

## Case Report

# A rare der(Y)t(Y;1)(q12;q12) in a patient with post-polycythemic myelofibrosis: a case report

Masahiro Manabe<sup>1</sup>, Osami Takeda<sup>2</sup>, Junya Okita<sup>1</sup>, Teruhito Takakuwa<sup>1</sup>, Naonori Harada<sup>1</sup>, Hirofumi Nakano<sup>1</sup>, Shuichiro Okamoto<sup>1</sup>, Yasutaka Aoyama<sup>1</sup>, Takeo Kumura<sup>1</sup>, Tadanobu Ohta<sup>1</sup>, Yoshio Furukawa<sup>1</sup>, Atsuko Mugitani<sup>1</sup>

<sup>1</sup>Department of Hematology, Seichokai Fuchu Hospital, 1-10-17 Hiko-cho, Izumi, Osaka 594-0076, Japan; <sup>2</sup>Department of Gastroenterology, Seichokai Fuchu Hospital, 1-10-17 Hiko-cho, Izumi, Osaka 594-0076, Japan

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**Abstract:** We describe a case of post-polycythemic myelofibrosis harboring der(Y)t(Y;1)(q12;q12). The patient was a 69-year-old man and was initially diagnosed with polycythemia vera. During the clinical course of his condition, the polycythemia developed into myelofibrosis. Chromosome analysis detected der(Y)t(Y;1)(q12;q12). We discuss the association between der(Y)t(Y;1)(q11~12;q12~21) and tumorigenesis along with a review of literature.

**Keywords:** Post-polycythemic myelofibrosis, der(Y)t(Y;1)(q12;q12), chromosomal abnormality

## Introduction

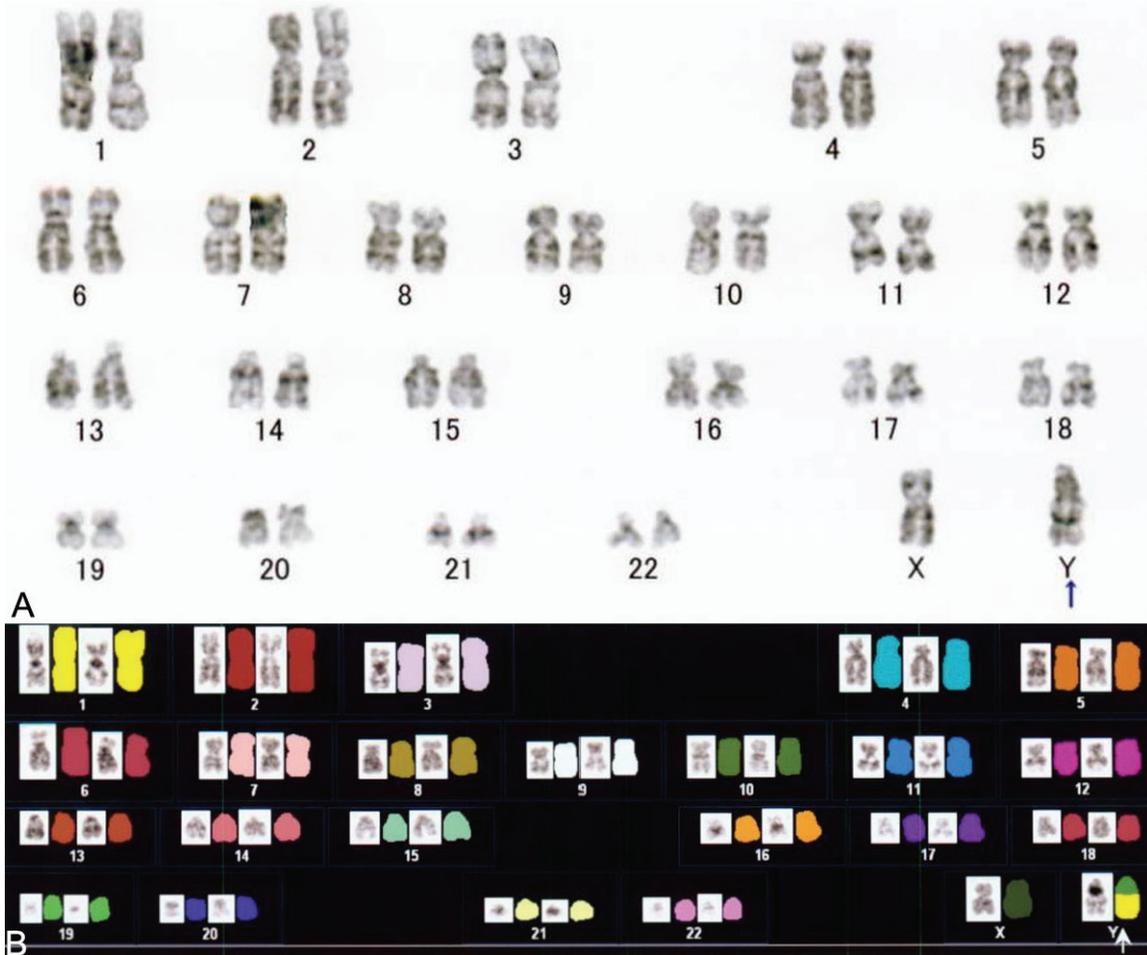
Many chromosomal abnormalities, such as t(8;21)(q22;q22), t(15;17)(q22;q12), and t(9;22)(q34;q11), are common in hematological diseases. However, structural abnormalities involving the sex chromosomes are rare in hematological malignancies [1]. der(Y)t(Y;1)(q11~12;q12~21) is reported to be a recurrent, but rare, chromosomal abnormality that is associated with hematological malignancies [2-18]. We encountered a patient with post-polycythemic myelofibrosis that harbored the der(Y)t(Y;1)(q12;q12) abnormality. In this report, we discuss the association between der(Y)t(Y;1)(q11~12;q12~21) and tumorigenesis.

