Chronic neutrophilic leukemia evolving from polycythemia vera with multiple chromosome rearrangements: a case report

Chronic neutrophilic leukemia (CNL) is a rare disorder defined by a persistent increase of mature peripheral neutrophils in the absence of monocytosis, basophilia, eosinophilia, Philadelphia chromosome, occult infection or malignancy.[1] Although CNL is considered a distinct entity, it was recently reported in association with polycythemia vera (PV).[2] We report one case of CNL associated with chromosomal abnormalities evolving from a long history of PV.

A female patient with PV, diagnosed in 1984 at the age of 55 years, was treated with hydroxyurea and phlebotomy until 1998 when splenectomy was performed because of massive splenomegaly. At that time, bone marrow examination revealed severe fibrosis associated with chronic myeloproliferative syndrome without signs of blastic transformation. After two months, despite treatment with hydroxyurea, progressive neutrophilic leukocytosis in the range of 120,000/mm^3 developed.

The diagnosis of CNL was confirmed by the presence of granulocytic proliferation without morphologic dysplasia in a bone marrow biopsy, elevation of leukocyte alkaline phosphatase and absence of BCR/ABL hybrid gene transcripts of p210 and p185. Cytogenetic study performed on the only 5 available metaphases showed in 3 reciprocal translocations between the long arm of chromosome 8 and the long arm of chromosome 11: t(8;11)(q24.3?;q14?), reciprocal translocation between the short arm of chromosome 15 and short arm of chromosome 19: t(15;19)(p11.2?;p12?), loss of one chromosome X and presence of a marker chromosome of unknown origin (Figure 1). Southern blot analysis of the MLL gene did not reveal any rearrangement. Despite chemotherapy with etoposide and busulfan the patient died of bronchopneumonia 7 months after diagnosis of the CNL with a neutrophilic cell count of 180,000/mm^3.

CNL is a clonal myeloproliferative disorder[3] originating in hematopoietic progenitors capable of differentiating only into granulocytes.[4] The clinical picture is dominated by marked neutrophilic leukocytosis without the presence of blast cells in the peripheral blood or bone marrow. Although most of the cases described are associated with normal cytogenetic findings, the clonal nature of the disorder is supported by the few cases recently associated with karyotypic abnormalities of which the most common is mosaicism for partial deletion of chromosome 20, which appears to be linked to a good prognosis.[5] The CNL evolving from PV may represent a clinical entity distinct from *de novo* CNL, characterized by a worse prognosis and by a different pattern of *in vitro* growth of hematopoietic progenitor cells.[6] There are few data in the literature concerning CNL evolved from PV, and even more scanty data about karyotypic assessment.[2] In this case, for technical reasons, it was not possible to define the exact breakpoints in the chromosomes and we cannot rule out the presence of a dicentric chromosome derived from the rearrangement between chromosomes 15 and 19. However, the involvement of chromosome 15 has already been reported in one case of CNL-PV characterized by a very high neutrophilic leukocytosis in association with der (15) and der(20).[7] Moreover, an abnormality of chromosome 11: del(11)(q23)) associated with CNL was recently described by Terre *et al.*[8]

The clonal nature of CNL has been the subject of controversy, particularly when hyperleukocytosis is associated with other clonal processes. In our case, in accordance with the findings of Elliott *et al.*,[9] the extent and the progression of the leukocyte count argue reasonably against a reactive process.

In conclusion, we describe a case of aggressive and refractory hyperleukocytosis compatible with CNL evolving from PV. The documentation of the associated karyotypic abnormalities[10] may add some clues about the cytogenetic profile in PV-derived CNL.

Figure 1. Karyotype of the patient: 46, X,-X, t(8;11) (q24.3?;q14?), t (15;19)(p11.2?;p12?)+ mar.

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