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Translocation (2;3)(p21;q26) as the Sole Anomaly in a Case of Primary Myelofibrosis

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ABSTRACT: *Translocation t(2p;3q) is a rare but recurrent finding in myeloid disorders. We present the first case of primary myelofibrosis with t(2;3)(p21;q26) as the sole chromosomal anomaly. The comparison with the 11 other previously published myeloid-associated t(2p;3q) cases confirms that this nonrandom translocation involves a pluripotent stem cell and is associated with a poor prognosis.*

INTRODUCTION

Chromosomal translocations involving the short arm of chromosome 2 and the distal part of chromosome 3 long arm have been described in hematological malignancies. Several authors highlighted the nonrandom nature of these translocations in myeloid malignancies. Only 11 previous cases of t(2;3)(p13–23;q26–29) associated with myeloid disorders have been published [1–9] (Table 1). Except for three cases of acute myeloid leukemia M2 (AML M2), this nonrandom chromosomal rearrangement is observed with other anomalies and considered a secondary karyotypic aberration [1].

In the present report, we describe, to our knowledge, the first case of primary myelofibrosis with t(2;3)((p21;q26) as the sole anomaly.

PATIENT REPORT

A 68-year-old man was admitted to the hospital because of epistaxis, pallor, weight loss, and severe left upper quadrant pain. He reported chills, sweats, and dyspnea. Abdominal examination revealed moderate hepatomegaly and major splenomegaly. No lymphadenopathy was found. The hematologic data at diagnosis were the following: 10.2 g/dL hemoglobin, white blood cell count 16.99 $\times$ 10^9/L, 6% myelocytes, 1% promyelocytes, and 7% blasts. Bone marrow aspiration was difficult and disclosed no stroma. Mild basophil leucocytosis and thrombocytopenia were noted. An excess of myeloblasts (7.2%), elliptocytes, dacrocytes, schizocytes, and basophils was also observed. 71.5% (peripheral blood) and 82.8% (bone marrow) of the blasts showed a primitive immunophenotype CD34+/33−. A chronic myeloproliferative disorder was suspected. Cytogenetic studies performed at diagnosis on 24-hour BM cultures revealed a 46,XY[3]/46,XY,t(2;3)(p21;q26)[26] karyotype (Fig. 1). Fluorescence in situ hybridization using the BCR and ABL probes (Oncor Inc., Gaithersburg, MD) confirmed the absence of the chronic myeloid leukemia (CML)-associated molecular rearrangement.

Splenectomy was performed 2 weeks after diagnosis. The spleen was greatly enlarged (weight: 3,900 g) and deep purple-red with indistinct white pulp. The subcapsular area showed hematomas. Microscopic examination revealed variable degrees of fibrosis of all the hematopoietic cell lines in the red pulp sinuses and in the cords of Billroth. New samples of bone marrow and blood were received at the same time. Peripheral blood showed leucoerythroblastic blood film with striking poikilocytosis, including teardrop poikilocytes. Bone marrow again disclosed no stroma. Thrombocytopenia (38 $\times$ 10^9/L platelets) persisted; hyperleucocytosis (48.28 $\times$ 10^9/L) with 34% of blasts and 1.6% of micromegakaryocytes were observed. The diagnostic of myelofibrosis in transformation was made. The patient quickly developed pulmonary leukostasis and died.

DISCUSSION

To the best of our knowledge, this is the first report of a t(2;3)(p21;q26) translocation in a case of myelofibrosis. Similar translocations have been published previously in

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Table 1 Patient, diagnostic, and cytogenetic data from the 11 previously published t(2;3) cases associated with myeloid disorders

