Abstract

We present a case of acute myeloid leukemia (AML) with a balanced translocation between chromosomes 2q12 and 6q12, t(2;6)(q12;q12). This abnormality was defined by conventional cytogenetics and multicolor banding techniques using specific probes for chromosome 2. Blasts accounted for 2% of white blood cells in peripheral blood and approximately 30% of all nucleated cells in marrow aspirates. They were medium-to-large cells with fine nuclear chromatin, indistinct nucleoli and basophilic cytoplasm. Immunophenotyping indicated the blasts were of myeloid lineage with aberrant CD7 expression. Therefore, the patient was diagnosed as 'Acute myeloid leukemia, NOS, AML with maturation' according to the WHO classifications. In literature review, this case should be considered as the first report of AML with t(2;6)(q12;q12). Interestingly, a bone marrow smear showed dysmegakaryopoietic findings, such as multinucleated or mononucleated megakaryocytes and micromegakaryocytes. After diagnosis, the induction chemotherapy was given with idarubicin and cytosine arabinoside according to the protocol of intermediate-prognostic AML. After chemotherapy, the patient had been in remission for 13 months but relapsed with 54% blasts in marrow aspirates. The cytogenetic analysis revealed t(2;6)(q12;q12), which is same with karyotype shown at diagnosis. In this case report, the pathologic and clinical findings of AML with t(2;6)(q12;q12) were described, which are severe dysmegakaryopoiesis and poor prognosis. This report may be helpful for clinician to have a similar case treated.

Keywords: Acute myeloid leukemia; Cytogenetics; Multicolor banding analysis; Translocation; Prognosis; Relapse. t(2;6)(Q12;Q12)

Abbreviations: AML: Acute Myeloid Leukemia; mBAND: Multicolor Banding


t(2;6)(Q12;Q12)

Acute Myeloid Leukemia with t(2;6)(q12;q12) Reveals Dysmegakaryopoietic Finding and Poor Prognosis

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Figure 1a: Bone marrow aspiration smears. Wright-Giemsa.x1,000. Blasts were medium-to-large cells with fine nuclear chromatin, indistinct nucleoli and basophilic cytoplasm and accounted for approximately 30% of all nucleated cells in the marrow aspirates.

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Case Presentation

The patient was a 56-year-old female, previous healthy, with chief complaints of dizziness and general weakness. The patient's complete blood count parameters were as follows: white blood cell count, 1.29×10^9 cells/L; hemoglobin level, 4.5 g/dL; hematocrit 13%; and platelet count 31×10^9 cells/L. The differential count was 2% blasts, 43% segmental neutrophils, 53% lymphocytes, 1% monocytes, and 1% eosinophils. A blood smear showed normocytic hypochromic red blood cells with anisopoikilocytosis. The initial bone marrow biopsy revealed slightly hypocellular marrow with interstitially infiltrating immature cells. Blasts were medium- to large sized cells with fine nuclear chromatin, indistinct nucleoli and basophilic cytoplasm and accounted for approximately 30% of all nucleated cells in the marrow aspirates (Figure 1a). Auer rods were not found. Dysmegakaryopoietic characteristics were also observed, such as multinucleated or mononucleated megakaryocytes and micromegakaryocytes (Figure 1b). An immunophenotyping test demonstrated that the blasts expressed CD34, CD33, CD117, HLA-
DR, CD13, MPO and CD7. These cells were negative for CD10, CD19, CD20, CD22, CD3, CD5, CD14, CD56 and TdT. Therefore, the blasts were of the myeloid lineage with aberrant CD7 expression.

A conventional chromosomal analysis of bone marrow was performed using pokeweed stimulation and standard techniques. The metaphases were banded using Giemsa-Trypsin-Wrights staining at a 400-band resolution. The chromosomal analysis showed the balanced translocation between chromosomes 2q12 and 6q12 in 18 cells among the 20 assessed metaphases (Figure 2a). The karyotype is described as 46,XX,t(2;6)(q12;q12)[18]/46,XX[2], according to the International System for Cytogenetic Nomenclature 2013 [1]. This karyotypic abnormality was confirmed by multicolor banding (mBAND) analysis using mBAND probe sets for chromosome 2 (MetaSystems, Altlussheim, Germany). The mBAND results were evaluated using MetaSystems software (Figure 2b). Multiplex RT-PCR was also performed, but it was negative for the 28 known leukemia-causing translocations. The multiplex RT-PCR experiment was performed using the HemaVision kit (DNA Technology A/S, Aarhus, Denmark) according to the manufacturer's instructions. The kit allows for the detection of 28 leukemia-causing chromosomal translocations, including the most commonly occurring variants: t(1;19), t(12;21), inv(16), t(8;21), t(4;11), t(15;17), and t(9;22). Positive controls for the individual translocations are provided with the kit. The overall findings were interpreted as 'Acute myeloid leukemia, NOS, AML with maturation' using the WHO classifications [2].

