Blast Cell Phenotype Defined by Flow Cytometry Correlates with Clinical Features and Prognosis in Pediatric Acute Lymphoblastic Leukemia

Anna Kuzina, Sergey Nikulshin [1], Zhanna Kovalova, Anda Bartule [1], Dagne Gravele [1]

Rīga Stradiņš University, Latvia
[1] Children's Clinical University Hospital, Latvia

Introduction. Acute leukemia is the most frequent malignancy in children; acute lymphoblastic leukemia (ALL) accounts for 75% cases. Differences in clinical presentation and survival between phenotypically defined B and T-cell ALL have been recognized. On the other hand, there is little data on the association of other diagnostically relevant antigens with clinical features and prognosis.

The aim, materials and methods. The aim of the study was to find significant correlations between leukemic cell phenotype and clinical presentation and prognosis in Latvian children with ALL. 74 consecutive 0–18 year-old patients treated at Children's Clinical University Hospital Department of Oncohematology (the only specialized institution in Latvia) in 2007–2012 were enrolled. The diagnosis and follow-up for minimal residual disease (MRD) was made by 4-color flow cytometer Coulter Epics XL (Beckman-Coulter, USA) in 2007–2010 and 8-color flow cytometer FacsCanto II (Becton-Dickinson, USA) since 2011. Data on symptoms, objective findings (examination, USG and RX studies, laboratory changes), cytogenetics and flow cytometry results were obtained from medical documentation and analyzed by IBM *SPSS* Statistics v.21. Two-sided correlations (Spearman rho) and survival (Kaplan-Meier) were calculated.

Results. B-cell ALL was diagnosed in 64 cases (86.5%) and T-ALL in 10 cases. T-cell phenotype correlated with male gender ($p = 0.027$), higher leukocyte count ($p = 0.008$), higher relapse rate ($p = 0.025$) and mortality ($p = 0.001$). Five year event-free survival for B-ALL was 0.81 and for T-ALL 0.36 ($p = 0.0006$). Overall, five year survival was 0.89 and 0.36, respectively ($p = 0.0002$).

Statistically significant correlation of CD9, CD10, CD19, sCD22, CD34, CD45 and TdT antigens expression with either clinical features or outcome was found. CD9 expression correlated with female gender ($p = 0.025$) and hyperdiploidy ($p = 0.001$) and negatively with fever at presentation. CD10 expression correlated with bone pain ($p = 0.016$), lower risk group ($p = 0.050$) and lower chance of MRD at day 33 ($p = 0.0002$). CD19 expression correlated with higher leukocyte count ($p = 0.018$) and lower chance of relapse ($p = 0.038$). Surface CD22 expression was associated with hyperdiploidy ($p = 0.006$), which is a feature of a favorable outcome, with higher hemoglobin level ($p = 0.040$), lower leukocyte count ($p = 0.001$), less frequent hemorrhagic rush ($p = 0.004$) and less frequent hepatomegaly ($p = 0.040$) at presentation. High CD34 was associated with male gender ($p = 0.023$), higher risk group ($p = 0.050$) and MRD both on day 15 ($p = 0.008$) and day 33 ($p = 0.0007$). CD45 correlated with older age at diagnosis ($p = 0.012$) and neurological symptoms ($p = 0.018$) and negatively with hyperdiploidy ($p = 0.002$). Higher TdT was associated with MRD on day 15.

Conclusions. It was confirmed that statistically significant correlations exist between blast cell phenotype and clinical features and prognosis. The study supported literature data on worse outcome of T-ALL and clinical relevance of CD10 and CD34 antigens. In addition, previously unrecognized clinical, cytogenetic and prognostic correlations of CD9, CD10, CD19, sCD22, CD34, CD45 and TdT antigens expression were statistically proven. Further analysis is necessary to evaluate the practical value of the findings. The study demonstrates the merit of flow cytometry in ALL management.