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Case Report

A novel deletion in the Yq-chromosome of a patient with chronic myelomonocytic leukemia

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Abstract: At present the pathogenesis and therapeutic effect of chronic myelomonocytic leukemia (CMML) is still not very clear. There are no specific molecular biology characteristics in it. We report a novel deletion in the Yq chromosome of a patient with CMML, as well as the treatment and prognosis, and review the relevant literature, and put forward that the Y chromosome abnormality may be involved in the development process of malignant blood diseases.

Keywords: Chronic myelomonocytic leukemia, Y chromosome abnormalities

Introduction

Chronic myelomonocytic leukemia (CMML) is a heterogeneous disease and characterized by morphologic dysplasia with accumulation of monocytes. CMML was classified as a myelodysplastic syndrome (MDS) under the French-American-British scheme [1], but it is in a group of myeloproliferative disease (MPD) in the World Health Organization (WHO) classification [2]. The pathogenesis of CMML remains poorly understood. Although clonal cytogenetic abnormalities are detected in 20% to 40% of the patients with CMML, none is specific [3] and the related risk factors for CMML are still unclear. In this report we first describe a CMML patient, who had a missing part of chromosome Y (Yq^-) and was sensitive to hydroxycarbamide (HU) therapy.

Patient and methods

Patient

A chronic myelomonocytic leukemia (CMML) was diagnosed in our male patient at 54 years of age in 2008. The patient had a medical history of ankylosing spondylitis (AS) dating from 1992. The patient showed an elevated number of monocytes in the blood, with a monocyte count of 7.2×10^9/L. The amounts of blasts including myeloblasts, monoblasts and promonocytes in the bone marrow were 8%, 5%, and 8% respectively. High expression levels of CD13, CD33, CD14, CD11c and HLA-DR were detected in his bone marrow cells. Enlarged spleen was found in the patient. HU therapy was conducted at an initial dose of 2,000 mg daily and a maintenance dosage of 500~1,000 mg daily. The patient's condition in five years was significant improved. His white blood cell count varied between 8.0×10^9/L and 20.0×10^9/L, hemoglobin level was higher than 12.0 g/dl continuously, and platelet count fluctuated between 70.0×10^9/L and 180.0×10^9/L.

Chromosome analyses

Chromosome analyses were performed on bone marrow samples. Bone marrow specimens were cultured for 24 hr. Metaphase analysis was done for G-bands using conventional cytogennetic analysis technique.

FISH analysis

Fluorescence in situ hybridization (FISH) analysis was performed according to the manufacturer's instructions with commercially available FISH probes (Beijing Golden Beijia Medical Technology Co, Ltd). The CSPX and CSPY DNA probes were used for both X and Y chromosomes analyses.

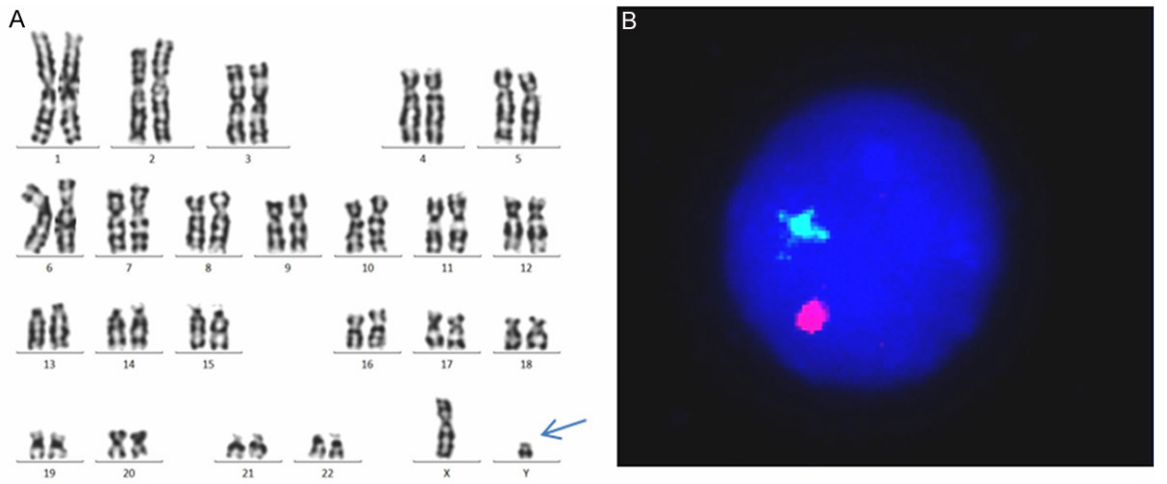

Figure 1. Cytogenetic characterization of the Yq (-) transiocation. A. Detailed characterization of the translocation was made using G-banding method. The arrow indicates the deletion of the Yq chromosome. B. Two different colour FISH (Beijing GP Medical Technology Co., Ltd.). Red signal shows centromeric specific probe for X chromosome (CSPX) and green signal shows for Y chromosome (CSPY).

