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Leukaemia Section
Short Communication

t(9;14)(q33;q32) IGH/LHX2

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Abstract

Short Communication on t(9;14)(q33;q32) IGH/LHX2, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

Chronic myeloid leukemia (CML) in B-cell lymphoid blast crisis

Phenotype/cell stem origin

B cell phenotype (CD19, CD10) with 2 aberrant myeloid markers (CD13 and CD33).

Etiology

Unknown.

Epidemiology

Only one case to date, a 10-year-old male patient (Nadal et al., 2012).

Clinics

Lymphadenopathies, enlarged spleen and liver. Central nervous system involvement.

Cytology

High WBC with blast cells (44%), myelemia, eosinophilia and basophilia. Bone marrow aspiration showed 60% of undifferentiated blast cells with persistence of the granulocytic lineage.

Treatment

The patient was treated according to the European protocol ESPHALL (imatinib, asparaginase, vincristine, vindesine, daunorubicin, aracytine, VP16, ifosfamide, and methotrexate, followed by an allograft).

Evolution

After induction, minimal residual disease (MRD) detection by CMF and by molecular analysis was negative, whereas RT-PCR for BCR-ABL1 transcript was still positive. Chromosomal examination showed the presence of one metaphase out of 30 with only the t(9;22)(q34;q11), suggesting that the t(9;14) translocation was a secondary chromosomal abnormality.

Thus, the chemotherapy had eradicated the lymphoblast cells but a CML clone persisted, further supporting the diagnosis of CML in BC.

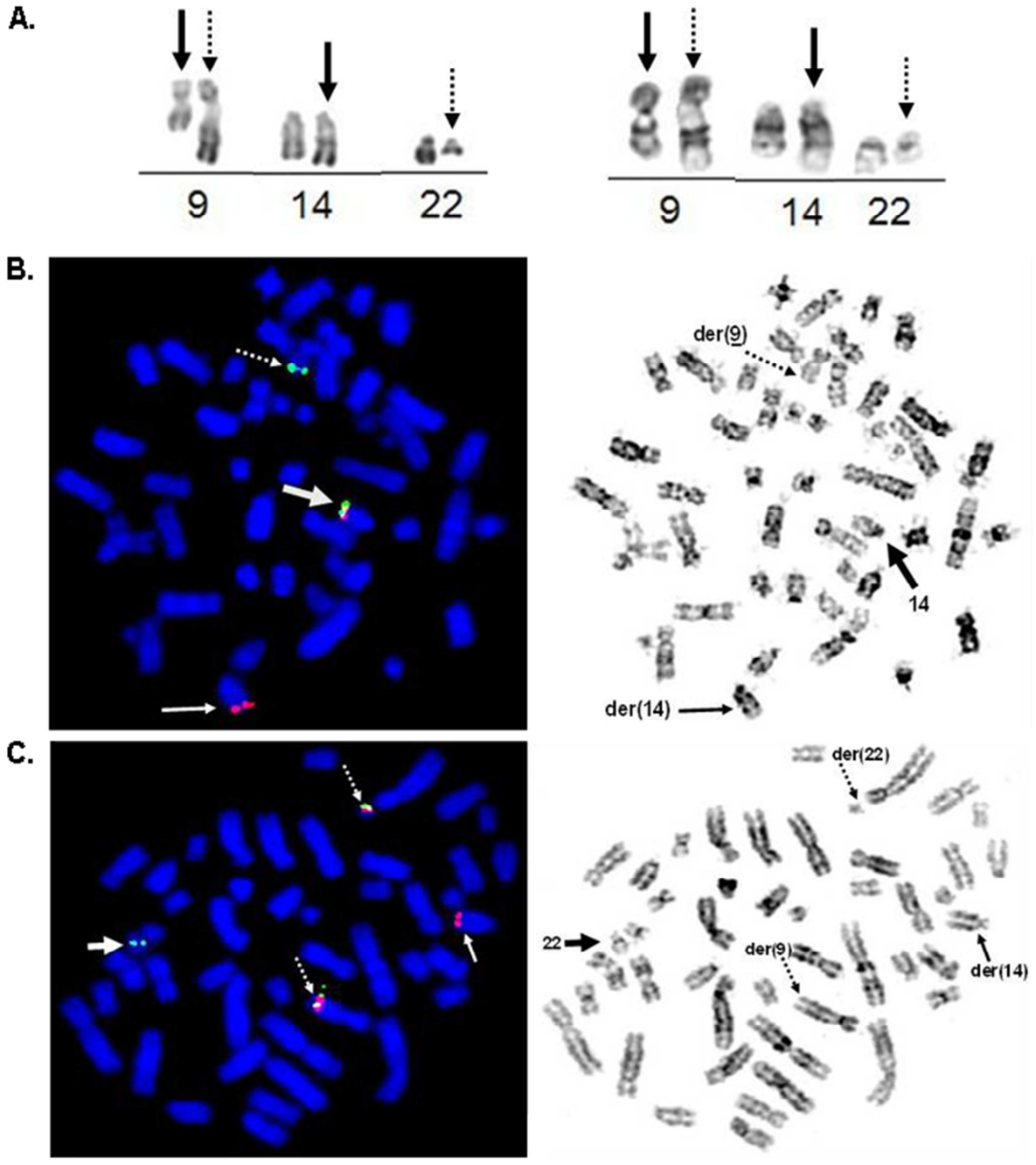
By 7 months after diagnosis, the patient underwent allogenic stem cell transplantation from his HLA-matched sister. At 2 years post-transplantation, the patient was alive and well. BCR-ABL1 transcript was undetectable (<0.001%).

