Leukaemia Section
Short Communication

t(9;12)(q34;p13)
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Clinics and pathology

Disease
Described in only 6 cases; acute lymphoblastic leukemia (ALL), acute non lymphocytic leukemia (ANLL) and chronic myeloid leukemia (CML).

Prognosis
Numbers small, but one CML case had allogeic BMT and is in complete remission, the remaining cases had rapid disease progression and died of shortly after diagnosis.

Cytogenetics

Cytogenetics morphological
t(9;12)(q34;p13), cryptic at the cytogenetic level.

Variants
t(9;12;14)(q34;p13;q22) and complex insertions of ETV6 into ABL.

Genes involved and proteins

ABL
Location: 9q34
DNA/RNA
ETV6 is fused to exon 2 of ABL in the three cases described.

Protein
Tyrosine kinase, localized primarily to the nucleus.

ETV6
Location: 12p13
DNA/RNA
9 exons; alternate splicing.

Protein
Contains Helix-Loop-Helix (HLH) at N-terminal end and ETS DNA binding domain at C-terminal end; wide expression; nuclear localization; ETS-related transcription factor.

Result of the chromosomal anomaly

Hybrid gene
Description
5' ETV6–3' ABL; two different fusion breakpoints have been described; ETV6 exon 4 fused in frame to ABL exon 2 (Type A) and ETV6 exon 5 fused in frame to ABL exon 2 (Type B); ETV6 maintains the HLH domain and ABL the tyrosine kinase domain.

Fusion protein
Description
a 155 kDa protein in Type A, 180 kDa protein in Type B; has elevated tyrosine kinase activity, localized in the cytoplasm and co-localizes with the actin filaments of the cells.

Oncogenesis
The HLH domain of ETV6 induces oligomerization, which results in the constitutive activation of the kinase domain of ABL; this is thought to result in phosphorylation of JAK2 and activation of the STAT pathway.

Biological activity very similar to BCR-ABL.

References
Papadopoulos P, Ridge SA, Boucher CA, Stocking C, Wiedemann LM. The novel activation of ABL by fusion to an ets-related gene, TEL. Cancer Res. 1995 Jan 1;55(1):34-8


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