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Amplification of the *BCR::ABL1* Fusion Gene: A Rare Phenomenon in B-cell Acute Lymphoblastic Leukemia

BCR::ABL1 Füzyon Geni Amplifikasyonu: B-hücreli Akut Lenfoblastik Lösemide Nadir Bir Olgu

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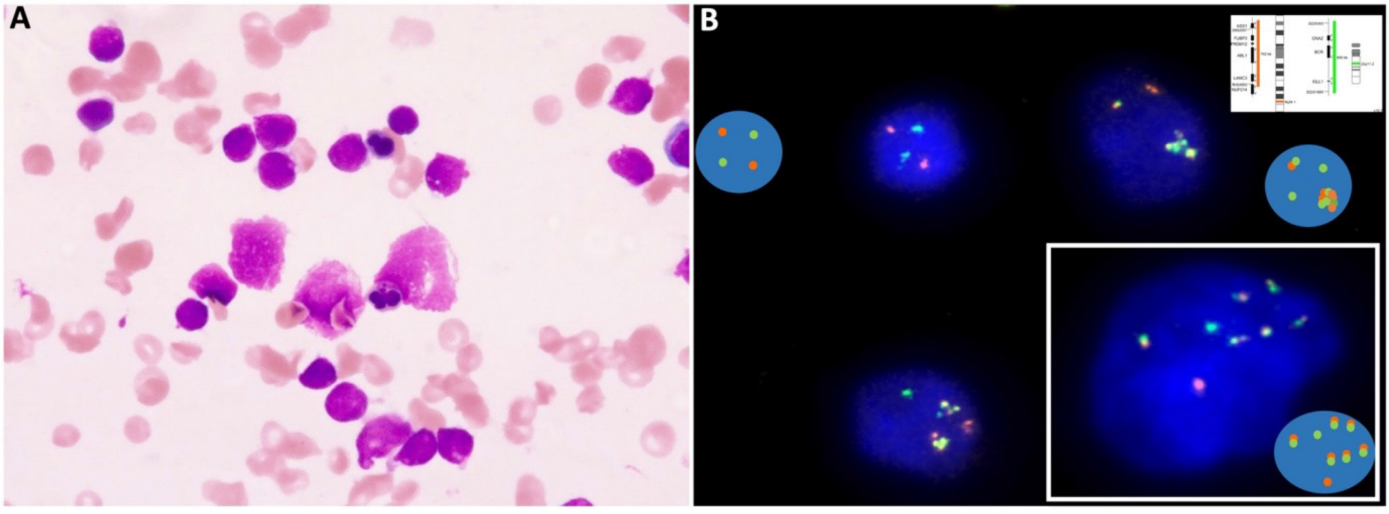

Figure 1. A) Bone marrow examination revealed predominantly small lymphoid blasts (May-Grünwald-Giemsa stain, 1000x). B) Fluorescent in situ hybridization (FISH) using BCR/ABL1 dual-color dual fusion probe revealed multiple extra copies of the *BCR::ABL1* fusion gene (yellow signals) in a cluster (inset) or separately in 70% of the interphase nuclei (*ABL1:* orange fluorescence-labeled probe, *BCR:* green fluorescence-labeled probe). Graphical images highlighting the design of the FISH probe, normal signal pattern (2 red, 2 orange), and amplified *BCR::ABL1* signals appearing separately and in a clustered manner are given.

A 48-year-old woman presented with fever for 1 month. On examination, she had hepatosplenomegaly. A complete blood count revealed pancytopenia (hemoglobin: 49 g/L, leukocyte count: $0.6x10^9$/L, platelet count: $6x10^9$/L). Bone marrow examination showed 55% blasts (Figure 1A). On a 10-color flowcytometry panel, 64% of precursor cells were positive for CD19, CD10, CD20, $CD38^{dim}$, $CD81^{dim}$, CD86, cytoplasmic CD79a, CD34, and terminal deoxynucleotidyl transferase (TdT) while they were negative for myeloid (CD13, CD33, CD117, CD14, CD64, CD36) and T-cell-associated markers. Hence, this case was diagnosed as B-cell acute lymphoblastic leukemia (B-ALL). Fluorescent in situ hybridization (FISH) was performed for the *BCR::ABL1* and *ETV6::RUNX1* translocations and the *TCF3* and *KMT2A* rearrangements, and the t(9,22)(q34;q11) *BCR::ABL1* translocation was revealed along with multiple copies of the fusion gene appearing separately (Figure 1B, inset) or in a

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clustered manner (Figure 1B) in 70% of the interphase nuclei, consistent with the amplification of the *BCR::ABL1* fusion gene. The patient died within a month of the diagnosis.

Additional Philadelphia (Ph) chromosomes are frequently seen in B-ALL and in cases of disease progression in chronic myeloid leukemia (CML). However, multiple extra copies of the *BCR::ABL1* fusion gene are rare genetic occurrences in CML signifying disease progression and imatinib resistance. This results from a second Ph chromosome, double minutes, isoderivative chromosome 22, and isodicentric Ph chromosome [1,2]. Although extra copies of the *BCR::ABL1* fusion gene were reported previously in T-ALL, they have never been documented in B-ALL [3]. This signal pattern highlights the need for FISH or other conventional cytogenetic approaches over reverse-transcriptase polymerase chain reaction studies to confirm disease progression.

Keywords: *BCR::ABL1*, Fluorescent in situ hybridization, B-cell acute lymphoblastic leukemia

Anahtar Sözcükler: *BCR:ABL1*, Floresan in situ hibridizasyon, B-hücreli akut lenfoblastik lösemi

Ethics

Ethics Committee Approval: The approval of the relevant institutional ethics committee was obtained and the research adhered to the guidelines set forth by that committee in line with the principles stipulated by the 1975 Declaration of Helsinki, revised in 2008.

Informed Consent: Written informed consent was obtained from the patient included in this study.

Authorship Contributions

Surgical and Medical Practices- D.R., S.S., P.S., A.J.; Concept- S.S.; Design- S.S.; Data Collection or Processing- D.R., S.S.; Analysis or Interpretation- S.S., P.S., A.J.; Literature Search- D.R.; Writing- D.R., S.S.

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