## Case presentation

A 69-year-old male was referred to our hospital because of anemia in October 2010. He had a past history of polycythemia vera (without chromosomal abnormalities) and was treated with intermittent phlebotomy in 1995, but he refused further treatment due to a lack of symptoms. A physical examination detected mild splenomegaly and anemic conjunctivae.

Peripheral blood analysis demonstrated a white blood cell count of 21900/ $\mu$ L including 11.5% myelocytes, 73.5% neutrophils, 6% lymphocytes, 3% monocytes, 4.5% eosinophils, 1.5% basophils. In addition, the patient had a hemoglobin level of 8.5 g/dL, a platelet count of 313000/ $\mu$ L, and a serum lactate dehydrogenase level of 731 U/L. Anisocytosis and teardrop cells were detected on his peripheral blood film, and the polymerase chain reaction revealed that his peripheral blood cells were homozygous for the JAK2 V617F mutation. Bone marrow aspiration was not performed because of dry tap, but a bone marrow biopsy revealed massive fibrosis. A chromosomal study of his peripheral blood cells revealed his karyotype to be 46, X, der(Y)t(Y;1)(q12;q12) [9] / 46, XY [11] (**Figure 1**). A diagnosis of post-polycythemic myelofibrosis was made due to the presence of bone marrow fibrosis and the patient's history of polycythemia vera. His anemia gradually progressed; hence, red cell transfusions were started from December 2010, and he required about 4 units of packed red blood cells per month. His leukocyte count remained stable at between 10000~30000/ $\mu$ L without any evidence of leukemic transformation. The most recent chromosomal analysis of his peripheral blood cells,

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**Figure 1.** A. G-band karyotype analysis revealed the following karyotype: 46, X, der(Y)t(Y;1)(q12;q12). B. Multicolor fluorescent in situ hybridization (FISH) image (pseudocolor labeled) of metaphase spreads after spectrum-based classification.

which was performed in January 2013, did not reveal any abnormalities apart from der(Y)t(Y;1)(q12;q12).

