t(8;9)(p22;p24)
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Clinics and pathology

Disease
The PCM1-JAK2 resulting from a t(8;9)(p22;p24) fusion gene occurs in both myeloid and lymphoid malignancies: CML-like chronic phase disease with associated eosinophilia and marrow fibrosis and possible evolvement to secondary AML and B-ALL ('blast crisis'), de novo B-ALL and T-ALL/T-NHL. Striking male predominance.

Phenotype / cell stem origin
Atypical chronic myeloid leukemia; chronic eosinophilic leukemia; pre-B-cell acute lymphoblastic leukemia; acute myeloid leukemia M6; T-cell acute lymphoid leukemia; myelodysplastic syndrome / myeloproliferative disease, unclassifiable; secondary acute myeloid leukemia.

Epidemiology
15 published cases (plus 3 unpublished), striking male predominance, only 2 females, median age 45.5 years (range, 12-74).

Clinics
CML-like chronic phase disease with associated eosinophilia and marrow fibrosis and possible evolvement to secondary AML and B-ALL ('blast crisis'), de novo B-ALL and T-ALL/T-NHL. Striking male predominance, clinical course highly variable.

Treatment
Allogeneic stem cell transplantation; interferon; hydroxyurea; no specific JAK2 inhibitor currently available.

Prognosis
PCM1-JAK2 positive disease is an aggressive disease compared to patients with MPD and associated V617F JAK2 mutation. Acute leukemias (de novo and secondary) seen in approximately 50% of all cases.

Cytogenetics

Cytogenetics morphological
t(8;9)(p22;p24).

Probes
First probe: 5´ and 3´ regions of PCM1 (RP11-49F3 and RP11-3K23). Second probe: 5´ and 3´ regions of JAK2 (RP11-3H3 and RP11-28A9).

Genes involved and Proteins

PCM1 (pericentriolar material 1)
Location: 8p22-p21.3
DNA / RNA
41 exons; alternate splicing.
Protein
PCM1 is involved in recruiting proteins necessary for centrosome replication and predicted to contain multiple coiled-coil motifs.

JAK2 (Janus kinase 2)
Location: 9p24
DNA / RNA
23 exons.
Protein
JAK2 is a tyrosine-protein kinase with transmembrane and tyrosine kinase domains.
Results of the chromosomal anomaly

Hybrid gene

Description

5' PCM1 - 3' JAK2.

Transcript

PCM1-JAK2 chimeric RNA constantly present; variable positions of the breakpoints within PCM1 and JAK2; reciprocal transcript may be present.

Fusion protein

Diagrammatic representation of normal JAK2, normal PCM1 and the PCM1-JAK2 fusion protein.

Description

PCM1-JAK2 mRNA is predicted to encode a protein that retains several of the predicted coiled-coil domains from PCM1 and the entire tyrosine kinase domain of JAK2.

Oncogenesis

As has been found for other tyrosine kinase fusion proteins, e.g. BCR-ABL, it is likely that one or more of the coiled-coil motifs from PCM1 result in dimerization or oligomerization of the PCM1-JAK2 chimera, with consequent constitutive activation of the JAK2 kinase domain.

References


Bousquet M, Brousset P. Myeloproliferative disorders carrying the t(8;9) (PCM1-JAK2) translocation. Hum Pathol 2006;37:500.

This article should be referenced as such: