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613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

ETV6-ABL1 Fusion Gene Was Associated with a Poor Prognosis in Patients with Acute Myeloid Leukemia

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Background: Acute myeloid leukemia (AML) is commonly characterized by chromosomal abnormalities that result in the formation of chimeric genes involved in leukemogenesis. ETV6-ABL1-a fusion gene results from a complex rearrangement involving translocation, inversion, or insertion of ETV6 into chromosomal band 9q34 or ABL1 into 12p13. This rare but recurrent genetic aberration is found in AML patients and is associated with a poor prognosis.
Methods:A retrospective review was conducted of three relapsed AML patients with ETV6-ABL1 fusion genes screened by multiplex RT-PCR who were treated at Beijing Lu Daopei Hospital and Hebei Yanda Lu Daopei Hospital between November 2019 and January 2022.
Results: At diagnosis, the median age was 32 years (range 32-42 years), and two patients were male(Pt.2,3). AML subtypes included M2 (Pt.2) and M4 (Pt.1,3), and no patient had a prior history of myeloproliferative neoplasms. Clinical and laboratory characteristics at diagnosis included: hepatosplenomegaly (Pt.3), lymphadenopathy (Pt.1), leukocytosis (median 209.71×10^9/L, range, $60.28\text{-}687.2\times10^9$/L),but no significant eosinophilia($\geq1.5\times10^9$/L). Cytogenetic analyses showed a normal karyotype in all three patients. FLT3-ITD gene mutation was found in two patients(Pt.1,2). All there patients received the same IA regimen(idarubicincytarabine) as induction chemotherapy and achieved complete remission, followed by multi-agent chemotherapy as consolidation treatment.Pt.1 received additional targeted therapy with sorafenib. However, after a median duration of remission (DOR) of 4 months (range 3-8 months), all patients experienced relapse and sought for further therapy at our hospital. Upon re-evaluation by laboratory tests, ETV6-ABL1 fusion gene was detected by multiplex RT-PCR, and additional NUP98-NSD1 fusion was also found in Pt.2. FLT3-ITD gene mutation was confirmed in Pt. 1 and Pt. 2, but the characteristic t(9;12) (q34;p13) chromosomal abnormalities were not present in any of the patients. Pt. 2 presented with an abnormal karyotype of 46, XY, t(3;17)(q12;p11.2),add (10)(q22)[5] / 46,XY[15], while the rest 2 patients had a normal karyotype. Pt.1 died rapidly from serious infection after relapse. Pt. 2 and Pt. 3 received dasatinib-containing combination regimens as salvage therapy and achieved partial remission. Pt. 2 underwent haploidentical allogeneic hematopoietic stem cell transplantation (allo-HSCT) with an enhanced myeloablative conditioning regimen in March 2021, and has maintained molecular remission until now. Pt. 3 is currently undergoing HSCT preparation.
Conclusion: ETV6-ABL1 fusion gene is a rare but recurrent genetic aberration in AML, and its rearrangement is not uniform across eachpatient, typically involving cryptic insertions. Routine chromosome G-banding analysis may not identify this fusion gene, and the combined use of fluorescence in situ hybridization and PCR is recommended for better detection for ETV6-ABL1. Patients with this fusion gene have a high relapse rate and a poor prognosis. Tyrosine kinase inhibitors (eg. Dasatinib)are a reasonable treatment option, and allo-HSCT may be considered for potential cure.

Disclosures No relevant conflicts of interest to declare.

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