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Myelodysplastic Syndrome that Progressed to Acute Myelomonocytic Leukemia with Eosinophilia Showing Peculiar Chromosomal Abnormality
: A Case Report

Myelodysplastic syndrome is a closely related group of acquired bone marrow disorders characterized by ineffective and dysplastic hematopoiesis. These clonal disorders frequently progress to acute leukemia. Acute myelomonocytic leukemia with eosinophilia is characterized by an increase in abnormal eosinophils in the bone marrow, relatively good clinical course and inv (16) chromosomal abnormality. We experienced one case of refractory anemia with excess blasts which progressed to refractory anemia with excess blasts in transformation and finally to acute myelomonocytic leukemia with eosinophilia showing peculiar chromosomal abnormalities of der (1;7).

Key Words: *Myelodysplastic syndromes; Leukemia, myelomonocytic, acute; Eosinophilia; Chromosome abnormalities*

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INTRODUCTION

Though myelodysplastic syndrome has been known to progress to acute myelogenous leukemia, transformation to myelomonocytic leukemia with eosinophilia (M4Eo) is infrequent. M4Eo shows characteristic cytogenetic abnormality (inversion of chromosome 16). We experienced one patient with M4Eo who did not show inversion of chromosome 16 but had other rare cytogenetic abnormalities, which resulted from myelodysplastic syndrome (refractory anemia with excess blasts).

CASE REPORT

A 37-year-old man admitted to our hospital because of dizziness, easy bruisability and fatigue for two months. His past history revealed benzene exposure for one year just prior to admission.

On physical examination, there was no organomegaly or lymphadenopathy. Complete blood counts were hemoglobin 6.6 g/dL, platelets 39,000/μL, and leukocytes 3.6 $\times 10^9$/L, with 50% neutrophils, 41% lymphocytes, 5% monocytes, 2% eosinophils and 1% blasts. Bone marrow examination showed 6% blasts, 9.8% eosinophils, and signs of dyserythropoiesis, dysgranulopoiesis and dysmegakaryopoiesis, compatible with refractory anemia with excess blasts (RAEB) (Fig. 1A). Cytogenetic analysis of bone marrow cells showed only normal karyotypes (Fig. 1B). He was then followed up via OPD with intermittent packed RBC transfusion without any specific treatment.

One and half year later, complete blood counts were hemoglobin 7.6 g/dL, platelets 25,000/μL, and leukocytes 15.9 $\times 10^9$/L, with 2% blasts and 84% monocytes and bone marrow examination revealed dysplastic features with 25% myeloblasts, compatible with refractory anemia with excess blasts in transformation (RAEB-t).

Six months later, he was hospitalized because of cellulitis of the left lower leg which was resolved without any problems with the appropriate antibiotic regimen, and bone marrow examination during admission showed 56% myelomonoblasts and increased eosinophils (9%),

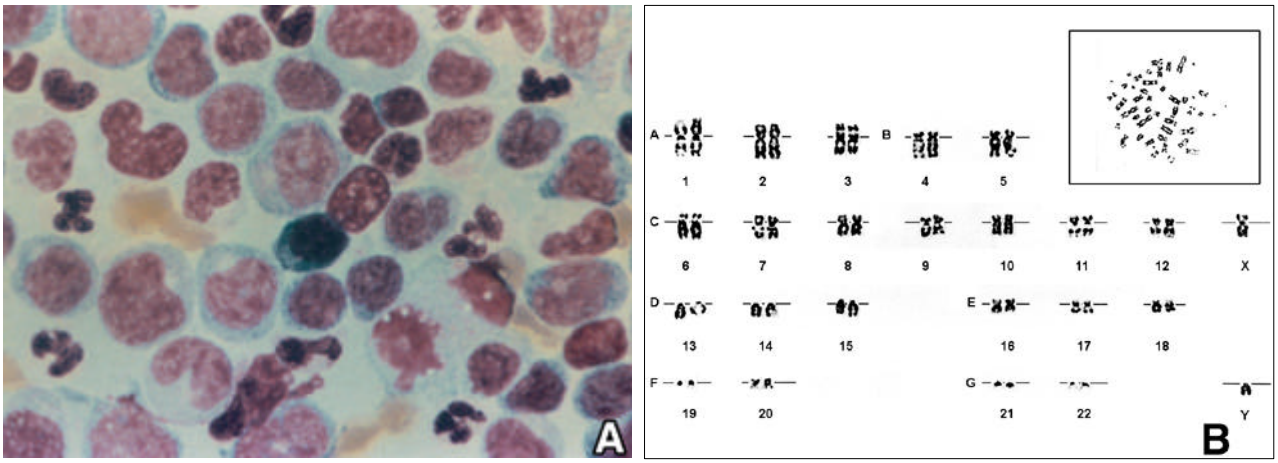

Fig. 1. A) Bone marrow at initial diagnosis showing dyshematopoiesis (Wright stain, ×1,000). B) Bone marrow karyotype at initial examination showing normal 46, XY.

