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BRIEF REPORT

# Evidence for BCR/ABL1-positive T-cell acute lymphoblastic leukemia arising in an early lymphoid progenitor cell

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## Abstract

BCR-ABL1-positive leukemias have historically been classified as either chronic myelogenous leukemia or Ph+ acute lymphoblastic leukemia. Recent analyses suggest there may be a wider range of subtypes. We report a patient with BCR-ABL1 fusion positive T-cell ALL with a previously undescribed cell distribution of the fusion gene. The examination of sorted cells by fluorescence in situ hybridization showed the BCR-ABL1 fusion in the malignant T cells and a subpopulation of the nonmalignant B cells, but not nonmalignant T cells or myeloid or CD34+ progenitor cells providing evidence that the fusion may have occurred in an early lymphoid progenitor.

**KEYWORDS**
BCR-ABL1, discordant MRD, T-cell ALL

## 1 | INTRODUCTION

The BCR-ABL1 fusion gene is the hallmark of chronic myelogenous leukemia (CML) and is also present in a subtype of acute lymphoblastic leukemia (ALL). Hovorkova et al[1] provided evidence that patients presenting with BCR-ABL1 fusion-positive ALL might represent a spectrum of leukemia subtypes. They demonstrated that minimal residual disease (MRD) measured by the BCR-ABL1 fusion gene polymerase chain reaction (PCR) and the immunoglobulin gene/T-cell receptor (TCR) gene PCR was concordant in the majority of cases and that the fusion gene was confined to the lymphoid blasts. However, in about 20% of the cases, the MRD was discordant and the fusion gene was present not only in the malignant blasts but also in nonmalignant cells, suggesting that the fusion might have occurred in a multipotent progenitor cell. The BCR-ABL1 fusion gene is almost always found in malignant B cells and has been reported only rarely in malignant T cells.[2–4] We describe a patient with BCR-ABL1 transcripts in the malignant T cells and in a subpopulation of nonmalignant B cells. Progenitor cells, myeloid cells, nonmalignant T cells, and a population of normal B cells were BCR-ABL1 negative. The TCR beta and gamma genes were not rearranged in the malignant T cells. These combined results suggest that the BCR-ABL1 fusion may have occurred in an early lymphoid progenitor. Determining the cell type of origin is important, as each cell type may have distinct biological properties and may require different treatment.[5–7] Including fluorescence in situ hybridization (FISH) analysis for BCR/ABL1 fusions in fluorescent-activated cell sorter (FACS)-sorted cells and genomic analysis during induction may lead to a better understanding of the frequency and outcome of the different BCR-ABL1-positive leukemia subtypes.

## 2 | CASE DESCRIPTION AND METHODS

A 13-year-old male presented with a white blood cell count of $426 \times 10^9$/L, hemoglobin 11.5 g/dL, and platelets $115 \times 10^9$/L. The review of the peripheral blood (PB) smear showed 84% blasts, 1% myelocytes, 1% metamyelocytes, 1% bands, 3% neutrophils, 12% lymphocytes, and 1% monocytes. His creatinine was 0.6 and uric acid 7.7. A computed tomography scan was remarkable for splenomegaly and enlarged abdominal lymph nodes; there was no mediastinal mass. Blasts comprised 77% of the marrow cellularity and were positive for CD34 (minimal), CD7, CD5, CD4, CD8 (partial), CD1a (partial), CD38, cytoplasmic CD3, and TdT but negative for B-cell and myeloid markers. The cerebrospinal fluid was negative. FISH was positive for the BCR-ABL1 fusion gene. The ABL kinase domain mutation analysis of his BCR-ABL1 fusion protein (p190) was negative. Cytogenetic studies revealed no other abnormalities. He was started on four-drug induction and the tyrosine kinase inhibitor, dasatinib. His initial clinical course was complicated by tumor lysis syndrome and acute kidney injury requiring continuous venovenous hemodiafiltration.

Abbreviations: ALL, acute lymphoblastic leukemia; BM, bone marrow; BP, blast phase; CML, chronic myelogenous leukemia; FACS, fluorescent-activated cell sorter; FISH, fluorescence in situ hybridization; HSCT, hematopoietic stem cell transplant; MRD, minimal residual disease; PB, peripheral blood; PCR, polymerase chain reaction; RT, reverse transcription; TCR, T-cell receptor.