Der(2)t(2;11)(p21;q23), a Variant form of t(2;11), in Biphenotypic Acute Leukemia with T Lymphoid Lineage and Myeloid Lineage Differentiation

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We describe a patient with biphenotypic acute leukemia (BAL) with T-lymphoid lineage and myeloid lineage differentiation [BAL (T/M)]. Cytogenetic analysis revealed complex chromosomal abnormalities, including der(2)t(2;11)(p21;q23). Neither leukemia cells nor T-cell receptor gene rearrangements were detected in the bone marrow samples after four courses of high dose cytosine arabinoside regimen. However, der(2)t(2;11)(p21;q23) anomaly persisted in most of metaphases. Fluorescence in situ hybridization (FISH) analysis with a probe for MLL did not detect the split signal. Forty-five cases of hematological disorder with t(2;11)(p21;q23) abnormality have been previously reported. The majority of such cases have been classified as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). This is the first case BAL (T/M) associated with a t(2;11)(p21;q23) anomaly. (Kitakanto Med J 2012; 62: 287-290)

Key words: t(2;11)(p21;q23), biphenotypic acute leukemia, hematopoietic stem cell

1. Introduction

Biphenotypic acute leukemia (BAL) is a rare subgroup of acute leukemia. Diagnosis of BAL is based on immunophenotyping proposed by the European group for the immunological classification of leukemia (EGIL). While leukemia cells express B-lymphoid and myeloid antigens in most of cases with BAL, cases with expressing myeloid and T-lymphoid antigens are rare. As for chromosome, BAL has been reported to associated with Philadelphia (Ph) chromosome and translocation of 11q23,2 but t(2;11)(p21;q23) anomaly has not been reported so far. Here we report a case of BAL with T-lymphoid and myeloid antigen expression with complex type of chromosome abnormality containing t(2;11)(p21;q23).

2. Case report

A 48 year-old male was admitted to our hospital complaining malaise, high-grade fever, and diarrhea in December 2004. Physical examination revealed hepatosplenomegaly and swelling of cervical, axillary, as well as inguinal lymph node. On computed tomography, systemic lymphadenopathy, hepatosplenomegaly, mediastinal mass and bilateral pleural effusion were observed (Fig. 1). Laboratory examinations were hemoglobin 6.1 g/dl, platelets count 27×10⁹/l and a white blood cell count of 39.7×10⁹/l with 92% blasts,

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serum lactate dehydrogenase 681 IU/l, and C-reactive protein levels 21.0 mg/dl. Both of serum (33.9 mg/ml) and urine lysozyme (41.5 mg/ml) were elevated. The naphthol ASD chloroacetate esterase, α-naphthyl butyrate esterase and myeloperoxidase staining of blast cells were negative. Flow cytometric analysis revealed leukemia cells were positive for cyclCD3, CD5, CD7, CD13, CD33, CD34, CD56, CD117 and terminal deoxynucleotidyl transferase (TdT), and negative for CD2, CD4, CD8, CD10, CD14, CD19 and CD20 antigens. The karyotype of leukemia cells at diagnosis was 46XY, der(2)t(2;11)(p21;q23)del(2)(q2), der(11)t(2;11), der(12)t(2;12)(?;q24), del(16)(q12), idic(17)(p11). The Fluorescence in situ hybridization (FISH) analysis with the MLL gene probe (Vysis, Downers Grove, IL, USA) did not detect a split signal on chromosome 11 indicating that MLL gene was not related to this translocation. Southern blot analysis showed clonally rearranged band when T-cell receptor (TCR) gamma-chain as well as beta-chain genes were used as a probe. Based on these results, the diagnosis of BAL with T-lymphoid and myeloid differentiation (T/M) [BAL (T/M)] were established by the scoring system proposed by the EGIL.3

Though he did not achieve complete remission (CR) acute lymphoblastic leukemia (ALL) induction therapy,3 disappearance of leukemia blasts in bone marrow was obtained by high dose cytosine arabinoside (HD–AraC) regimen. With three courses of HD–AraC as consolidation therapy, blast cells decreased to less than 5% in bone marrow (BM) and TCR rearrangement was not detected. However, lymphadenopathy of cervix, axilla, and mediastinum did not resolved and t(2;11)(p21;q23) chromosome anomaly persisted in BM cells. In receiving radiotherapy to the lymphadenopathy, the leukemia cells regrew quickly, and he died of fungal infection.

3. Discussion

In the cytogenetic analysis of BAL with B-lymphoid and myeloid differentiation [BAL (B/M)], the 11q23 anomaly and Ph chromosome have frequently been documented.4–6 On the contrary, there is no report on BAL (T/M) with these abnormalities, rather, normal karyotype or complex abnormalities have been reported in this type of leukemia.7,8

Concerning t(2;11)(p21;q23) anomaly, only 45 cases have been reported; 26 with myelodysplastic syndrome (MDS), 12 with de novo acute myeloid leukemia (AML), 4 with ALL and 3 with Chronic myeloproliferative diseases (Table 1).9–30 Thus, there has been no report of BAL (T/M) with t (2;11)(p21;q23). Approximately half of 45 cases with t (2;11) (p21; q23) have additional karyotype. Of note, 16 out of 26 MDS cases have del (5q) anomaly.

In the 11q23 anomaly, most of cases are associated with MLL gene rearrangement. However, in the present case with t (2;11) (p21; q23), MLL gene rearrangement was not detected suggesting that the breakpoint did not related to this translocation. In the reported cases with t (2;11) (p21; q23), 4 of 9 cases detected MLL rearrangement. There might be heterogeneity in the involved gene in this translocation.

As BAL (T/M) is rare and poorly documented, there is little information as to the treatment modalities. The usefulness of HD–AraC regimen for ALL has been reported when compared to the conventional chemotherapy. However, post–remission regimen as well as the usefulness of hematopoietic stem
cell transplantation remains controversial.31

Leukemia cells with t(2;11)(p21;q23) might be transformed at the level of hematopoietic stem cells or earlier progenitor stage, because the BAL in the present case showed marked expression of CD34 antigen and early stage T-cell markers such as CD7 and CD5; the later stage T-cell markers such as CD4 and CD8 were lacking. This might be one of the reasons why this case was chemo-resistant. Moreover, in this case, sole t(2;11)(p21;q23) chromosomal abnormality remained more than 90% in BM cells even when leukemia cells microscopically disappear in BM; this suggests the difficulty of evaluation of chemotherapy in BAL (T/M), which was also observed in a past report.32

In summary, we describe a first case of BAL (T/M) with a t(2;11)(p21;q23) abnormality. Additional cases need to determine the prognostic significance and clinical implications of this chromosomal finding with biphenotypic profile and immature morphology. 

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