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Teaching cases

Transformation of primary myelofibrosis with 20q− in Philadelphia-positive acute lymphoblastic leukemia: Case report and review of literature

Vladimir Jurisic[a,*], Natasa Colovic[b,c], Tatjana Terzic[b,c], Vesna Djordjevic[b], Milica Colovic[c]

[a] University of Kragujevac, Faculty of Medicine, Kragujevac, Serbia
[b] Institute of Hematology, Clinical Center of Serbia, Belgrade, Serbia
[c] University of Belgrade, Faculty of Medicine, Belgrade, Serbia

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ABSTRACT

A 56-year-old male with chronic idiopathic myelofibrosis and cytogenetic finding of 20q− after a period of 10 months developed acute Philadelphia-positive lymphoblastic leukemia. Immunophenotyping of peripheral blood by flow cytometry showed HLA-DR, CD34, CD19, CD22, CD10, CD33, and CD11b positivity. Cytogenetic analysis revealed the presence of 20q− and Philadelphia chromosome t(9;22)(q34:q11) at the time of disease transformation to ALL. The JAK2V617F mutation was not found. This is a very rare case of simultaneous presence of two cytogenetics abnormalities and evolution of primary idiopathic myelofibrosis to Philadelphia-positive acute lymphoblastic leukemia.

Introduction

Primary myelofibrosis (PMF) or agnogenic myelofibrosis with myeloid metaplasia is a myeloid disorder that results from abnormal clone proliferation of stem cells with multilineage potential and is characterized by myelofibrosis and extramedullary hematopoiesis.

PMF can progress to acute leukemia in 14–20% of the cases. Usually, the disease terminates as acute myeloid leukemia (AML), but transformation to acute lymphoblastic leukemia (ALL) is extremely rare. There are only several cases reported so far, including 2 pediatric cases and 4 adults [1]. Leukemic transformation has been attributed to gene loss or/and inactivation without clear explanation, based on the possibility that the malignant cell clone is unstable.

We here report a very rare case of PMF transformation to Philadelphia-positive ALL confirmed by cytogenetic and RT-PCR analyses.

Case report

A 56-year-old male developed malaise and fatigue in April 2004. Physical examination disclosed splenomegaly (160 mm in diameter). The laboratory analyses showed hemoglobin (Hb) 80 g/l, platelets 1058×10^9/l, white blood cell count (WBC) 8.7×10^9/l, with 2% myelocytes, 4% metamyelocytes, 7% bands, 65% segmented neutrophils, 2% monocytes, and 22% lymphocytes in the differential leukocyte formula, leukocyte alkaline phosphatase (LAP) score of 43 (normal 20–80). Peripheral blood smear showed anisocytosis, polychromasia, dacryocytes and immature granulocytes. Bone marrow cytology disclosed hypocellularity with the persistence of all cell lines and without increased blasts. Cytogenetic studies (Fig. 1I) revealed the following karyotype: 46,XY,del(20)(q11)(3)/46,XY(17). The RT-PCR analysis showed that JAK2 mutation was negative. The growth of cell colonies *in vitro* showed the presence of spontaneous growth of erythroid and granulocyte cell colonies (CFU-GM and BFU-E). The histological examination of the bone marrow trephine biopsy revealed hypercellularity with presence all three hematopoietic cell lines (Fig. 2a). The myeloid series was abundant and showed no dysplastic cytological features; however, there were immature myeloid precursors localized centrally in the medullar space. There was megakaryocyte hyperplasia with pleomorphic morphology, and there was emperipolesis of other hematopoietic cells within megakaryocytes. There was reticulin and collagen fibrosis (Grades

* Corresponding author at: University of Kragujevac, Faculty of Medicine, P.O. Box 124, 34000 Kragujevac, Serbia.
E-mail address: vdvd@mailcity.com (V. Jurisic).

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