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Case Report Section

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Inversion(11)(p15q22) as a secondary anomaly in a case of relapsed MDS-RAEB after unrelated donor hematopoietic cell transplantation

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Clinics

Age and sex
38 years old female patient.

Previous history
Preleukemia previous diagnosed as MDS-RAEB, with isolated deletion 20q.
No previous malignancy, no inborn condition of note.

Organomegaly
No hepatomegaly, no splenomegaly, no enlarged lymph nodes, no central nervous system involvement.

Blood

WBC: 2.58 X 10^9/l (neutrophils 36.30%, lymphocytes 47%, monocytes 13.90%)
HB: 103g/dl
Platelets: 42X 10^9/l
Blasts: 6.59%
Bone marrow: 5% (the bone marrow was normocellular with 5% myeloblasts, 8% promyelocytes, with dysplasia in myeloid and erythroid lineages).

Cyto-Pathology Classification

Immunophenotype
There were 10% myeloid blasts positive for C34, CD117, CD13, CD33, and HLA-DR and partially positive for cMPO.

Diagnosis
Relapsed MDS-RAEB 4 months after unrelated donor HCT.

Survival

Date of diagnosis: 02-2012

Treatment: Date of the first HCT: 02-2012, a second HCT: 10-2012

Complete remission: complete remission 1 month after the first HCT (03-2012)

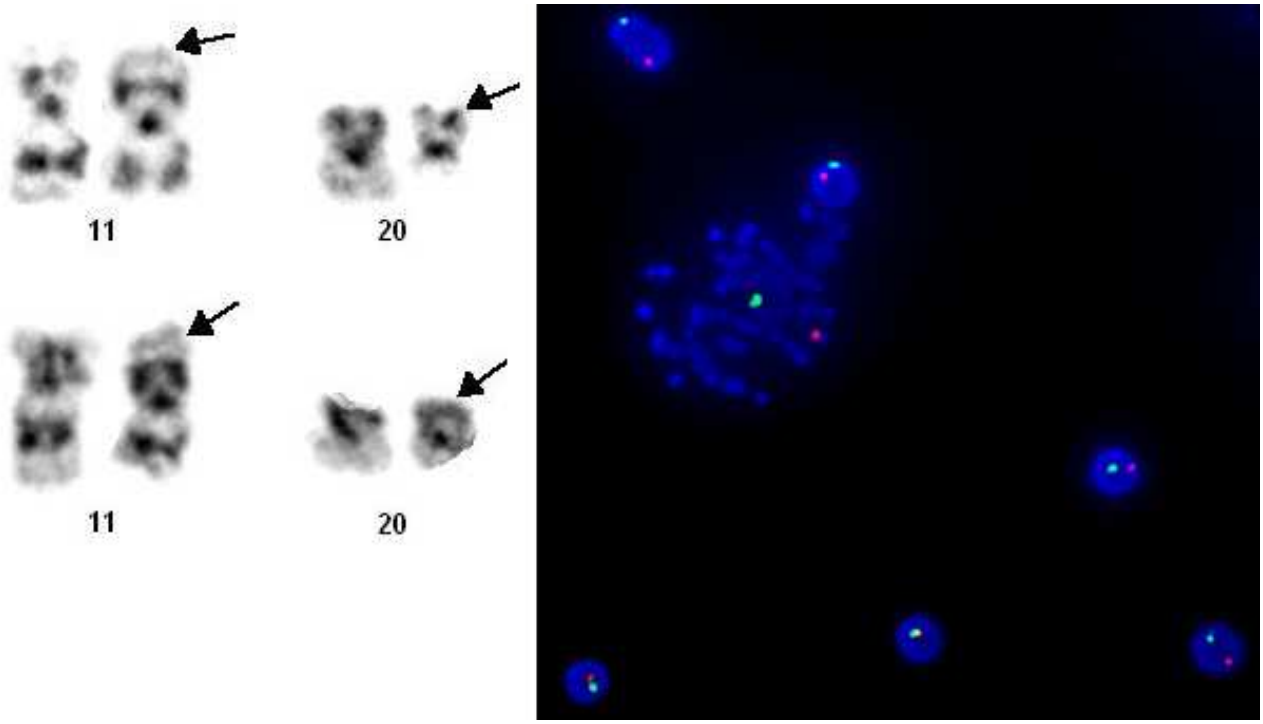
Treatment related death: died of acute graft versus host disease and serious infection

Relapse: four months after the first HCT (07-2012)

Status: Death

Last follow up: 12-2012

Survival: 10 months from the date of first HCT.



Left: G-banded partial karyogram at relapse, showing the inv(11)(p15q22) and del(20)(q11). Right: FISH result using centromeric XY DNA probe (Vysis) after the second HCT showing 99.8% XY signal (donor-originated).

