Detection of FLT3 Oncogene Mutations in Acute Myeloid Leukemia Using Conformation Sensitive Gel Electrophoresis

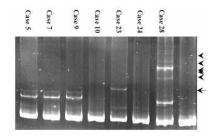
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Abstract: FLT3 (fms-related tyrosine kinase 3) is a receptor tyrosine kinase class III that is expressed on by early hematopoietic progenitor cells and plays an important role in hematopoietic stem cell proliferation, differentiation and survival. FLT3 is also expressed on leukemia blasts in most cases of acute myeloid leukemia (AML). In order to determine the frequency of FLT3 oncogene mutations, we analyzed genomic DNA of adult de novo acute myeloid leukemia (AML). Polymerase chain reaction (PCR) and conformation-sensitive gel electrophoresis (CSGE) were used for FLT3 exons 11, 14, and 15, followed by direct DNA sequencing. Two different types of functionally important FLT 3 mutations have been identified. Those mutations were unique to patients with inv(16), t(15:17) or t(8;21) and comprised fifteen cases with internal tandem duplication (ITD) mutation in the juxtamembrane domain and eleven cases with point mutation (exon 20, Asp835Tyr). The high frequency of the flt3 proto-oncogene mutations in acute myeloid leukemia AML suggests a key role for the receptor function. The association of FLT3 mutations with chromosomal abnormalities invites speculation as to the link between these two changes in the pathogenesis of acute myeloid leukemiaAML. Furthermore, CSGE method has shown to be a rapid and sensitive screening method for detection of nucleotide alteration in FLT3 gene. Finally, this study reports, for the first time in Saudi Arabia, mutations in the human FLT3 gene in acute myeloid leukemia AML patients.

Keywords: AML; Flt3; ITD; CSGE; Mutational analysis



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