

Leukaemia Section

Mini Review

Essential thrombocythemia (ET)

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Clinics and pathology

Disease

Chronic myeloproliferative syndrome

Phenotype / cell stem origin

The disease is a chronic myeloproliferative disorder originating from a mutated pluripotent stem cell capable of producing red blood cells, granulocytes and megakaryocytes. In some cases, B-lymphocyte involvement by the clonal proliferation was documented. T-lymphocytes are not involved by the malignant process and nonclonally derived granulocytes may coexist with clonal cells in patients with ET.

Epidemiology

ET has an annual incidence of 1.5 to 2.4 patients /100,000. The disease incidence may show a peak around 30 years in females, with a second peak in the elderly with a 1:1 male-to-female ratio. The average age at diagnosis is 50-60 years.

Clinics

The disease is diagnosed in the presence of a sustained increase of the platelet count ($>600 \times 10^9/L$) over at least 1 month without an obvious explanation.

In the majority of patients the disease remains asymptomatic for many years. The disease symptoms are usually related to arterial thrombosis and, less frequently, deep venous thrombosis, which are more frequent in the untreated patient. Death may occur following major ischemic events or leukemic transformation.

Cytology

The peripheral blood smear shows thrombocytosis without obvious morphologic abnormalities of the

white blood cells and erythrocytes. Megathrombocytes may be seen. The bone marrow is hypercellular with enlarged megakaryocytes, which may tend to aggregate in small clusters. At diagnosis a moderate increase of reticulin fibers may be observed, whereas the presence of marked fibrosis is a diagnostic exclusion criteria.

Treatment

Treatment should be considered for patients at risk of thrombosis (age > 60 years, previous ischemic events, platelet $> 1500 \times 10^9/L$). Low-dose aspirin or other anti-platelet agents are used. Hydroxyurea is effective in reducing the platelet count and the incidence of thrombotic events. Interferon or anagrelide may be used in young patients.

Evolution

Leukemic transformation may occur in 3-10% of the cases. Transformation into a stage indistinguishable from idiopathic myelofibrosis was documented in 5% of the cases.

Prognosis

The large majority of the patients survive > 10 years. No significant difference between life expectancy of ET patients and age-matched subjects was observed in a study.

Cytogenetics

Cytogenetics morphological

Less than 10% of the patients show a clonal chromosome defect at diagnosis.

Recurrent abnormalities include total/partial trisomy 1q, trisomy 8 and trisomy 9, del(13q) and del(20q). Rearrangements of chromosome 17, leading to 17p deletion can be frequently associated with Leukemic transformation.

Cytogenetics molecular

a) Fluorescence in situ hybridization (FISH) and molecular studies :

FISH may be more sensitive than conventional karyotyping for the detection of chromosome deletions

b) Janus Kinase JAK2 mutation :

A valine to phenylalanine substitution at position 617 (JAK2 V617F mutation) is present in 50-75% of the patients leading to constitutive kinase activity. Unlike polycythemia vera, mutated homozygous cells are not found in ET. In 1% of the patients a gain-of-function mutation of the thrombopoietin receptor (MPL) gene can be found, determining activation of the JAK-STAT pathway.

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