A Case of Myelodysplastic Syndrome Associated with an Isolated del(5q) Chromosomal Abnormality Showing Poor Prognosis

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Typical myelodysplastic syndrome (MDS) associated with isolated del(5q) consists of an interstitial deletion of the band between q13 and q33 on chromosome 5. Generally, patients with isolated deletion 5q have better outcomes than those who have the deletion 5q with additional karyotypic abnormalities. Here we report a 47 year-old female with an isolated del(5q) chromosomal abnormality with an atypical breakpoint of 5q11q35 and rapid progression to acute leukemia, which had an exceptionally poor outcome. The peripheral blood revealed pancytopenia and occasional giant platelets, and the patient had hypercellular bone marrow with 4.8% blasts, as well as dysmegakaryopoiesis and dyserythropoiesis. Cytogenetically, the patient was del(5q)(q11.2q35)[18]/46,XX[2], showing that her deleted region was larger than that found for typical del 5q syndrome. Three months later, the patient presented with acute myelomonocytic leukemia with multilineage dysplasia. The cytogenetic findings were identical. Two months after allogeneic bone marrow transplantation, the patient died from severe graft-versus host disease. (Korean J Hematol 2007;42:43-47.)

Key Words: Myelodysplastic syndromes, Isolated deletion(5q)

INTRODUCTION

Interstitial deletion of 5q is the most common chromosomal aberration in patients with myelodysplastic syndromes (MDS),1,2) with the proximal breakpoint usually being from q11 to q31 and the distal breakpoint from q21 to q33. The most common deletion is an interstitial deletion of the band from q13 to q33. MDS associated with isolated del(5q) is one of the seven categories of MDS by WHO definition. This disease shows favorable prognosis with long survival1-4) and clinically the patients in this category is classified as refractory anemia. 5) We report here a case of MDS associated with isolated del(5q) which was associated with exceptionally poor prognosis.
CASE REPORT

A 47-year-old woman visited hospital complaining of dyspnea. No abnormalities were noted during physical examination, but unexplainable pancytopenia was detected. The peripheral complete blood count was as follows: hemoglobin, 7.9g/dL; MCV, 97.6fL; white blood cells, $2.1 \times 10^9$/L with differentials of 1% band, 26% segments, 1% basophil, 1% eosinophils, 16% monocytes, 53% lymphocytes; and platelet, $31 \times 10^9$/L. Frequent giant platelets were noted. Bone marrow (BM) aspiration revealed hypercellular marrow, with 4.8% of all nucleated cells being blasts. The BM showed multilineage dysplasia involving cells of the megakaryocytic and erythroid lineages. Dysmegakaryopoietic features included hypolobulation, nu-

Fig. 1. The findings at the diagnosis of myelodysplastic syndrome associated with isolated del(5q). (A) Occasional micromegakaryocytes with hypolobulated nucleus in the bone marrow aspirates (Wright stain, $\times 1,000$). (B) Numerous megakaryocytes of various sizes. Frequent hypolobulated micromegakaryocytes in the hypercellular bone marrow biopsy specimen (H&E stain, $\times 1,000$).

Fig. 2. The findings of bone marrow aspiration at the diagnosis of acute myelomonocytic leukemia with multilineage dysplasia (AML M4 according to the FAB classification). (A) Blasts with prominent nucleoli and relatively abundant cytoplasm with small vacuoles (Wright stain, $\times 1,000$). (B) Erythroid dysplasia, including multinucleation, nuclear fragmentation, and basophilic stippling in the bone marrow aspirates (Wright stain, $\times 1,000$).
clear separation, and micromegakaryocytes, and
dyserythropoiesis features included nuclear budding,
multinucleation, basophilic stippling, and
Howell-Jolly bodies (Fig. 1). Sideroblasts were not
detected. Conventional cytogenetic analysis showed del(5q)(q11.2q35) in 18 of 20 metaphases and 46,XX in the remaining two. The deleted region was larger than that of typical MDS associated with isolated del(5q) (Fig. 2). Three months later without treatment, the peripheral blood showed 6% blasts and 24% monocytes with pancytopenia sustained. The leukoerythroblastic reaction was noted. Repeated BM aspiration revealed 31% blasts with dysplastic features, and the patient was classified as acute myelomonocytic leukemia (AML M4 according to the French-American-British classification with multilineage dysplasia. The dysplasia became aggravated into three lineages with additional myeloid lineage (Fig. 3). Cytologically, the blasts showed positive myeloperoxidase and non-specific esterase reaction. The blasts expressed CD13, CD33, CD117, CD14, and aberrant CD7. Repeated cytogenetic analysis showed del(5q)(q11.2q35), with no additional changes, in 18 of 20 metaphases. The patient received bone marrow transplantation (BMT) from unrelated donor after a scheduled pre-BMT BuCy regimen (Busulfan 4mg/kg/dx4, Cyclophosphamide 60mg/kg/dx2). But, 2 months after BMT, the patient died from severe graft-versus host disease (GVHD).

DISCUSSION

The MDS associated with isolated del(5q) classically, is characterized by hypolobulated micromegakaryocytic hyperplasia and a clonal cytogenetic abnormality, consisting of an interstitial deletion in the long arm of chromosome 5. According to the new classification of MDS by World Health Organization (WHO), this is defined as a subgroup of MDS showing single cytogenetic abnormality of del(5q) and <5% blasts in the BM. Cytogenetically, individuals with isolated del(5q) have a fairly good prognosis. The significance of >5% BM blasts in a patient with an isolated del(5q) is not clear, but it has been suggested that these patients have poorer prognosis.

Variable breakpoints of 5q have been reported in MDS associated with isolated del(5q), with the usual proximal breakpoint being from q11 to q31 and the usual distal breakpoint from q21 to q33. The most common form, del(5q)(q13q33), has the best prognosis. In this patient, however, the deletion region was between bands q11.2 and q35, larger than that observed frequently in del(5q). It may be noteworthy that in this patient, MDS evolved into acute leukemia with multilineage dysplasia, without additional cytogenetic abnormalities, only 3 months after the initial diagnosis. Following the development of splenomegaly, she died from GVHD soon after BMT.

Although many genes that encode hematopo-
Table 1. Clinical and pathologic characteristics of MDS associated with isolated del(5q) and the comparison with this patient

| Isolated del(5q) | This patient |
|------------------|--------------|
| • Clinical presentation | • Clinical presentation |
| Older age (median 68 years) | Old age (47 year-old) |
| Female predominance (7:3 female to male) | Female |
| Refractory anemia | Pancytopenia |
| Low risk of leukemic progression | Leukemic progression |
| Good prognosis | Poor prognosis |
| • Hematologic presentation | • Hematologic presentation |
| Macrocytic anemia | Normocytic anemia |
| Modest leukopenia | Modest leukopenia |
| Normal/High platelet counts del(5q)(q13q33) | Low platelet count del(5q)(q11.2q35) |
| BM erythroid hypoplasia | No BM erythroid hypoplasia |
| Hypolobulated megakaryocytes in BM <5% BM blast count | Markedly hypolobulated megakaryocytes in BM 4.8% of BM blast count |

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In conclusion, we have described a patient with MDS associated with isolated del(5q), which was rapidly transformed to acute leukemia. In this patient, poor prognosis has been due to the 5q breakpoint, which included the band at 5q12.

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