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Letter to the Editor

Acute T cells lymphoblastic leukemia associated with t(1;19)(q23;p13)/*E2A–PBX1* in an adult

1. Introduction

The recurring chromosome abnormalities involving special genes are closely associated with the distinct subsets of leukemia with morphological, immunophenotypic and clinical features. The t(l;19)(q23;pl3) structurally interrupts the *E2A* gene located at 19p13, which codes for the helix-loop-helix transcription factors E12 and E47, and fuses it to the chromosome 1 gene *PBX1* for a homeobox gene [1]. The translocation leads to product a novel E2A/PBX1 chimeric transcription factors [2,3]. It was demonstrated that *E2A–PBX1* transforms cells by constitutively activating transcription of genes regulated by *PBX1* or by other members of the *PBX* protein family [4]. The t(l;19)(q23;pl3), the one of the frequent recurring translocation in childhood ALL, is present in about 5% of ALL cases, including 20–25% of pre-B ALL (leukemias that express cytoplasmic Ig [cIg] but not surface Ig), making it the most common chromosomal rearrangement in children with leukemia [5]. It is also observed in a small percentage of early pre-B (cIg^-, sIg^-) and transitional pre-B (cIg^+, sIg^+) [5]. The cases with t(1;19) had an identical, complex phenotype characterized by homogeneous expression of CD19, CD10, and CD9; complete absence of CD34; and at least partial absence of CD20 [6]. In addition, this translocation is detected occasionally in adults with ALL and in acute myelogenous leukemia (AML), and lymphomas [5]. We found one case of adult T cells ALL associated with translocation of t(1;19) and fusion of *E2A–PBX1*.

2. Case report

The patient was a 26-year-old male who had noted progressive asthenia. Physical examination revealed petechia on the skin of limbs, stern tenderness, surface lymphadenopathy of 1–3 cm in diameters, and splenomegaly of 4 cm below left costal margin. The computed tomography scan also showed mediastinal lymphonodes enlargement. The hemoglobin value was 142 g/L, white cell count was 61.7×10^9/L with 73% blasts, platelet count was 33×10^9/L, and LDH value was 2436 IU/L. The bone marrow examination revealed marked hypercellularity with over 85.5% lymphoblasts. Immunophenotypical markers of the leukemic cells were analyzed by the direct immunofluorescence method using flow cytometric analysis and monoclonal antibodies. The blast cells were positive to CD2, CD3, CD7, cytoplasmic CD3 (cyCD3), CD10, CD13, CD15, and HLA-DR, while the markers of B cells, such as cyCD79a, CD19, CD20, were weak. The blast cells also did not express CD34, and the myeloid antigen including cyMPO, CD14, CD33. Cytogenetic analysis showed unbalanced translocation, and the karyotype was as follows: 47, XY, 9p+, 15p+, 17q−, der(19), t(1;19)(q23;pl3)[5]/46, XY[15]. The *E2A/PBX1* fusion mRNA was demonstrated by the reverse transcriptase-polymerase chain reaction (RT-PCR) for detecting 29 translocations/chromosomal aberrations in patients with acute leukemia [7]. Oligonucleotide primers used in this study were 5′GCTTCGCTCAG3′ for *E2A* and 5′CCCTCCAGAAG3′ for *PBX1*.

Then the patient was diagnosed as *E2A*/*PBX1*$^+$ t(1;19) T cells ALL. After leukapheresis, he was induced with hyperCVAD (300 mg/m^2 cyclophosphamide every 12 h for 6 doses on days 1 through 3, 2 mg vincristine on days 4 and 11, 50 mg/m^2 adriamycin on day 4, and 40 mg/d dexamethasone on days 1 through 4 and 11 through 14) alternating cycles with high dose methotrexate/high dose cytosine arabinoside (HD-MTX/HD ara-C)(1 g/m^2 MTX over 24 h on day 1 and 3 g/m^2 ara-C every 12 h for 4 doses). The patient achieved complete clinical and hematologic remission after 1 cycle of hyperCVAD. Intrathecal (IT) chemotherapy with MTX and ara-C for central nervous system prophylaxis was conducted after complete remission, and no leukemic cells were isolated from spinal fluid.

3. Discussion

Troussard et al. [8] have reported one patient with an isolated t(1;19) was shown to have T-ALL, based on the expression of CD2, CD7, CD5 and CD8 and the absence of expression of the CD19 and CD10. The diagnosis was also confirmed by the presence of a TCR beta rearrangement and the absence of any IgH rearrangement. But the case failed to show any *E2A–PBX1* transcript by RT-PCR, including after hybridization with an internal probe. Rearrangement of the *E2A* gene was not observed by Southern blotting and normal sized transcript of *E2A* was showed by Northern hybridization with a cDNA probe. It is therefore unlikely that the chromosome 19 breakpoint involves the *E2A* gene. The case we reported here was the first T cells ALL associated with translocation of t(1;19) and fusion of *E2A–PBX1*.

The malignant potential of chimeric E2a/Pbx1 proteins have demonstrated in fibroblasts [2], myeloid cells [9], and T lymphocytes [10], but not in B lymphocytes, despite the fact that almost all reported cases of *E2A–PBX1*$^+$ t(1;19)$^+$ have occurred in B-lineage acute lymphoblastic leukemia (ALL) [5]. It indicated that the oncogenic potential of chimeric E2a/Pbx1 proteins is not limited to the latter lineage. Sykes and Kamps [11] demonstrated that E2a/Pbx1 induces immortal proliferation of stem cell factor-dependent pro-T thymocytes by a mechanism dependent upon both its transactivation and DNA-binding functions. Pro-T-cell clone immortalized by E2a/Pbx1 causes pro-T-ALL but induces AML when converted to factor independence by Bcr/Abl [11], and Bourette et al. [12] found E2a–Pbx1 immortalized pro-T cells could proliferate and shifted from lymphoid to myeloid lineage after signaling through exogenously expressed macrophage-colony-stimulating factor, irrespective of the presence of estradiol. These results suggested that unique functions of cooperating signaling oncoproteins or specific cellular environment signals could influence the lymphoid versus myeloid character of E2a/Pbx1 leukemia.

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It is possible that the blast cells subjected to expansion by E2a/Pbx1, converted to acute leukemia after a second mutation which affected proliferation pathway, the properties of this second signaling oncoprotein permit or facilitate different phenotype, including pre-B ALL, T-ALL, and AML.

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