Y-STR analysis

Microdeletion analysis of the Y chromosome was performed using AmpFISTR Identifiler TM fluorescently labeled multiplex amplification system and ABI9700 PCR approach. 16 Y-chromosome-specific short tandem repeat (Y-STR) were selected. Sixteen Y-STR loci (DYS456, DYS389I, DYS390, DYS389II, DYS-458, DYS19, DYS385, DYS393, DYS391, DYS-439, DYS635, DYS392, Y-GATA-H4, DYS437, DYS438, and DYS448) were investigated.

Results and discussion

A novel deletion in the Yq chromosome of a patient with CMML

Cytogenetic abnormalities occur 20~40% of cases of CMML, although none are entirely specific. The most chromosome abnormalities seen in CMML include trisomy 8, monosomy 7 or deletions of 7q [4]. Other cytogenetic abnormalities were also discovered in CMML. A case of CMML with 46, XY, der (9) t(1;9)(q11;q34) was reported [5]. An unbalanced translocation of the entire 1q onto the short arm of chromosome 14 as a sole cytogenetic abnormality was found in a patient with CMML [6]. In this report we describe a CMML patient, who had 46, XY, Yq (-) and Hu therapy sensitive (**Figure 1**). However, the prognostic implication of the cytogenetic abnormalities in CMML is not fully understood. A patient with CMML who showed 46, XY, t(11;19)(q23;q13.1) eventually developed into acute myeloid leukemia (AML) in a short time [7]. A patient of CMML with t(5;21)(q13;q22) was characterized by a progressive platelet reduction, who required a platelet transfusion to maintain a tolerable quality of life [8]. Our patient's prognosis seems to be better than those patients with above other abnormal chromosome karyotype.

Microdeletion analysis of Y-STR in a patient with CMML

Compared with the normal expression level of the Y-STR in the patient's oral mucosa cells, four Y-STR loci (DYS456, DYS458, DYS19, DYS393) located in the short arm of the Y chromosome were normal in the bone marrow cells of the same patient. The other twelve Y-STR loci (DYS389I, DYS390, DYS389II, DYS385, DYS-391, DYS439, DYS635, DYS392, Y-GATA-H4, DYS437, DYS438, DYS448) located in the long arm of the Y chromosome were not amplified (**Figure 2**). Y chromosome karyotype abnormalities were often found in male sperm production barriers and male infertility. In recent years, it was also discovered in some tumor diseases and hematologic disorders. Loss of Y chromosome as a frequent event occurring in male pancreatic tumors and bladder cancer has been reported [9, 10]. Some patients with acute leukemia or myelodysplastic syndrome