After diagnosis, the patient had received the induction chemotherapy with idarubicin 12 mg/m²/day in day 1-3 and cytosine arabinoside 200 mg/m²/day in day 1-7 according to the protocol of intermediate-prognostic AML and become the remission state including cytogenetically normal karyotype. Remission stated was continued during 13 months but AML was relapsed with 54% blasts in marrow aspirates. In relapse, the cytogenetic analysis revealed t(2;6)(q12;q12), which is same with karyotype shown at diagnosis. The immunophenotyping test also demonstrated that the cellular expression was not changed. After relapse, the induction chemotherapy was carried out to patient using idarubicin 12 mg/m²/day in day 1-3 and cytosine arabinoside 100 mg/m²/day in day 1-7. Then, she was treated by consolidation chemotherapy of cytosine arabinoside 3,000 mg/m²/ day in day 1, 3 and 5. At now, we are monitoring the patient on the remission state.

**Discussion**

Recurrent cytogenetic abnormalities are frequently identified in acute leukemia [2]. A clonal abnormality may assist in establishing a diagnosis or in prognostication. To date, a number of aberrations have been identified through cytogenetic and molecular analyses. Here, we describe a novel case of acute myeloid leukemia (AML) with a balanced translocation between chromosomes 2q12 and 6q12, t(2;6), (q12;q12) including pathologic and clinical information during 18 month. The
translocation t(2;6)(q12;q12) was defined by conventional cytogenetics and mBAND analysis. In hematologic malignancy associated literature search, I couldn’t find any case of t(2;6)(q12;q12) as sole or combined abnormality. Therefore, this case should be considered as the first report for AML with t(2;6)(q12;q12). Interestingly, this case showed severe dysmegakaryopoiesis and relapsed at 13 months after remission. This report may broaden the current knowledge of translocation-related leukemia.

Although, the cytogenetic abnormality in our case was confirmed by mBAND analysis, their associated genes were not identified. In several cases of hematologic malignancies, leukemia-associated genes in 2q11-13 or 6q11-13 regions were reported such as AFF3, PAX8, SMAP1 and EEFA1. The AFF3 (2q12) and SMAP1 (6q13) genes are MLL fusion partners reported in cases of acute leukemia [3-6]. The AFF3 gene was also found in other translocations. An AFF3-BCL2 fusion from t(2;18)(q11.2;q21.33) and an AFF3-RUNX1 fusion from t(2;21)(q11;q22) were reported in follicular lymphoma and T-cell acute lymphoblastic leukemia, respectively [7,8]. The PAX8 (2q13) gene may be a candidate for the upregulation of WT1 in acute myeloid leukemias [9]. The EEFA1 (6q13) gene could be involved in cancer development, progression and survival in hematopoietic tumors [10,11]. However, abnormal morphologic features of megakaryocytes were not described in these reports. Therefore, it is possible that the genes associated with our case have yet to be reported in leukemia or that a new function has evolved due to the gene translocation. Generally, megakaryocyte dysplasia should be carefully looked for on BM marrow biopsies and aspirate from patient at diagnosis, which may be the diagnostic hallmark of hematologic malignancy, especially myelodysplastic syndrome and acute myeloid leukemia. However, clonal cytogenetic or molecular abnormalities for dysmegakaryopoiesis are not definitive as the sole abnormality.

In summary, we report here the AML case of t(2;6) showed severe dysmegakaryopoiesis and poor prognosis. This report may be helpful for clinician to have a similar case treated. However, further studies would be needed to identify of the involved genes and the frequency of this translocation and to assess its potential prognostic value.

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References