INTEGRATED CYTOGENETIC CHARACTERIZATION OF A PREVIOUSLY UNIDENTIFIED t(9;12;14)(p13;p13;q32) REARRANGEMENT IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Ağaran, Sema Nur[1]; Guner Izmir, Sebnem[2]; Akalin, Ibrahim[1]; Ascioglu, Huriye[1]; Akbas, Hacer[1]; Ozgumus, Toluy[3]

[1]Metagentech Center for Genetic Diseases, [2]Faculty of Health Sciences, Istanbul Gelisim University, [3]Atlas University Faculty of Medicine

Background: Cytogenetic abnormalities are central to the diagnosis and risk stratification of B-cell acute lymphoblastic leukemia (B-ALL), yet rare structural rearrangements remain incompletely characterized. Although t(7;14)(p13;q11) has been reported predominantly in T-lineage malignancies and only exceptionally in B-ALL, abnormalities involving chromosomal regions 9p13, 12p13, and 14q32 encompass leukemia-associated loci, including PAX5, ETV6, and IGH, which are critical for B-cell development and leukemogenesis. The coexistence of these uncommon abnormalities may provide insight into clonal evolution and disease biology. Purpose: To characterize a cryptic marker chromosome and define the underlying cytogenetic abnormalities in a patient with B-ALL.

Methods: Conventional karyotyping, RT-PCR, interphase FISH, follow-up chromosome analysis, and metaphase FISH using the ETV6/RUNX1 dual-fusion probe were performed.

Results: A 20-year-old woman with B-ALL demonstrated 46,XX,t(7;14)(p13;q11),dic(9;12)(p13;p13),+mar[20] at diagnosis. RT-PCR was negative for BCR::ABL1, TCF3::PBX1, and KMT2A::AFF1. Interphase FISH was negative for BCR::ABL1, ETV6::RUNX1, KMT2A, MYC::IGH, chromosome 13q deletion, trisomy 8, and ATM abnormalities, but revealed partial ETV6 deletion in 94% of nuclei and signal patterns compatible with trisomy 14/IGH rearrangement in 90%. Follow-up cytogenetic analysis showed 46,XX,del(12)(p13),t(7;14)(p13;q11),t(9;12;14)(p13;p13;q32),+14. Metaphase FISH localized ETV6 signals to the previously unidentified marker chromosome, demonstrating that it represented the derivative chromosome generated by t(9;12;14)(p13;p13;q32). Subsequent chromosome analysis showed a marked reduction of the abnormal clone. Due to the persistence of the jumping translocation, the patient underwent bone marrow transplantation.

Conclusions: Integrated cytogenetic analysis and metaphase FISH were essential for resolving a cryptic marker chromosome, documenting clonal evolution, and supporting therapeutic decision-making in B-ALL. The chromosomal breakpoints map to genomic regions containing PAX5, ETV6, and IGH, suggesting potential biological relevance despite the absence of recurrent molecular fusion transcripts. This case expands the cytogenetic spectrum of B-ALL and highlights the diagnostic value of metaphase FISH for characterizing cryptic chromosomal abnormalities.