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Akutne limfoblastične leukemije

A GIRL WITH RARE DOUBLE PHILADELPHIA CHROMOSOME POSITIVE PRE-B ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute lymphoblastic leukemia (ALL) is the most common malignant disease in children. ALL with Philadelphia (Ph) chromosome is found in up to 5% of pediatric patients with ALL. Ph chromosome is a derivative chromosome 22 originated from reciprocal translocation t(9;22)(q34;q11) of genetic material between chromosomes 9 and 22 and contains a fusion gene called BCR-ABL1.

Materials and Methods: 12-year-old girl with Ph pos. ALL treated in UHC Zagreb, presented with rare double Philadelphia chromosome

Results: A 12-year-old girl was admitted to hospital with pancytopenia in peripheral blood. Bone marrow cytology showed 98% blasts of small and medium-size with sparse and agranulated cytoplasm. Chromosome analysis revealed a hyperdiploid clone with translocation of t (9; 22) and additional derived chromosome 22 (double Ph), trisomy of chromosome 21, and a 9p21 deletion. Immunophenotype analysis revealed immature and aberrant pre-B phenotype cells among mononuclear cells. On the total number of cells in the sample, the proportion of immature B-lymphoblasts was 94%. Her final diagnosis was pre-B ALL with a double Ph chromosome. Initial treatment consisted of conventional chemotherapy according to *EsPh ALL BFM* protocol with regular intrathecal chemotherapy. Imatinib (300 mg/m2) was included alongside conventional chemotherapy on day 15. She had a good initial treatment response. Bone marrow biopsy revealed MRD 7.2% on day 15 and 0% on day 33. BCR-ABL1 was 0.26% on day 33. After 12 months of conventional therapy her MRD continued to be immeasurable and her bcr-abl1 at 0.005%. She is currently on maintenance therapy with daily imatinib mesylate and 6-mercaptopurine and weekly methotrexate administration.

Conclusion: The clinical significance of the double Ph chromosome in pediatric and adult patients remains unknown. Scare published reports suggest that double Ph chromosome is associated with a lower probability of complete remission, shorter time to disease progression, and decreased overall survival compared with a single Ph chromosome. The contemporary treatment standard for Ph chromosome-positive ALL consists of chemotherapy with TKI imatinib. Allogenic stem cell transplantation (SCT) after the first remission is believed to be the treatment of choice in adult. In the pediatric patients alloSCT is option only in a case of late remission or relapsed disease.

ARRAY COMPARATIVE GENOMIC HYBRIDIZATION IN DIAGNOSTICS OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Array comparative genomic hybridization with single nucleotide polymorphism (aCGH+SNP) is a powerful method for detection of copy number (CN) alterations and copy neutral loss of heterozygosity (CN-LOH) in hematologic malignancies. Acute lymphoblastic leukemias (ALL) partially rely on cytogenetics for prognostica-

tion and therapy decision since they frequently harbor deletions (IKZF1, CDKN2A/B, PAR1, PAX5, ERG, Rb1), amplifications (iAMP21) and hiper- or hypodiploidy. The aim of the study was to determine efficacy of aCGH+SNP in diagnostics of ALL in comparison to G-banding.

aCGH+SNP was performed on sixteen patients with newly diagnosed ALL (13 B-ALL and 3 T-ALL). aCGH+SNP revealed prognostic markers in 94% of samples (N=15). CN alterations that are of prognostic significance but could not be detected by classical G-banding were as follows (N=8/16, 50%): hiper- or hypodiploidy in cases where no metaphases could be found (N=2) or only normal karyotype was detected (N=1). In addition, we were able to detect a patient with PAR1 deletion (Ph-like phenotype), a patient with IKZF1 and ERG gene deletions, a patient with iAMP21 and RB1 deletion, a patient with CDKN2A/B double deletion and MYB, ABL1 and NUP214 duplications, and a patient with CDKN2A deletion in combination with IKZF2 and C-MYC deletions. In remaining 50% of samples where both G-banding and aCGH+SNP found prognostically relevant markers, aCGH+SNP did detect additional CN alterations that could not be detected by G-banding due to limitations in the resolution of the method (deletions, duplications, amplifications <5MB). Additionally, we were able to detect multiple CN-LOH >5MB that are considered to be a part of the malignant clone in 8/15 patient samples (50%). Major drawback of the method is the inability to detect balanced translocations in the samples.

In conclusion, aCGH+SNP is a powerful method in diagnostics of ALLs that covers entire genome and can detect relatively novel prognostic markers in ALL (delPAR1, delIKZF1, IKZF1plus category). In addition to G-banding, FISH and molecular analysis, it reveals relevant information about the genetics underlying the disease.