Acquired Philadelphia Chromosome with Transformed Myelodysplastic Syndrome

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Received 14 January 2013; Accepted 15 May 2013

Abstract Transformation to acute myeloid leukemia (AML) frequently occurs in patients with myelodysplastic syndrome (MDS), and genetic evolution probably plays a critical role in this transformation. However, late appearance of the Philadelphia (Ph) chromosome during the course of transformed MDS is extremely rare. We report a 77-year-old man with transformed MDS and an acquired Ph chromosome. He was initially diagnosed with refractory anemia with 45,XY,del(5)(q?),-7,-14,-17,+mar1,+mar2 [7/20] as the major clone. After 4 months, hematological studies showed progression of anemia with increased number of blast cells. Conventional chromosome analysis revealed 45,XY,del(5)(q?),-7,t(9;22)(q34;q11.2),-14,-17,+mar1,+mar2 [20/20], a subclone with an acquired Ph chromosome derived from a stem clone observed at MDS diagnosis. RT-PCR results were positive for major BCR-ABL transcript. Although a comparison of whole-genome sequences between original and transformed clones would be informative, the acquired Ph chromosome probably played a role as a “class-I mutation,” which increases cell proliferation in transformed MDS.

Keywords Philadelphia chromosome; myelodysplastic syndrome; acute myeloid leukemia

1. Introduction

Transformation to acute myeloid leukemia (AML) frequently occurs in patients with myelodysplastic syndrome (MDS), and genetic evolution probably plays a critical role in this transformation [5]. However, late appearance of the Philadelphia (Ph) chromosome during the course of transformed MDS is extremely rare [3]. We report the case of a patient with transformed MDS and a newly acquired Ph chromosome.

2. Case presentation

A 77-year-old man visited our hospital because of general fatigue. Laboratory findings were as follows: hemoglobin (Hb), 8.3 g/dL; mean cell volume (MCV), 85.0 fL; white blood cells (WBCs), 4.5 × 10⁹/L (myelocytes: 1%, band: 2%, segmented neutrophils: 46%, monocytes: 14%, and lymphocytes: 37%); and platelets, 51 × 10⁹/L. Bone marrow film showed slightly hypercellular marrow with 4.6% myeloid blast cells and erythroid dysplasia (Figure 1(a)). He was initially diagnosed with refractory anemia with 45,XY,del(5)(q?),-7,-14,-17,+mar1,+mar2 [7/20] as the major clone. After 4 months, hematological studies showed progression of anemia with increased number of blast cells. Conventional chromosome analysis revealed 45,XY,del(5)(q?),-7,t(9;22)(q34;q11.2),-14,-17,+mar1,+mar2 [20/20], a subclone with an acquired Ph chromosome derived from a stem clone observed at MDS diagnosis. RT-PCR results were positive for major BCR-ABL transcript. The patient was diagnosed with Ph-positive AML. Imatinib was administered as induction therapy against Ph-positive AML. Combination chemotherapies were not administered because of serious medical complications related to acute pneumonia. The patient died of pneumonia 3 weeks...
Figure 1: Bone marrow morphology and G-banding revealed clonal evolution. (a) Bone marrow smear (Wright-Giemsa, 1,000×) showed MDS at diagnosis. (b) Karyotype at MDS diagnosis was 46,XY,del(5)(q?)[1]/45,XY,idem,-7,-14,-17,+mar1,+mar2[7]/45,XY,-5[4]/46,XY[8]. A major abnormal clone is shown in Figure 1(b). (c) Bone marrow smear (Wright-Giemsa, 1,000×) showed AML with multilineage dysplasia upon progression of anemia 4 months after MDS diagnosis. The size of the blast cells ranged from medium to large; they showed a high nuclear:cytoplasmic ratio and visible nucleoli. (d) Karyotypes at diagnosis of transformation to AML was 45,XY,del(5)(q?),-7,t(9;22)(q34;q11.2),-14,-17,+mar1,mar2[20]. The Philadelphia chromosome is marked by an arrowhead.

4. Conclusion
The clinical course and clonal evolution in our patient suggest that an acquired mutation such as Ph chromosome is an important mechanism in the transformation to AML.

References