Patient data	Disease	Karyotype	Ref.
M/3.5y	AML M2	45,XY,t(2;3)(p21;q29),−7,del(12)(p12)	Berger et al. [1]
F/10	AML M2	46,XX,t(2;3)(p22;q28)	Berger et al. [1]
M/74	AML M2	46,XY,t(2;3)(p13;q28)	Prigogina et al. [2]
M/16	AML M2	46,XY,t(2;3)(p13;q26)	Fleischman et al. [9]
M/72	AML M2	45,XY,t(2;3)(p23;q26),−7	Levaltier et al. [3]
M/55	AML	46,XY,t(2;3)(p23;q29),del(7)(q31)	Whang-Peng et al. [4]
F/80	RA	45,XX,t(2;3)(p14;q26),5q−,−18	Mecucci et al. [5]
F/57	RA	46,XX,t(2;3)(p23;q27),del(5)(q22q35),7q−	Yunis et al. [6]
F/64	RAEB	45,XX,t(2;3)(p21;q27),−7	Bitter et al. [7]
F/30	CML (blastic phase)	46,XX,t(9;22)(q34;q11)[3]46,XX,t(2;3)(p13;q26), t(9;22)(q34;q11)[8]	Kwong et al. [8]
M/16	CML (blastic phase)	46,Y,der(X)t(X;9)(p22;q22),t(2;3)(p13;q26), t(9;22)(q34;q11)	Fleischman et al. [9]

11 patients with other myeloid disorders (6 AML cases, 3 MDS, and 2 CML blast phase patients) (Table 1). In the great majority of these reports, t(2;3) appears to be a secondary event, indicative of a poor prognosis. Only three cases of AML M2 showed the translocation as an isolated anomaly. In the other reports, the chromosomal rearrangement was found associated with other chromosomal aberrations, mainly loss and/or deletions of chromosomes 5 and 7 (Table 1), confirming the already mentioned strong association between these rearrangements and 3q26 abnormalities [10–12]. In our case, however, t(2;3) was the sole anomaly but its presence coincided with rapid blastic transformation of myelofibrosis. The same conclusion can be drawn from CML patients where the detection of the t(2p;3q) coincided with rapid conversion to blast crisis [8, 9]. Our observation also confirms previously established correlations between rapid blastic transformation and 3q abnormalities [13, 14]. Other common features of 3q26 aberrations are also encountered, such as an abnormal platelet count and micromegakaryocytes [14]. Finally, our observation further confirms that t(2;3) appears in a pluripotent stem cell, is associated with a poor prognosis, and constitutes a nonrandom chromosomal anomaly associated with myeloid disorders [1–9, 13].

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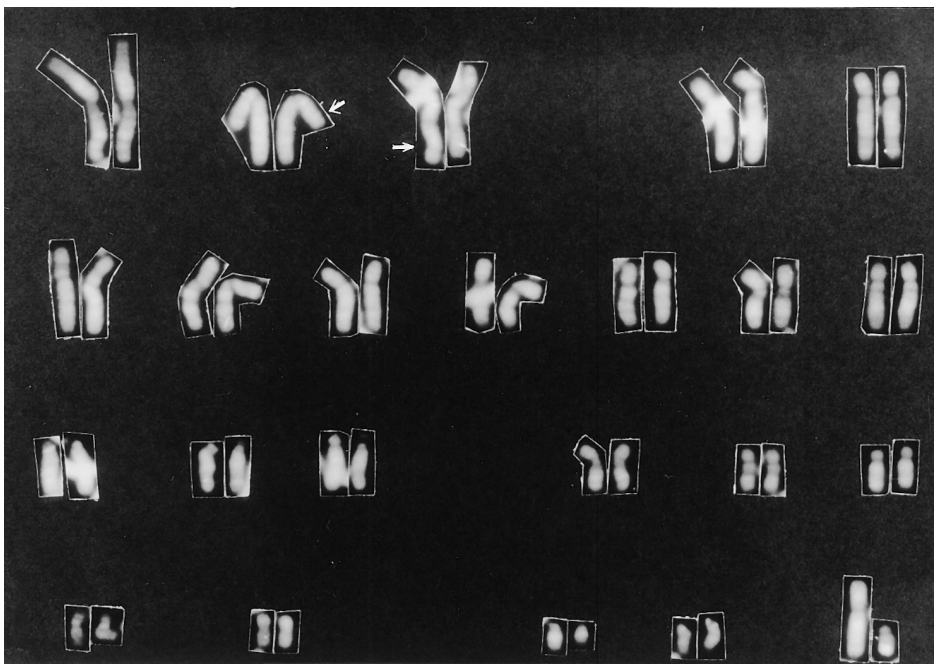
Figure 1 Karyotype of the bone marrow cells at diagnosis. Arrows indicate the abnormal chromosomes.



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