Cytogenetics

Additional anomalies

The t(9;14)(q33;q32) translocation appears as a secondary abnormality occurring at acutisation of a CML with the usual t(9;22)(q34;q11) with a breakpoint in the mBCR region. The latest is usually observed in BCR-ABL1+ de novo acute lymphoblastic leukemia but is rare in CML.

i(7)(q10), present in 2 out of the 20 metaphases analyzed using conventional karyotype, and in 3/100 metaphases using FISH (7q22/7q36 Dual-Color probe, Kreatech Diagnostics).



A. Conventional karyotype: partial R and G-banded karyotype. The derivative chromosomes of translocations t(9;14)(q33;q32) and t(9;22)(q34;q11) are denoted by solid and dotted arrows, respectively.
B. FISH: representative metaphase hybridized with dual color break-apart IGH probe (Abbott, Rungis, France). A fusion signal is seen on normal chromosome 14 (large arrows), a red signal on derivative chromosome 14 (small solid arrows) and a green signal on derivative chromosome 9 (small dotted arrows).
C. FISH: representative metaphase hybridized with a BCR/ABL ES probe (Abbott). A green signal is seen on a normal chromosome 22 (large arrows), and two fusion signals on derivative chromosomes 9 and 22 (small dotted arrows), confirming the BCR-ABL1 rearrangement with a breakpoint in the mBCR region. A red signal is observed on derivative chromosome 14 (small solid arrows), indicating that the breakpoint of t(9;14) was centromeric to the ABL1 gene in chromosome 9.

Genes involved and proteins

LHX2

Location
9q33

Note
LIM homeobox gene LHX2 is a member of the LIM homeobox family of transcription factors characterized by a DNA binding homeodomain and a cystein-rich LIM-domain. LHX2, initially identified as an early marker in B-lymphocyte differentiation (Xu et al., 1993), is involved in the neurogenesis, hair follicle, and hematopoietic development (Porter et al., 1997).

IGH

Location
14q32

Result of the chromosomal anomaly

Hybrid gene

Note
The translocation links sequence located 148 kb centromeric of LHX2 on chromosome 9 to JH6 segment on chromosome 14.

Fusion protein

Note
No fusion protein.

Oncogenesis
LHX2 juxtaposition with the IGH locus results in strong over-expression of LHX2, which may have contributed to the rapid progression in the blastic phase. It has been shown that over-expression of LHX2 in murine hematopoietic precursors leads to the development of chronic myeloproliferative disorders (Richter et al., 2003). Thus, transcriptional deregulation of LHX2 plays a recurrent role in leukemogenesis.

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