Abstract

Acute leukemia is the most common malignancy in children. According to the origin of the leukemic blasts, two types of leukemia are distinguished – lymphoid (ALL) and myeloid (AML). The focus of this thesis is lineage plasticity of the leukemic blasts. In about 2-5% of leukemias, blasts share immunophenotypic features of both lymphoid and myeloid lineages. In international retrospective study we showed superior overall survival in patients treated according to lymphoid type of protocol compared to patients treated to myeloid type of protocol, especially in cases with CD19 positivity on the blasts.

Another type of the plasticity and diagnostic uncertainty in leukemia is ALL with early switch to monocytic lineage. About 8% of B cell precursor ALL underwent monocytic switch in our consecutive cohort. This phenomenon is more common among *DUX4r*, *PAX5-P80R* and *ZNF384r* leukemias. Discrepancy between minimal residual disease (MRD) measured by flow cytometry and quantitative assessment of immunoreceptor rearrangements method occurs because of the loss of B-lymphoid markers. We investigated transdifferentiation process by mass cytometry. By the multilabel panel we were able to determine the sequence of changes in proteins and transcription factors by new tviblindi algorithm.

Targeted treatment, such as monoclonal antibodies, are becoming part of the treatment protocols, recently. Daratumumab is a new promising drug targeting CD38 molecule used experimentally in relapsed ALL. We treated five patients with relapsed ALL with daratumumab. In patients with resistant disease the apparent loss of the surface CD38 can be observed due to daratumumab binding to CD38 protein causing steric hindrance for diagnostic anti-CD38 antibody.

We evaluated MRD at day 8 in bone marrow in 290 patients treated by ALL IC BFM 2002 protocol. The survival of patients having more than 60% of blasts was inferior compared to those with <60%. Nevertheless, aspiration at day 8 can be substituted with day 15 aspiration.

Keywords: acute leukemia, flow cytometry, immunotherapy, lineage plasticity of leukemic cells, mass cytometry, minimal residual disease, switch to monocytic lineage