### Discussion

Structural abnormalities involving the sex chromosomes, particularly the Y chromosome, are uncommon in hematological disease [1]. Furthermore, to the best of our knowledge, only about 20 cases of hematological disease harboring der(Y)t(Y;1)(q11~12;q12~21) have been reported [2-19] (**Table 1**). Among them, there were 6 cases of myelodysplastic syndrome, 4 cases of acute myeloid leukemia, 3 cases of chronic myelomonocytic leukemia, 2 cases of polycythemia vera (including our case), 2 cases of acute lymphoblastic leukemia, 2 cases of lymphoma, and 1 case each of atypical chronic myeloid leukemia and myelofibrosis. Several

previous studies have reported that the der(Y)t(Y;1)(q11~12;q12~21) was strongly associated with myelodysplastic syndrome [8, 13, 14]; however, although myelodysplastic syndrome is the hematological condition that is most frequently associated with der(Y)t(Y;1)(q11~12;q12~21), cases of other diseases, such as acute myeloid leukemia [16, 19] or Burkitt's lymphoma [15], involving the abnormality have also been reported. Accordingly, it seems that der(Y)t(Y;1)(q11~12;q12~21) is not restricted to myelodysplastic syndrome, and might play an important role in tumorigenesis in hematological disease.

As for its involvement in 1q abnormalities, der(Y)t(Y;1)(q11~12;q12~21) results in the partial loss of Yq and the partial gain of 1q. Trisomy 1q, regardless of whether it is complete or partial, might be implicated in leukemogenesis

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**Table 1.** Cytogenetic findings of previously reported cases involving der(Y)t(Y;1)(q11~12;q12~21)

	Age	G-banded Karyotype including der(Y)t(Y;1)	Diagnosis	Author
1	52	46, XY, t(12;17)(q13;p11)/47, X, der(Y)t(Y;1)(q12;q21), +9	PV	Testa JR (1981)
2	60	46, XY, del(20)(q11)/46, X, der(Y)t(Y;1)(q12;q21)	RAEB-1	Hollings PE (1988)
3	74	46, X, der(Y)t(Y;1)(q12;q21)	CMML	Hollings PE (1988)
4	60	47, X, der(Y)t(Y;1)(q12;q21), t(2;8)(q14;q24), +3, t(14;19)(q32;q13)	ML, SNC*	Tanaka S (1990)
5	22	51, X, der(Y)t(Y;1)(q12;q21), +6, +8, t(9;11)(p21;q23), +13, +18, +19	AML	Haupt R (1991)
6	15	46, X, der(Y)t(Y;1)(q12;q21)	RA	Thompson PW (1991)
7	62	46, X, der(Y)t(Y;1)(q12;q21)	AML	Singh S (1993)
8	59	47, X, der(Y)t(Y;1)(q12;q21), +8	RAEB-2	Wei DCC (1993)
9	10	46, X, der(Y)t(Y;1)(q11~12;q12~21), t(8;14)(q24;q32)	ALL	Dayton VD (1994)
10	65	46, X, der(Y)t(Y;1)(q12;q12)	MF	Michaux L (1996)
11	69	46, X, der(Y)t(Y;1)(q12;q12), del(11)(q13)	CMML	Michaux L (1996)
12	63	47, X, der(Y)t(Y;1)(q12;q12), +9	MDS	Raymakers R (1996)
13	0	46, XY, t(1;19)(q23;p13)/46, idem, der(Y)t(Y;1)(q12;q12)/46, idem, der(15)t(1;15)(q12;p11)/46, idem, der(22)t(1;22)(q12;p11)	ALL	Heerema NA (1999)
14	47	46, X, der(Y)t(Y;1)(q12;q12)	RAEB-1	Wan TSK (2001)
15	65	46, X, der(Y)t(Y;1)(q11;q12)	aCML	Ohsaka A (2002)
16	11	46, XY, t(8;14)(q24;q32)/46, idem, der(Y)t(Y;1)(q12;q21)	BL	Lones MA (2004)
17	81	46, X, der(Y)t(Y;1)(q11;q21)/46, idem, +der(12)t(3;12)(q26;q15), -21	AML	Bao L (2006)
18	37	46, X, der(Y)t(Y;1)(q12;q12)	RA	Djordjević V (2008)
19	NR	46, X, der(Y)t(Y;1)(q11;q21)	CMML	Chen B (2010)
20	71	47, X, der(Y)t(Y;1)(q12;q21), +6, t(8;16)(p11;p13)/47, idem, del(13)(q3?;q3?)	AML	Brown T (2012)
21	69	46, X, der(Y)t(Y;1)(q12;q12)	PV	present case