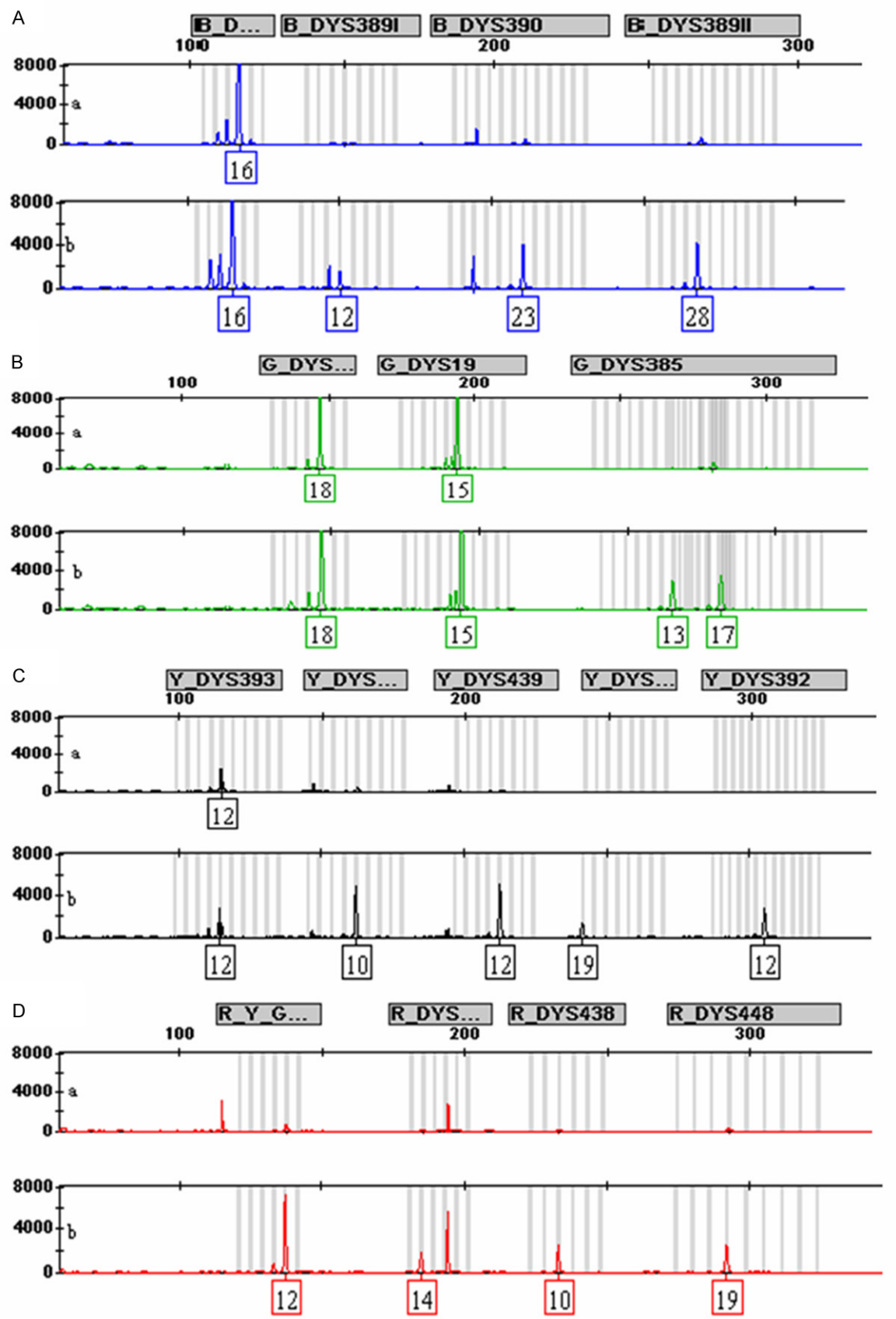
A
B_D...
B_DYS389I
B_DYS390
B_DYS389II
100
200
300
8000
4000
0
a
16
b
16
12
23
28
B
G_DYS...
G_DYS19
G_DYS385
18
15
13
17
C
Y_DYS393
Y_DYS...
Y_DYS439
Y_DYS...
Y_DYS392
12
10
19
D
R_Y_G...
R_DYS...
R_DYS438
R_DYS448
14

Figure 2. 16 Y-chromosome-specific short tandem repeat (Y-STR) were selected. Each picture consists of two parts of a and b. a is the bone marrow of patient with leukemia cells Y-STR loci map, b is the patient' oral mucosa cell Y-STR loci map. Four Y-STR loci (DYS456, DYS458, DYS19, DYS393) located in the short arm of the Y chromosome were normal in the bone marrow cells of the same patient. The other twelve Y-STR loci (DYS389I, DYS390, DYS389II, DYS385, DYS391, DYS439, DYS635, DYS392, Y-GATA-H4, DYS437, DYS438, DYS448) located in the long arm of the Y chromosome were not amplified.

(MDS) showed the Y chromosome loss, which may be associated with the development of disease [11, 12]. It is reported that Y-STR loci (D2S1338, D7S820, D18S51, D13S317, and CSF1PO) and amelogenin gene were involved in the blast crisis in the patients with chronic myelocytic leukemia (CML). In our case, we first report a CMML patient with Yq-, which suggest the correlation between the pathogenesis of CMML and Y chromosome abnormality.

Conclusions

In combination with the miss of the long arm of the Y chromosome in our reported patient with CMML, suggesting that the Y chromosome abnormality may be involved in the pathogenesis of malignant blood disease and the mechanism needs further study.

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Disclosure of conflict of interest

None.

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