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Congress Abstract

Immunophenotypic Signature of Immature Granulocytes as a Key Predictor of Genetically Confirmed Acute Promyelocytic Leukemia

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Introduction: Acute promyelocytic leukemia is a specific and hematologically emergent subtype of acute myeloid leukemia that requires the fastest possible verification due to the high risk of developing severe coagulopathy. Multicolor flow cytometry enables rapid verification of atypical promyelocytes and the establishment of their immunophenotypic signature even before molecular genetic study results are obtained.

Objective: To study the specific immunophenotypic profile of "immature granulocyte" populations and to evaluate its predictive value in verifying genetically confirmed acute promyelocytic leukemia in comparison with a blast phenotype group.

Materials and Methods: The results of examination of 54 patients with a primary diagnosis of acute leukemia (37 women, 17 men; mean age — 43.7±12.3 years) were analyzed. Based on flow cytometry data, two groups were formed: 1. Main group (n=45): patients with an immature granulocyte phenotype (29 women, 16 men; mean age — 41.8 years). 2. Additional group (n=9): patients with a defined blast phenotype (CD34+/-, HLA-DR-, with expression of myeloid markers). Immunophenotyping was performed by multicolor flow cytometry using a panel of monoclonal antibodies (CD34, CD117, HLA-DR, CD64, CD33, CD13, CD15, CD16, CD11b, CD11c, MPO, CD4). Genetic status verification was performed by FISH (t(15;17)) and polymerase chain reaction (PML-RARα).

Results: Signature profile of the "immature granulocytes" group (n=45): A) Absolute expression of the pan-myeloid marker CD33 (100%, 45/45); B) High frequency of expression of CD13 (93.3%, 42/45), CD117 (91.1%, 41/45), CD64 (91.1%, 41/45), and cytoplasmic MPO (91.1%, 41/45); C) Virtually complete absence of HLA-DR expression (negative in 95.6% of patients); D) Moderate expression of the stem cell marker CD34 (40.0%, 18/45) and CD4 (44.4%, 20/45); E) Complete absence of mature granulocyte markers (CD15, CD16, CD11b, CD11c — 0%). Predictive value: Of 41 examined patients in the main group, the presence of t(15;17) translocation / PML-RARα chimeric gene was confirmed in 97.6% (40/41); only 1 patient (2.4%) tested negative. In 4 patients, testing was not performed. Comparison group ("blasts," n=9): in this group, expression of the stem cell marker CD34 was significantly more frequently recorded (66.7%); CD33 expression was 100%, CD117 — 88.9%, CD13 — 88.9%, MPO — 77.8%, CD64 — 66.7%; HLA-DR was negative in 88.8% of cases. Genetic confirmation (PML-RARα) was obtained in 55.6% of patients; in 44.5% the result was negative, indicating other variants of acute myeloid leukemia.

Conclusions: Detection of the cytometric signature "immature granulocytes" with the specific profile $CD33^+$ $CD117^+$ MPO^+ $CD64^+$ $HLA\text{-}DR^-$ is a highly accurate predictor of acute promyelocytic leukemia, with confirmation of molecular genetic status (PML-RARα) in 97.6% of cases. The blast phenotype is associated with a higher proportion

of PML-RARα-negative variants, which requires differential diagnosis with other subtypes of myeloid leukemias.

Keywords: Acute Promyelocytic Leukemia; Flow Cytometry; Immunophenotyping