NR, not reported; PV, polycythemia vera; RAEB, refractory anemia with excess of blasts; CMML, chronic myelomonocytic leukemia; ML, malignant lymphoma; SNC, small noncleaved cell; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MF, myelofibrosis; MDS, myelodysplastic syndrome; aCML, atypical chronic myeloid leukemia; BL, Burkitt's lymphoma; RA, refractory anemia. The karyotype description was according to the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer [25]. \*The diagnosis was taken from the original paper.

due to gene dosage amplification and hematopoietic tissue degeneration, e.g., trilineage dysplasia [17, 20]. In addition, this might explain why der(Y)t(Y;1)(q11~12;q12~21) abnormalities are most frequently detected in myelodysplastic syndrome. On the other hand, 3 cases of chronic myeloproliferative disorders involving der(Y)t(Y;1)(q11~12;q12~21) have been reported, including 2 cases of polycythemia vera (including our case) and 1 of myelofibrosis. As Caramazza et al. showed that chromosome 1 abnormalities are most common in chronic myeloproliferative disorders, it is probable that der(Y)t(Y;1)-induced partial 1q trisomy was responsible for the tumorigenesis in these cases [21]. Concerning polycythemia vera, clonal chromosomal abnormalities are

observed in 15% to 25% of cases at diagnosis, but abnormal karyotypes are much more common at the onset of hematological complications, as indicated by additional clonal events [22]. Furthermore, in post-polycythemic myelofibrosis, the high frequency of 1q duplication is striking (this anomaly is seen in 70% to 90% of patients at the fibrotic phase versus the 10% to 15% incidence observed at the diagnosis of polycythemia vera). In our case, no chromosomal abnormalities were detected at diagnosis; however, der(Y)t(Y;1)(q12;q12) subsequently appeared after the patient's condition progressed to the fibrotic phase. In addition, similar to our case, Raymakers et al. reported a case of secondary myelodysplastic syndrome harboring der(Y)t(Y;1)(q12;q12), in which the

patient's karyotype did not show any abnormalities at the initial diagnosis of polycythemia vera [11]. It seems that the der(Y)t(Y;1)-induced partial 1q trisomy plays a crucial role in the development of polycythemia vera. Although we were not able to perform any detailed genetic evaluations in the present case, the further accumulation of cases is necessary to evaluate which genes on 1q are responsible for the development and/or progression of hematological disease.

Finally, regarding *JAK2* mutation, it was reported that 100% of post-polycythemic myelofibrosis patients possessed *JAK2* V617F mutation [23]. Although our case also exhibited *JAK2* mutation, the effects of *JAK2* mutations and cytogenetic abnormalities on patient prognosis and clinical variables are poorly understood [24]. Recently, the efficacy of *JAK2*-inhibitors against chronic myeloproliferative disorders was confirmed; therefore, we think that further evaluations of the prognostic utility of *JAK2* mutations and cytogenetic abnormalities are necessary.

**Address correspondence to:** Dr. Masahiro Manabe, Department of Hematology, Seichokai Fuchu Hospital, 1-10-17 Hiko-cho, Izumi, Osaka 594-0076, Japan. Phone: 81-725-43-1234; Fax: 81-725-41-0900; E-mail: m1153564@med.osaka-cu.ac.jp

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