p53 GENE MUTATION IN THE CHRONIC PHASE WAS NOT DETECTED IN THE MYELOID CRISIS OF A CHRONIC MYELOCYTIC LEUKEMIA CASE

To the Editor:

Although the molecular mechanisms of blast crisis have not been clarified so far, chronic myelocytic leukemia (CML) almost always transforms from a chronic phase (CP) into a more aggressive phase (BC). The p53 gene is well known as a tumor-suppressor gene and its alterations have been reported in various human malignancies. Several reports suggested that the p53 gene alterations may frequently be associated with BC of CML, especially with a myeloid phenotype. It has been documented that the p53 gene alterations are rather less frequent in CP than in BC, and there were very few reports regarding follow-up of the p53 gene alterations at BC in CML cases with the p53 gene alterations in CP.

We reported a case of CML where p53 gene mutation observed in CP was not detected in BC, suggesting that some clones without p53 gene mutation probably evolved into BC. To our knowledge, there were no reported cases similar to this case.
A 27-year-old woman was diagnosed as having Ph'-positive CML in CP with thrombocytosis and mild myelofibrosis. She was treated with natural interferon-α, Ranimustine, or hydroxyurea in CP for about 3 years. Then she was transformed into myeloid crisis, whereas the karyotype was 46,XX,t(9q'::22q-') without additional chromosomal abnormalities. We analyzed p53 gene in samples obtained from the peripheral blood several times through CP to BC by polymerase chain reaction single-strand conformation polymorphism (PCR-SSCP) and subsequent nucleotide direct sequencing. We examined exons 5 through 8 containing evolutionarily highly conserved regions of the p53 gene, in which the majority of alterations of p53 clustered. Although we detected only normal mobility bands in BC, we detected mobility shifts suggesting mutation within exon 6 in CP by PCR-SSCP analysis (Fig 1). Both the aberrant and the normal mobility bands were observed in CP. Sequencing was performed for samples in both CP and BC (Fig 2). In CP, sequencing of exon 6 showed 3-bp insertion between codon 207 and 208, and 2-bp deletion in codon 210. These mutations resulted in formation of a novel stop codon after 5 codons. The wild-type allele was also observed. In BC, sequencing of exon 6 showed no abnormality. This result suggests that the p53 gene mutation may not be responsible for clonal evolution of CML in the present case.

In conclusion, the present case shows a variety of relevance of p53 gene to the progression from CP to BC in CML.

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REFERENCES


p53 gene mutation in the chronic phase was not detected in the myeloid crisis of a chronic myelocytic leukemia case [letter] [see comments]

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