Aberrant Methylation and Impaired Expression of Tumor Suppressor Gene in Chronic Myeloid Leukemia

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Background: CML (chronic myeloid leukemia) is a type of leukemia that starts in the bone marrow. The BCR-ABL fusion oncogene plays a key role in the disease’s pathogenesis. It was translated into the BCR-ABL oncoprotein, which regulates hematopoietic cell development and survival by stimulating a number of signaling pathways. The molecular processes that cause leukemogenesis, on the other hand, are still unclear. The Phosphatase and Tensin Homolog (PTEN) tumor suppressor gene is lost or inactivated in several cancers. Its absence is connected to disease development because BCR-ABL inhibits its production in CML stem cells. PTEN’s role as a tumour suppressor in people with the Philadelphia chromosome, however, is uncertain.

Materials and Method: There were a total of 109 cases for detecting promoter methylation mutations and PTEN gene protein expression. A methylation specific PCR was used to determine the methylation status. Mutations were detected using DNA sequencing, while protein expression was assessed using western blot. Finally, the above data were associated with clinicopathologic characteristics.

Results: Positive hypermethylation was found in a slightly higher percentage of patients (61%) than control samples, and 72 percent of cases showed decrease of protein expression. In 8.3 percent of the cases, new PTEN mutations were discovered. PTEN expression was lost in all mutant cases, and 7/9 instances had positive promoter methylation. Furthermore, 79 percent of the total methylation positive samples showed a reduction of PTEN expression, which was substantially associated (p=0.06).

Conclusion: We discovered that promoter methylation is linked to the decrease of PTEN expression which suggests, PTEN hypermethylation may play a role in the pathogenesis of CML progression and provide crucial prognostic information to improve treatment strategies.

Keywords: PTEN, BCR-ABL, Chronic myeloid leukemia, Hypermethylation, Mutation, Expression