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abstract

SETBP-1 mutations favors transformation to AML in PTPN-11 positive JMML

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SETBP-1 mutations favors transformation to AML in PTPN-11 positive JMML

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Introduction: Juvenile myelomonocytic leukemia (JMML) is a rare and aggressive malignancy found in children. The genomic landscape of the JMML shows that the most common mutated genes found in the RAS. The risk stratification and the management of JMML patients are determined by the precise evaluation of the underlying genetic mutations. The co-occurring mutations along with the RAS pathway mutations may affect the outcomes of the disease. PTPN11 is the most common mutation found in JMML. In this study, we describe the outcomes of JMML patients who had an underlying PTPN11 mutation along with a mutation in the SETBP1 gene.

Methodology: DNA was extracted from the 43 cases with JMML after confirmation of the diagnosis. Whole exome sequencing was performed to find out the underlying germline and somatic mutations.

Results: We found that about 35% (n=14) of patients harboured a PTPN11somatic mutation. A coexisting SETBP1mutation was found in 5 patients out of 14 cases.

In our cohort of patients, we found that the SETBP1 was exclusively associated with PTPN11and all 5 patients transformed into AML. The median time to AML transformation was12 months (13 days-35 months). PTPN11 mutation with co-existing SETBP1 mutation showed a worse outcome compared to otherPTPN11 positive patients and all 5 patients died within 3 months of transformation.

Conclusion: In with PTPN11 positive JMML a coexisting SETBP1 mutation confers a poorer prognosis. These patients have a high risk of AML transformation. These patients should be candidates for consideration of early hematopoietic stem cell transplantation (HSCT).