Case No.	Sex	Age (yr)	Diagnosis	Karyotype	References
1	F	4	t-MDS-RA	46,XX,inv(11)(p15q22)[16]	Arai Y, et al[2]
2	M	7	MDS-RAEBT	46,XY,inv(11)(p15q22)[20]	Arai Y, et al[2]
3	M	10	AML-M1	47,XY,inv(11)(p15q22),+21[16]	Arai Y, et al[2]
4	M	61	t-AML-M4	46,XY,t(3;5)(p13;q35),inv(11)(p15q22)[9]/46,XY[1]	Arai Y, et al[2]
5	M	51	t-CMMoL	46,XY,inv(11)(p15q22)	Ikeda T, et al[3]
6	M	58	CML	46,XY,t(9;22)(q34;q11), inv(11)(p15q22)[15]	Yamamoto M, et al[4]
7	M	6	AML	46,XY,inv(11)(p15q22)[3]/46,XY,idem,der(17)t(17;?)(q?11;?)[10]/46,XY,idem,del(2)(p?22),der(17)t(17;?)(q?11;?)[5]/46,XY[2]	Nebral K, et al[5]
8	M	18	t-AML-M4	46,XY,inv(11)(p15q22)[20]	Nebral K, et al[5]
9	F	47	t-AML	46,XX,inv(11)(p15q22)[17]/46,XX[6]	Romana SP, et al[6]
10	F	55	t-MDS	46,XX,t(11;11)(p15;q22)[9]/ 46,XX[11]	Romana SP, et al[6]
11	F	60	AML-M4	46,XX,inv(11)(p15q22),del(12)(p13)[20]	Romana SP, et al[6]
12	M	12	AML-M5b	46,XY,inv(11)(p15q22)	Morerio,C, et al[7]
13	F	Unknown	AML-M6	46,XX,inv(11)(p15q22)	Xue YQ, et al[8]
14	F	38	MDS-RAEB	46,XX,del(20)(q11.2)[5]/46,XX,inv(11)(p15q22),del(13)(q22q32),add(16)(q22),add(19)(q13.3),del(20)(q11.2)[cp13]/ 46,XX[2]	Present case

Table 1. Summary of publicly reported cases with inv(11)(p15q22) and NUP98-DDX10 fusion gene.

Karyotype

Sample: Bone marrow

Culture time: 24h

Banding: G banding

Karyotype at Relapse

46,XX,del(20)(q11.2)[5]/46,XX,inv(11)(p15q22),del(13)(q22q32),add(16)(q22),add(19)(q13.3),del(20)(q11.2)[cp13]/46,XX [2]

Other molecular cytogenetics technics

Karyotype 17 days after the second HCT: 46,XY[30]

Other molecular cytogenetics results

Fluorescence in situ hybridization (FISH) result 17 days after the second HCT (using XY DNA probe): 99.8% XY signal (donor-originated)

Other Molecular Studies

Technics:

RT-PCR: Not done because no sample left to extract RNA.

Comments

Inversion(11)(p15q22) is a rare entity.

It has been found as abnormal clone in MDS or myeloid leukemia, either de novo or secondary, in both children and adults. There seems to be male predominance. To our knowledge, this is the first case report that presents inv(11)(p15q22) as an additional cytogenetic abnormality besides deletion 20q, a common aberration in MDS. Previously, Yamamoto M et al reported the appearance of an inv(11)(p15q22) as a secondary anomaly in a chronic myeloid leukemia (CML) patient undergoing treatment with imatinib, suggesting a possibility that this abnormality might be involved in drug resistance and disease evolution.

Our patient was diagnosed as MDS-RAEB with isolated deletion 20q at admission. One month after unrelated donor HCT, the patient reached complete hematologic and cytogenetic remission. However, about four months after transplantation, myeloblasts recurred in the bone marrow. Flow cytometry examination revealed about 10% abnormal cells with characteristic immunophenotype of myeloblasts. Cytogenetical detection revealed two abnormal clones, one with sole deletion 20q, the other with inv(11)(p15q22) and other aberrations besides deletion 20q. We speculate the occurrence of inv(11)(p15q22) with two possibilities: (1) clonal evolution, because the patient had isolated deletion 20q at initial diagnosis, which is common in MDS patients. In general condition, clonal evolution means disease progression and leukemic transformation in MDS, so acquisition of inv(11)(p15q22) might be a cause of relapse after HCT. (2) therapy-related aberration, as the patient received high-dose pretreatment before donor stem cell infusion, although this is unlikely.

Until now 13 cases with inv(11)(p15q22) have been reported by literature review (Table 1). This inversion leads to fusion of DDX10, a putative RNA helicase gene at 11q22 with the nucleoporin gene NUP98 at 11p15.

The previously described cases with this chromosome anomaly and NUP98-DDX10 fusion gene comprising 5 children,7 adults and 1 unknown. 8 cases had diagnosis of de novo or secondary AML, 4 cases had primary or therapy-related MDS, and one CML case was found with this chromosome abnormality in acute phase. NUP98-DDX10 fusion, another type of NUP98 rearrangements, might be associated with the poor clinical course.

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