Remission of acute monocytic leukemia, secondary to treatment with epipodophyllotoxins, in a patient with t(8;16)(p11;p13) and MYST3–CREBBP fusion

The balanced t(8;16)(p11;p13) is found in less than 1% of acute myeloid leukemia (AML) patients, usually associated with specific clinicopathologic findings such as blast differentiation (French–American–British [FAB] subtypes M4/M5), absence of previous MDS in young individuals of both sexes, presence of erythrophagocytosis, and poor response to chemotherapy, with a poor prognosis and mean survival less than 1 year [1]. This translocation results in the fusion of the CREBBP gene (alias CBP) located at 16p13.3 with the MYST3 gene (previously known as RUNXBP2; alias MOZ) located at 8p11.2 [2,3], which have been suggested to be targets for topoisomerase II inhibitors and anthracyclines, respectively. There are, however, very few reported cases of patients with both this translocation and AML secondary to treatment with these drugs [3–7].

A 24-year-old man was diagnosed with a mediastinal seminoma on May 2001. He received four cycles of chemotherapy with cisplatin, etoposide, and dexamethasone; the remaining mediastinal mass was surgically removed. He was diagnosed with acute monocytic leukemia (FAB subtype M5b) in November 2002, presumably secondary to treatment with epipodophyllotoxins. Bone marrow aspirate revealed infiltration with 92% large blasts weakly positive for myeloperoxidase staining and negative for chloroacetate esterase staining. Immunophenotyping with forward scatter–side scatter (FS/SS) gating identified two separate populations of blasts, both of which were CD33+/H11001, CD15+/H11001, CD4+/H11002, CD56+/H11002, and CD34+. Weak erythrophagocytosis was observed. Cytogenetic analysis revealed the karyotype 46,XY,t(8;16)(p11;p13) in 7% of the metaphases analyzed (Fig. 1A). Remission was achieved after treatment according to the PETHEMA protocol, and all metaphases were normal by December 2002. The patient received a bone marrow transplant and was, at writing, in molecular and cytogenetic remission.

Fluorescence in situ hybridization (FISH) studies with bacterial artificial chromosomes (BACs) RPCI-11 461A8 and RPCI-11 95J11 were consistent with a rearrangement of CBP (Fig. 1B). Reverse transcriptase-polymerase chain reaction (RT-PCR) [3] confirmed the presence of the in-frame 1128-bp MOZ–CBP fusion transcript (only type I transcript; Fig. 1C) and also the presence of the CBP–MOZ transcript (data not shown). The sequence of the chimeric transcripts (Fig. 1D) revealed breakpoints similar to those described previously, fusing exon 16 from MOZ to exon 3 from CBP.

In summary, we describe a t(8;16)(p11;p13) with MOZ-CBP fusion in a patient with AML 5b secondary to treatment...
with epipodophyllotoxins. The presence of this translocation is usually associated with strong erythrophagocytosis and CD34⁻/CD56⁺ blasts [7]. This patient, however, displayed weak erythrophagocytosis and CD56⁻ blasts, with a low percentage of cells showing the translocation. Moreover, RT-PCR detected only type-I (in-frame) fusion transcripts, but no type II (out-of-frame) transcripts. All these peculiarities could account for the good prognosis of this patient, who responded well to conventional therapy and is in cytogenetic and molecular remission after bone marrow transplantation, in contrast to other published cases.

Acknowledgments

This study was supported by grant no. 05/903 from the Department of Health of the Government of Navarra, Spain, and by a grant from the PIUNA Projects from the University of Navarra, Spain.

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