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CHRONIC MYELOID LEUKEMIA

Epidemiology and pathogenesis

The incidence of chronic myeloid leukemia (CML) is 1-2 cases/100,000 persons/year. CML is responsible for 15-20% of adults' leukemias. CML is most frequently diagnosed between the fifth and sixth decades of life. In most cases, the disease is due to a specific chromosomal rearrangement at the level of the stem cell: the translocation between the long arms of chromosomes 9 (q34 band) and 22 (q11 band). The two genes involved in the translocation (ABL and BCR) form a new fusion gene, BCR-ABL, with constitutive tyrosine kinase activity.

Clinical picture

CML is characterized on peripheral blood by leukocytosis of variable degree, accompanied by myeloid progenitors. Thrombocytosis, basophilia, and eosinophilia may also be seen. Splenomegaly is evident in approximately 30% of cases. CML is usually diagnosed in a chronic phase, mostly asymptomatic. If left untreated, however, there is a risk of transformation into an accelerated phase to an acute phase, called blasts crisis, of myeloid or lymphoid type.

Diagnosis

The approach to the diagnosis of CML begins with the exclusion of reactive causes of leukocytosis and/or thrombocytosis and of other chronic myeloid neoplasms. Important is the morphological study of peripheral and marrow blood, in order to evaluate abnormalities of blood cells and their precursors. The diagnostic suspicion must be confirmed by the finding of translocation (9;22) in bone marrow blood cytogenetics analysis and of BCR-ABL transcript on peripheral blood, by gene amplification techniques (PCR).

Prognosis

The Sokal index is the oldest and takes into consideration four prognostic factors: age, percentage of blasts on peripheral blood, spleen volume, and platelet values. Other prognostic classification systems have been developed more recently, based on the outcome of patients treated with current therapies. Among these, the Hatsford score and EUTOS are routinely calculated. Finally, the EUTOS Long Term Survival score (ELTS) was introduced in 2016. These models variably take into account age, percentage of blasts, eosinophils and/or basophils on peripheral blood, platelet levels, and splenomegaly.

Treatment

Therapy with first-, second-, and third-generation tyrosine kinase inhibitors (TKIs) has made it possible to radically change the prognosis of patients with CML, who now have a life expectancy very similar to that of the population of the same age. The choice of first-line therapy is based on the definition of the prognostic risk at diagnosis, the accurate assessment of comorbidities and the feasible goal in the individual patient (e.g., the possibility of discontinuing TKI after obtaining a profound and durable response). The criteria for treatment response and the patient's monitoring schedule are defined by the "European LeukemiaNet Guidelines" (*Hochhaus et al, 2020*). Allogeneic hematopoietic stem cell transplantation is reserved, even in younger age groups, for the few patients resistant to multiple inhibitors or in advanced disease.