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MYELOPROLIFERATIVE NEOPLASMS

Epidemiology and Pathogenesis

Chronic myeloproliferative neoplasms (MPNs) include Polycythemia Vera (PV), Essential Thrombocythemia (ET), and Myelofibrosis (described in a separate section). The incidence of PV is estimated between 2.3 and 2.8 per 100,000 persons per year, and that of TE between 1.5 and 2.4 per 100,000 persons per year. The hyperactivation of the JAK-STAT pathway is fundamental in the pathogenesis of MPNs, due to some acquired gene mutations: JAK2 (95% PVs, 60% ETs), CALR (30% ETs) and MPL (about 7% of TEs).

Clinical picture

PV is an MPN characterized by erythrocytosis (hemoglobin increased), often associated with leuko-thrombocytosis (increase of leukocytes and platelets). ET presents with a persistent increase in platelet count (>450,000/mmc). In both diseases, patients may report microvascular disorders such as headache, paresthesias, scotomas and tinnitus. More frequently in PV, aquagenic pruritus, constitutional symptoms, and splenomegaly may be seen. The natural history of PV and TE is marked by high rates of thrombotic (arterial and venous, even in atypical sites) and hemorrhagic complications.

Diagnosis

The diagnostic criteria for PV and ET have recently been revised by the 2016 WHO classification. In PV, the diagnosis is confirmed by the presence of erythrocytosis and trilinear myeloid hyperplasia at bone marrow level, in association with the presence of the JAK2 mutation or reduced erythropoietin levels. In cases of suspected ET, in addition to elevated platelet count and demonstration of JAK2, MPL or CALR mutations, bone marrow histological findings are essential for a correct differential diagnosis with prefibrotic myelofibrosis. Useful information is also provided by cytogenetic analysis.

Prognosis

In view of the increased risk of vascular events, patients with ET and PV should be stratified into two prognostic categories: "low risk" if patients are younger than 60 years without previous thrombosis, "high risk" if they are older than 60 years and/or have had a previous thrombotic event. In the long term it is also possible the evolution in secondary myelofibrosis or acute myeloid leukemia.

Treatment

Therapy depends on the vascular risk of the patients. In case of "low risk" patients, cytoreductive therapy is not usually indicated: in PV, phlebotomies and antiplatelet prophylaxis (low dose aspirin) are prescribed, while in ET low-dose aspirin in the absence of extreme thrombocytosis. In "high risk" subjects and in patients with uncontrolled symptoms it is necessary to start a cytoreductive treatment. In the first line, hydroxyurea (HU), anagrelide, or pegylated interferon derivatives are available in ET and HU in PV. In addition when PV patients become resistant/intolerant to HU, ruxolitinib is indicated ana available.