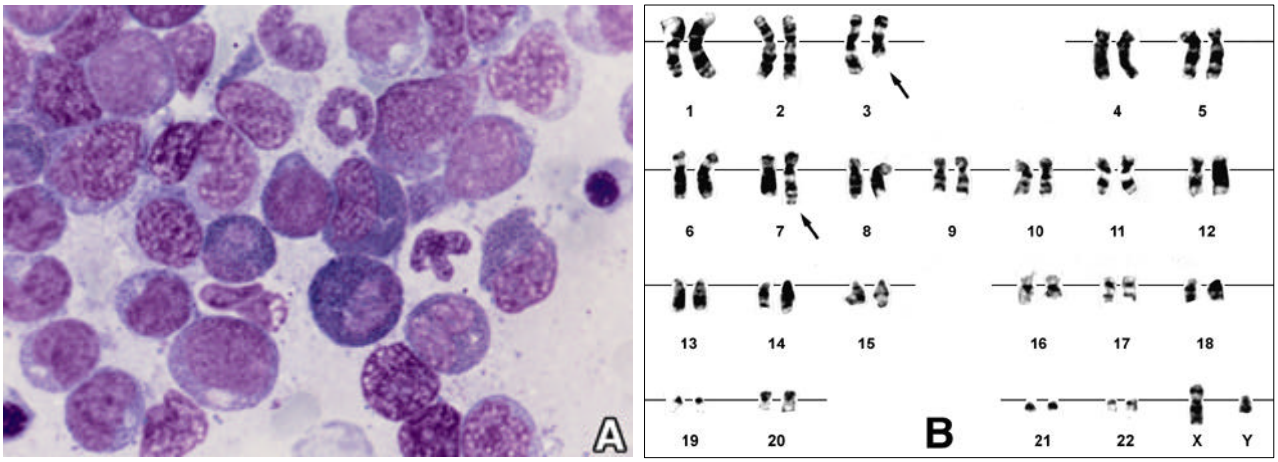

Fig. 2. A) Bone marrow at the time of overt leukemia showing dysgranulopoiesis and dysplastic eosinophils with coarse and basophilic granules (Wright stain, ×1,000). B) Bone marrow karyotype at the time of overt leukemia showing 46, XY, +1, der(1;7)(q10;p10), del(3)(q11q21). Chromosome abnormalities are indicated by arrows.

consistent with acute myelogenous leukemia (AML), FAB classification M4Eo (Fig. 2A). Sudan black B stain was positive. Periodic acid-Schiff and non-specific esterase stain were negative. On immunophenotyping, CD7 and CD14 were positive. Cytogenetic study showed 46, XY, +1, der (1;7)(q10:p10), del (3)(q11q21) (Fig. 2B). Induction chemotherapy with cytosine arabinoside and daunorubicin was started, but he failed to achieve complete remission after induction chemotherapy. He died of sepsis and pneumonia three weeks after reinduction chemotherapy.

DISCUSSION

Various portions of MDS progress to acute leukemia, especially acute myelocytic leukemia, and 30~60% of MDS reported to have chromosomal abnormality. The most frequent abnormalities were due to the whole or a partial loss of chromosome 7 (−7 or 7q−) and a partial loss of chromosome 5 (5q−) (1).

This was a case of refractory anemia with excess blasts which progressed into refractory anemia with excess blasts in transformation and finally into acute myelomonocytic leukemia with eosinophilia. At the point of transformation into AML-M4Eo, his chromosomal abnormalities were der (1;7), monosomy 7, and del (3q). The first two defects are often seen in MDS while the latter is rarely seen in MDS. There was no inv (16) known to be specific to AML-M4Eo in our patient. However, the combination of t (1;7) and inv (16) has never been reported previously, except for Tasaka's case (2).

Unbalanced translocation (1;7) was first reported in patients with treatment-related AML and MDS (3) and is most frequently associated with nonrandom chromosomal aberration with secondary MDS and AML (4). This chromosome abnormality has also recently been reported in patients with de novo MDS (1). The clinical significance of this karyotypic abnormality is characterized by resistance to conventional chemotherapy and susceptibility to severe infections (5, 6) and poor prognosis (7). With gene encoding, the neutrophil surface protein GP 130 is shown to be on the long arm of chromosome 7. Patients with monosomy 7 are defective in neutrophil chemotaxis (8) and tend to suffer from potentially lethal infections (2, 6). More recently, the breakpoint in this location has been accurately localized by employing fluorescence in situ hybridization (FISH) (9), resulting in the new denotation of der(1;7)(q10:p10) according to conventions adopted in ISCN 1991 (10).

Approximately one-half of MDS patients with the der (1q;7p) abnormality reported recent history of exposure to toxic agents. Because our patient had a past history of benzene exposure for one year, we presume there was a chromosomal abnormality in initial bone marrow which we failed to obtain on initial chromosomal analysis.

The pericentric inversion of chromosome 16 < inv (16) > has been reported as a characteristic chromosome abnormality of acute myelomonocytic leukemia with abnormal eosinophils (M4Eo). Leukemia patients with this chromosome aberration have a more favorable prognosis than those without this karyotypic abnormality (11).

Marrow eosinophilia is a rare occurrence in MDS. When eosinophilia is present, it is often difficult to distinguish whether it is reactive or part of the MDS process. Of all the reported cases of AML and MDS with t(1;7) abnormality, eosinophilia has not been a prominent feature. Matsushima et al. recently reported a study of MDS with eosinophilia in the bone marrow (12). In that study, MDS with bone marrow eosinophilia (MDS-Eo) was significantly correlated with major karyotype abnormality (MAKA) and poor prognosis. Our patient's initial bone marrow examination also showed 9.8% eosinophils, which may be due to immunologic abnormality. However, there have been no extensive investigations into immunologic abnormalities in patients with the chromosomal abnormality < −7, +der(1q;7p) >, and it is uncertain whether eosinophilia triggers the immunologic abnormality or a secondary reaction.

We report the first case of RAEB progressed into RAEB-t and finally into AML-M4Eo along with associated chromosomal abnormality.

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