Myeloid/Lymphoid neoplasms with abnormalities of PDGFRB
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Abstract

This insert represents a review of myeloid and lymphoid neoplasms with abnormalities of PDGFRB including clinical presentation, morphologic review, and cytogenetic findings.

**KEYWORDS**

Myeloid and lymphoid neoplasms with abnormalities of PDGFRB; PDGFRB; eosinophilia; chronic myelomonocytic leukemia; tyrosine kinase inhibitor

Clinics and pathology

**Disease**

Myeloid and lymphoid neoplasms with abnormalities of PDGFRB are neoplasms in which eosinophilia is typical, although not required. Gene fusions with PDGFRB were first described by Golub et al. in 1994 in a patient with features consistent with chronic myelomonocytic leukemia (CMML). Since that time, over 20 fusion partners have been described. The entity was first formally accepted in the 2008 edition of the World Health Organization's Classification of Tumours of Haematopoietic and Lymphoid Tissues along with abnormalities of PDGFRA and FGFR1. In the WHO 2016 edition, myeloid and lymphoid neoplasms with eosinophilia and t(8;9)(p22;p24.1) PCM1 / JAK2 is now recognized as a provisional entity.

**Phenotype/cell stem origin**

The cell of origin is a hematopoietic cell with commitment to eosinophilic differentiation.

**Epidemiology**

Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRB (as well as abnormalities of PDGFRA and FGFR1) are rare. Adult males are most commonly affected with a median age of onset in the late forties; however, older adults and rarely children have also been affected.

**Clinics**

Patients typically present with splenomegaly with hepatomegaly being less frequent; lymphadenopathy may also be seen. As with abnormalities of PDGFRA, skin and cardiac infiltration may be present at diagnosis with resulting cardiac damage.

**Pathology**

In patients with abnormalities of PDGFRB, peripheral blood and bone marrow are almost always involved with typical leukocytosis and possible concordant anemia and/or thrombocytopenia. Leukocytosis is usually dominated by monocytosis and eosinophilia imparting a chronic myelomonocytic leukemia (CMML)-like picture with eosinophilia (Figure 1 and 2). Eosinophils may have atypical morphology. Rarely, basophilia is also prominent. However, some patients present with...
features more suggestive of atypical chronic myeloid leukemia without BCR / ABL1 (aCML) or chronic eosinophilic leukemia (CEL) or more rarely, they present with phenotypic features of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), or juvenile myelomonocytic leukemia (JMML).

The bone marrow is typically hypercellular (Figure 3) with accompanying fibrosis. As in cases with PDGFRA abnormalities, mast cell aggregates (not meeting criteria for systemic mastocytosis) can be seen.

Monocytosis is seen along with atypical eosinophils with cytoplasmic vacuolation, uneven granule distribution, and increased nuclear lobes. (Wright Giemsa stained peripheral blood smear, original magnification 500x)
Leukocytosis is noted with increased monocytes and several blasts. In addition, an atypical eosinophil is noted with sparse uneven granule distribution. (Wright Giemsa stained peripheral blood smear, original magnification 1000x)

A markedly hypercellular bone marrow with myeloid hyperplasia including many eosinophils is appreciated. (Hematoxylin and Eosin stained bone marrow biopsy, original magnification 500x)

**Treatment**

Patients with abnormalities of PDGFRB are exquisitely sensitive to imatinib, like patients with abnormalities of PDGFRA, and this is the drug of choice. Primary and secondary resistance is uncommon; initial response typically occurs within 2 months.

**Prognosis**

Previously, this neoplasm was cited as an aggressive disease with a median overall survival of less than 2 years. However, after the universal initiation of imatinib as standard therapy, a recent study cited a 10-year overall survival of 90% (Cheah et al., 2014).
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Cytogenetics morphological
PDGFRB can have a variety of fusion partners with more than 20 currently described (Table 1), but by far the most common fusion is ETV6-PDGFRB. Conventional karyotyping usually readily identifies 5q33 (PDGFRB) rearrangements (Figure 4). Multicolor FISH has also been useful in recognizing PDGFRB rearrangements or confirming suspected fusion on karyotype by using probes that closely flank both ends of the gene.

Fusion partner genes and locations

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SPECC1 17p11
GOLGA4 3p22
HIP1 7q11
BIN2 12q13
MYO18A 17q11
NIN 14q22
SART3 12q23
ERC1 12p13
WDR48 3p21
DTD1 20p11
KANK1 9p24

Genes involved and proteins
PDGFRB (platelet-derived growth factor receptor, beta polypeptide)

Location
5q32

Note
Platelet Derived Growth Factor Receptor Beta (PDGFRB) is located on chromosome 5, band q32. It contains 23 exons and spans approximately 149.5 Mb. The encoded protein is 1067 amino acids. As with PDGFRα, it is a member of the type III class of tyrosine kinase receptors.
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Result of the chromosomal anomaly

Hybrid gene

Note
The most common fusion gene produced is the ETV6/PDGFRB, due to t(5;12)(q31~33;p13), which is typically detected via conventional karyotyping. However, many fusion partners are described as PDGFRB is known to be the most promiscuous of all of the genes involved in myeloid and lymphoid neoplasms with eosinophilia (and abnormalities of PDGFRA, PDGFRB, or FGFR1). This fusion gene produces an activated tyrosine kinase that transforms hematopoietic cells due to constitutive activation.

References


Savage NM, George TI, Gotlib J. Myeloid neoplasms associated with eosinophilia and rearrangement of PDGFRA, PDGFRB, and FGFR1: a review Int Jnl Lab Hem. 2013;35: 491-500

This article should be referenced as such: