t(4;12)(q12;p13) PDGFRA/ETV6

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Identity

Note: See also the t(4;12)(q11-q21;p13) with CHIC2 and ETV6 involvements in M0 acute myeloid leukaemia (M0-AML), keeping in mind that a t(4;12)(q13-21;p12-13) has also been described in B-cell acute lymphocytic leukaemia (ALL) (GFCH, 1993; Behm et al., 1996; Elghezal et al., 2001), B-cell non Hodgkin's lymphoma (NHL) (Schouten et al., 1990; Palanisamy et al., 2002), and in a case of adult T-cell lymphoma/leukemia (Sadamori et al., 1991).

Clinics and pathology

Disease
Myeloproliferative disease with eosinophilia

Epidemiology
Only one case to date, a 51 year old male patient.

Evolution
The disease was rather indolent for over 7 years; imatinib was then started with significant resolution of symptoms, and the patient remains in cytogenetic remission 9 months later.

Genes involved and proteins

PDGFRA
Location
4q12
Protein
Composed of an extracellular domain (the immunoglobulin-like motifs), a transmembrane domain, with an inhibitory juxtamembrane WW-like domain (Irusta et al., 2002), and an intracellular domain (kinase domain); receptor tyrosine kinase; forms homodimer, and heterodimer with PDGFRB; dimerization induces kinase domain activation, leading to the activation of intracellular signalling pathways (Kawagishi et al., 1995).

Somatic mutations
Hybrid genes between various partners and PDGFRGA occur in chronic myeloid leukaemia-like diseases with eosinophilia, mostly chronic eosinophilic leukemia (CEL), a clonal hypereosinophilic syndrome. PDGFRGA partners known so far are: STRN (2p24) (Curtis et al., 2007), FIP1L1 (4q12) (Cools et al., 2003, Pardanani et al., 2004), CDK5RAP2 (9q33) (Walz et al., 2006), KIF5B (10p11) (Score et al., 2006), ETV6 (12p13), herein described (Curtis et al., 2007), and BCR (22q11) (Baxter et al., 2002).

Mutations of platelet-derived growth factor receptor-alpha (PDGFRA) are observed in a subset of gastrointestinal stromal tumors (GISTs) (Heinrich et al., 2003).

Tumours with PDGFRA involvement are responsive to imatinib therapy (Cools et al., 2003; Debiec-Rychter et al., 2004).

ETV6
Location
12p13
Protein
Contains a HLH domain and a ETS-DNA binding domain; ETS-related transcription regulator.

Result of the chromosomal anomaly

Hybrid gene
Transcript
5' ETV6-3' PDGFRA; Fusion between ETV6 intron 6 and PDGFRA intron 11; reciprocal product not found -
Fusion protein

Description

The N-term ETV6- C-term PDGFRA fusion protein retains most of ETV6, including the pointed domain and the kinase domain of PDGFRA; although the WW-like domain is thought to act as an autoinhibitory element preventing kinase over-activation.

References


This article should be referenced as such: