Abstract: P1737

Title: HETEROGENEITY AND SIGNIFICANCE OF ETV6/RUNX1 FISH ANALYSIS FINDINGS IN CHILDREN WITH B-ALL

Abstract Type: e-Poster Presentation

Topic: Acute lymphoblastic leukemia - Biology & translational research

Background:

One of the most appropriate methods for detection of the majority of recurrent chromosomal aberrations in childhood acute lymphoblastic leukemia (ALL) is fluorescence in situ hybridization (FISH). ETV6/RUNX1 fusion FISH probes were created for visualization of *ETV6::RUNX1* fusion gene and detection of the most frequent translocation t(12;21)(p13;q22) in pediatric B cell lineage ALL (up to 35%). Wide application of these probes in routine procedures of genetic testing revealed a heterogeneous group of additional changes in ETV6 and RUNX1 gene regions in bone marrow cells of children with B-ALL.

Aims:

The aim of this study was detection and discussion of mentioned genetic changes.

Methods:

This study considered the 20 patients diagnosed with B-ALL and underwent genetic testing in the Laboratory for Medical Genetics, Mother and Child Health Care Institute of Serbia in 2023. According to ALLIC BFM protocol, cytogenetic analysis of bone marrow cells (conventional and G-bending) were performed along with RT-PCR for detection of *BCR::ABL, MLL::AF4, ETV6::RUNX1* and *PBX::E2A* fusion genes. In addition, FISH analyses using PBXB1/E2A plus translocation; dual fusion probe and ETV6/RUNX1 translocation, dual fusion probe (Cytocell) were performed in order to detect iAMP and *HLF::E2A* fusion.

Results:

Results revealed chromosomal changes in all 20 patients (100%). Numerical and/or structural chromosomal aberrations were seen in 18/20 (90%) patients by classical cytogenetic methods. Presence of recurrent fusion genes by RT-PCR were found in 10/20 (50%) cases. *ETV6::RUNX1* fusion was detected by RT-PCR and FISH in 9/20 cases (45%) while this fusion was present as more than one, two or four extra signals in 4/20 (20%). Additional RUNX1 signals were found in 10/20 (50%) patients, two of them as iAMP (10%), others as one or two additional RUNX1 signals (partial trisomy 21q22 or extra chromosome 21). Changes in a number of signals for ETV6 region (as addition or deletion of 12p13) were found in 4/20 cases (20%). Detected ETV6 and RUNX1 aberrations were presented as unique or simultaneously as a part of complex genotype in different combinations, also in one or more cell clones and will be listed precisely, for every patient. Reached results were in line with literature and discussed, concerning frequencies and prognostic significance and considering available clinical data for particular cases.

Summary/Conclusion: Regions of ETV6 and RUNX1 genes are involved in the molecular base of B-ALL in children with high frequencies. Aberrations of these regions appear as a heterogeneous group of changes (t (12;21), del12p13, add12p13, iAMP, +21, add 21q22), often simultaneously. Some of them have well established molecular mechanisms and prognostic impact but for the others and especially for their combinations, further and more extensive investigation will give precise and accurate conclusions. In this field, the FISH method remains an irreplaceable diagnostic and basic research tool.

Keywords: B cell acute lymphoblastic leukemia, Genetic, FISH, TEL-AML1