t(4;22)(q12;q11.2)
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Identity

Partial karyotype showing chromosomes 4 and 22.

Clincs and pathology

Disease
Reported in 3 cases; myeloproliferative disorder:

atypical chronic myeloid leukemia (aCML) (Philadelphia chromosome-negative).

Etiology
One case was post-treatment for lymphoma, thus suspected to be a secondary MPD.

Clinics
3 cases shared characteristics of splenic enlargement, eosinophilia and male predominance.

Prognosis
One patient on treatment with good response to imatinib mesylate.
**Cytogenetics**

Note
t(4;22)(q12;q11.2), easily distinguished cytogenetically.

**Cytogenetics molecular**

FISH for BCR-ABL1 is negative for fusion but will show extra signal for BCR when using the dual fusion probe set. BCR-ABL1 PCR is negative.

![Interphase FISH showing 3 signals for BCR (green), suggesting rearrangement. Two normal signals for ABL1 (red).](image)

**Probes**

BCR-ABL dual fusion probe set.

**Additional anomalies**

The t(4;22) was observed as the sole anomaly in the few reported cases to date.

**Genes involved and proteins**

**PDGFRA**

**Location**

4q12

**Note**

Member of the protein-tyrosine kinase receptor family subclass III that includes the colony stimulating factor-1, c-KIT, FLT1, and FLT3/FLK2. Suggested role for normal PDGFRA receptor expression during periods of glial cell development and connective tissue growth.

**DNA/RNA**

23 exons; includes 2 intracellular tyrosine kinase domains, TK1 and TK2 (exons 13-15 and 17-21), 5 extracellular Ig-like domains (exons 3-10), and a hydrophobic transmembrane domain (exon 10). The cytoplasmic region also encodes an ATP binding site.

**Protein**

170-kD transmembrane glycoprotein that normally binds all PDGF isoforms, AA, AB, and BB at its extracellular Ig domain.

**BCR**

**Location**

22q11.2

**DNA/RNA**

23 exons; alternate splicing.

**Protein**

160-kDa protein; contains a unique serine/threonine kinase activity and at least two SH2 binding sites encoded in its first exon and a C-terminal domain that functions as a GTPase activating protein for p21(rac).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Note**

5'BCR-3'PDGFRA fusion.

**Description**

Fusion of BCR exon 7, 12 or 17 (in 3 cases described) with PDGFRA exon 12, in frame, containing intronic sequence from BCR in two cases.

**Fusion protein**

**Description**

169 kDa protein in one case, somewhat smaller in two others.

**Expression / Localisation**

Predicted to be localized intracellularly.

**Oncogenesis**

Alteration of tyrosine kinase activity secondary to loss of regulatory and PDGF binding domains; also, BCR domains may significantly affect BCR-PDGFRA downstream signaling pathways as seen with BCR-ABL fusion.

**References**


This article should be referenced as such: