistically significant differences in aberrant expression.
- CD22 expression was identified with greater frequency in AML with complex karyotypes vs AML with normal karyotypes.
- Overall, patterns of aberrant antigen expression were variable, reflecting the heterogeneity of the AMLs.