

Mutations of FLT3 and CKIT genes in core binding factor with acute myeloid leukemia: IMR experience

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Abstract

Core binding factor (CBF) is a heterodimeric transcription factor made up of two subunits, CBF α (also known as RUNX-1) and CBF β . CBF plays a role in the transcriptional activation of a number of genes required for normal hematopoietic differentiation. CBF acute myeloid leukemia (AML) include 2 major subtypes, respectively associated with translocation t(8;21) (CBF α) and inversion inv(16)/t(16;16) (CBF β), which show a high rate of complete remission (CR) and prolonged CR duration. FLT3 internal tandem duplication (ITD) and D835 mutations is frequently observed aberration associated with poor prognosis in acute myeloid leukaemia (AML). CKIT mutations have been reported in core binding factor (CBF) AML. In CBF AML patients, frequently detected second mutations are FLT3 and c-KIT. This study aims to explore FLT3 and c-kit mutations in patients with acute myeloid leukaemia (AML). In this study, we retrospectively analysed the prevalence of FLT3 and CKIT mutations in 108 AML patients with t(8;21) and inv (16). The bone marrow and peripheral blood samples were extracted using QIAamp DNA MiniPrep Kit. The multiplex RT-PCR assay was performed using FLT3 Mutation Assay (Invivoscribe, USA). CKIT mutation was performed using AmoyDx CKIT Mutation and Human CKIT Gene D816V Mutation Detection Kit and run via Applied Biosystems 7500 Real-time PCR. The frequencies of FLT3-ITD, FLT3-D835, and CKIT mutations were 1.98%, 5.94%, and 14.8%, respectively. Double mutations of CKIT and FLT3-D835 were detected in 3 cases (2.97%). The occurrence rate of FLT3-ITD and CKIT mutations increased in adult with 21.4 % and 15.8% respectively compared to paediatric patients. Notably, the prevalence of FLT3-D835 and double mutations of FLT3-D835 and CKIT were observed only in adults. The frequencies of FLT3-ITD, FLT3-D835, and CKIT mutations in our AML patients are lower compared to other study. This may suggests that mutations of other genes also involve in stimulating proliferation of leukaemia cells. Identification of these mutations are important for prognostication and optimization of patient care.

Keywords: FLT3-ITD; FLT3-D835; CKIT; acute myeloid leukaemia; core binding factor

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