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Leukaemia Section

Mini Review

Atypical Chronic Myeloid Leukemia (aCML)

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Identity

Note: The nosology of aCML is controversial. The FAB classification includes aCML in the group of chronic myeloid leukemias. The WHO classification has classified aCML in the group of myelodysplastic/myeloproliferative diseases.

Clinics and pathology

Disease

aCML is a chronic myeloproliferative disorder with a clinical and hematological picture similar to chronic myelogenous leukemia (CML) but lacking Philadelphia chromosome and BCR - ABL or PDGFRBeta rearangements. Atypical CML is characterized by the combination of: 10-20% of immature granulocytes; marked granulocytic dysplasia and both less than 2% of basophils and less than 10% of monocytes.

Phenotype/cell stem origin

Presumably a multipotential stem cell.

Epidemiology

ACML is a rare disorder of old adults. No predominance of sex. The incidence is not established.

Clinics

Anemic syndrome. Splenomegaly. Malaise.

Cytology

Peripheral blood: Leukocytosis with a high count of immature granulocytes. By definition monocytes

are less than 10% and basophils less than 2%. Anemia is more frequent than thrombocytopenia.

Bone marow: Hypercellular with myelodysplastic features of the three series, most marked in granulocytic lineage. Blast cell infiltration ranges from 0% to 10%.

Treatment

Hydroxyurea is indicated, although not curative, in old patients. Complete remission may be achieved after chemotherapy based on anthracyclin and citarabine (an acute myeloblastic leukemia therapy schedule). Allogeneic bone marrow transplantation is the only curative therapy for those patients who are eligible. Some cases may achieve a complete hematological response after interferon therapy.

Prognosis

The median survival is about 24 months with standart therapy. Some cases have a progression to acute myeloblastic leukemia.

Cytogenetics

Cytogenetics morphological

By definition aCML cases lack in Philadelphia chromosome. Overall 50-65% of patients show cytogenetic abnormalities. The most frequent is +8 (25%). Other changes such as -7 and del(12p) have also been recurrently observed. Other abnormalities are: idic(Xq); del(5q); t(6;8)(p23;q22); -9; del(11q); del(12q); del(15q); del(17p); t(17;20) and add(21q). No specific cytogenetic changes have been associated with aCML. Rearrangements of PDGFRb gene, located at 5q33 have been described a t(5;10)(q33;q22) have been described in several patients.

Genes involved and proteins

Note

The mechanisms of oncogenesis in aCML remains to be elucidated. In the last years some cases displaying rearrangement PDGFRb have been reported. Most of these cases showed PDGFRb/ETV6 fusion, but also a fusion with H4 gene (located at 10q22), have been described. A total of 8 different genes have been found fused to PDGFRb gene. The diagnosis of these cytogenetic abnormalities are critical since most these cases could achieve a complete cytogenetic response with imatinib therapy. The JAK2V617F activating tyrosine kinase mutation is unfrequent in aCML.

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