**t(1;3)(p36;p21) as the Sole Clonal Abnormality in Refractory Acute Myeloid Leukemia**

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Acute myeloid leukemia (AML) is a heterogeneous group of diseases with a multitude of molecular genetic aberrations and variable clinical outcome. Clonal chromosomal abnormalities have been identified in over 50% of AML cases, and have been regarded as one of the most important prognostic markers. We present a case of a 56-year-old Hispanic man with AML with minimal differentiation. Morphologically, the bone marrow was hypercellular with trilineage hypoplasia and 80% blasts. Flow cytometry analysis showed that the blasts were of myeloid immunophenotype. Conventional cytogenetic analysis showed t(1;3)(p36;p21) as the sole cytogenetic abnormality in 5 of 20 metaphases analyzed. The patient received daunorubicin and cytarabine, and achieved first remission. He relapsed 4 months later, and was treated with fludarabine, cytarabine, idarubicin, and G-CSF, and consolidated with high-dose cytarabine. He then received matched related stem cell transplantation. However, the disease relapsed again, and the patient died 11 months after initial diagnosis. To our best knowledge, this is the first report of t(1;3)(p36;p21) as the sole cytogenetic abnormality.

**Key Words:** t(1;3)(p36;p21); acute myeloid leukemia, refractory

INTRODUCTION

Acute myeloid leukemia (AML) is a clonal hematopoietic stem cell disorder that is characterized by an uncontrolled proliferation of myeloid blasts in the bone marrow and defective production of normal blood cells, which may result in fatal infection, bleeding, and organ failure due to leukemic infiltration. It has been well-recognized that AML is a heterogeneous group of diseases with a multitude of molecular genetic aberrations and variable clinical outcome. Clonal chromosomal abnormalities have been identified in over 50% of AML cases, and have been regarded as one of the most important prognostic markers. Cytogenetic results have been integrated as an important part in the diagnosis, classification, risk stratification, treatment decision, and monitoring responses to therapy in the management of AML patients.

Numerous recurrent cytogenetic abnormalities have been described. Translocation between chromosome 1p36 and chromosome 3p21 is a rare recurrent cytogenetic aberration that has been reported in a variety of hematopoietic neoplasms including non-Hodgkin lymphoma (NHL), acute lymphoblastic leukemia (ALL), myelodysplastic syndrome (MDS), chronic myelogenous leukemia (CML) and AML. Thirteen cases have been reported to date. However, t(1;3)(p36;p21) is part of a complex karyotype in all cases reported. We report the first case of a 56-year-old Hispanic man with AML in which t(1;3)(p36;p21) occurred as the sole cytogenetic abnormality.

CASE REPORT

The patient was a 56-year-old Hispanic man who initially presented with mouth ulcers, eye infection, and fatigue in June 2008. He was found to be cytopenic with a white cell count of 5.9 K/uL, hemoglobin of 8.5 g/dL, and platelet count of 30 K/uL, with 45% circulating blasts. A bone marrow examination performed on June 25, 2008 revealed a hypercellular marrow with trilineage hypoplasia, dysgranulopoiesis, dyserythropoiesis, and 80% blasts. The blasts varied from small to intermediate-sized to large with fine chromatin, prominent nucleolus, and scant to moderate amount of cytoplasm. Immunohistochemical studies showed that the blasts were positive for CD34 and CD117, and negative for CD3, CD10, CD20, CD68, myeloperoxidase and terminal deoxynucleotidyl transferase. Flow cytometry was performed on June 25, 2008. He was found to be cytopenic with a white cell count of 3.9 K/uL, hemoglobin of 8.5 g/dL, and platelet count of 30 K/uL, with 45% circulating blasts.

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Key Words: t(1;3)(p36;p21); acute myeloid leukemia, refractory
The patient was admitted to a local hospital, and was treated with induction regimen of daunorubicin and cytarabine (7+3). A repeat bone marrow performed on July 30, 2008 showed no evidence of leukemia. The patient declined further chemotherapy. He remained well until November 2008 when a bone marrow examination revealed relapsed disease. He was treated with a salvage regimen with fludarabine, cytarabine, idarubicin, and G-CSF (FLAG), and came to our institution for further treatment options.

Upon presentation at our institution, his white cell count was 6.9 K/uL, hemoglobin 12.8 g/dL, and platelet count 355 K/uL, with a normal differential count. His serum lactate dehydrogenase level was 581 IU/L, and his serum β2-microglobulin level was 1.8 mg/L. There was no palpable hematosplenomegaly or lymphadenopathy. Bone marrow biopsy showed no morphologic or immunophenotypic evidence of AML. He received consolidation therapy with high-dose cytarabine in December 2008. He then received matched related stem cell transplantation in February 2009. However, the disease relapsed again in April 2009. The t(1;3)(p36;p21) was detected at the time of relapse. The patient decided not to receive any further treatment for AML, and he died 11 months after initial diagnosis.

DISCUSSION
Cytogenetic abnormalities have been regarded as one of the most important prognostic factor in AML. Clonal chromosomal aberrations have been detected in over 50% of AML, with +8, -7/del(7q), +21, -5/del(5q) being the most common. Hematopoietic neoplasms associated with t(1;3)(p36;p21) is a rare entity and has only been described in 2 cases of AML, both were classified as acute promyelocytic leukemia (APL). In both cases, t(1;3) presented as part of complex cytogenetic abnormalities. We report a case of AML with t(1;3)(p36;p21) as the sole cytogenetic abnormality.

In the two cases of APL, the first patient was a 55-year-old woman with a 3-way translocation involving 1p36 and 3p21 showing cytogenetic results of 46,XX.t(1;2;3)(p36;q21;p21).t(15;17)(q22;q11.2)[20]/46,XX [10]. No other clinical information was provided. The patient only survived 64 days. The second patient was a 44-year-old Japanese man who was initially diagnosed as APL with t(15;17) as the sole abnormality. The patient was treated with two courses of induction chemotherapy and achieved complete remission. t(1;3)(p36;p21) occurred at the third relapse (56 months after initial diagnosis). The patient died of sepsis 15 months after the detection of t(1;3)(p36;p21). This indicates that the t(1;3)(p36;p21), as well as its variant...
t(1;2;3)(p36;q21;p21) in the other case, was an acquired change that may be related to the patient’s chemotherapy as the authors suggested. However, in our case, t(1;3) was the sole cytogenetic abnormality at patient’s initial presentation of AML. It was not associated with any prior chemotherapy or radiation therapy, nor was it shown as an evidence of clonal evolution.

Based on the variable presentations of t(1;3)-associated neoplasms, it is likely that it is heterogeneous at the molecular level. It is also possible that other cytogenetic abnormalities in addition to t(1;3) in the reported cases might play roles in the heterogeneity of these diseases.

In summary, we report the first case of an AML with t(1;3)(p36;p21) as the sole cytogenetic abnormality in a 56-yea-old Hispanic man with immature phenotype, high blast count, resistance to multiple chemotherapy, and a poor clinical outcome. The t(1;3) was detected at initial presentation and was not associated with prior exposure to chemotherapy or radiation therapy.

CONFLICT OF INTEREST
The authors have no conflict of interest to disclose.

REFERENCES
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