Change of COMT Val158Met Genotype in Tumoral B Cells of a Chronic Lymphocytic Leukemia Patient: A Case Report

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Case Presentation

The venous blood sample was taken from a 64-year-old woman within a regular check-up. The patient had a 7-year history of chronic lymphocytic leukemia (B-CLL; Rai stage I and Binet stage A disease) and her hematological status was stable. As patient did not have any B symptoms, anemia or thrombocytopenia and she did not need any specific treatment according to the current CLL management approaches. Laboratorial findings revealed the white blood cell count (WBC) of 30x10^9/L with lymphocyte count of 25x10^9/L. Phenotype of lymphocytes was determined by NanoDrop 2000C spectrophotometer (Thermo Scientific). Because of the recent increasing interest in possible role of phase II enzymes and their genetic variants in carcinogenesis [8,14-20]. The single nucleotide polymorphism (SNP) G>A (rs4680) leads to an amino acid change of Val to Met from the non-B fraction of peripheral blood mononuclear cells of the patient, could indicate that Val158Met might play some role in the pathogenesis of CLL that certainly needs further investigations. The possible application of this polymorphism as a potential biomarker of CLL is also worth of further large-scale case-control studies.

Keywords: Biomarker; Catechol-O-methyltransferase; Chronic lymphocytic leukemia; O-methylation

Abstract

In this case report, a Chronic lymphocytic leukemia (CLL) female patient with a heterozygous polymorphism in the catechol-O-methyltransferase (COMT) gene is described. This functional change in the COMT enzyme Val158Met leads to a decreased efficacy to O-methylate different endogenous and exogenous compounds containing catechol structure, including hydroxylated estradiol intermediates, catecholamines and certain dietary flavonoids. The specific change found in tumoral B-cells as compared to the genomic DNA from the non-B fraction of peripheral blood mononuclear cells of the patient, could indicate that Val158Met might play some role in the pathogenesis of CLL that certainly needs further investigations. The possible application of this polymorphism as a potential biomarker of CLL is also worth of further large-scale case-control studies.

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Discussion

B-cell chronic lymphocytic leukemia (B-CLL) is the most frequent form of leukemia in adult population of the Western world being characterized by the progressive accumulation of mature non-functional B lymphocytes with dysregulated apoptotic pathways. Current conventional therapies have been focused mostly on controlling of the symptoms rather than curing of patients [2,3]. Also, the metabolism of chronic lymphocytic leukemia cells is still relatively less studied [4,5].

Catechol-O-methyltransferase (COMT, EC 2.1.1.6) is a significant phase II detoxification enzyme that catalyzes O-methylation reaction by relocating a methyl group from S-adenosylmethionine to one of the hydroxyl groups on substrate with catecholic structure [6-11]. This ubiquitous enzyme can be found in almost all mammalian tissues and it has a wide range of substrates, including endogenous catecholamines and catechol estrogens, but also exogenous compounds, such as certain dietary flavonoids [6-8,11,12]. The COMT gene is located on chromosome 22q11.2 and it encodes two different enzyme forms, a 221 amino acid length cytoplasmic protein and a membrane-bound form that contains additional 50 amino acid residues [6,7,13,14]. The most of the COMT occurring in human tissues is cytoplasmic [6,8,10,15,16]. However, COMT enzyme is polymorphic and its activity has significant differences among individuals [8,14-20]. The single nucleotide polymorphism (SNP) G>A (rs4680) leads to an amino acid change of Val to Met in the position 108/158 in cytoplasmic/ membranous enzyme form.
from various solid tumors, there are still no epidemiological studies available about the possible role of COMT variants in the risk of CLL, although a report of Skibola, et al. indicated an increased susceptibility of American women with low activity enzyme variant (Met/Met, AA) toward non-Hodgkin lymphoma [33,34]. We are currently completing a study about the distribution of COMT Val158Met genotypes in the Estonian CLL patients in comparison with the age- and gender-matched population-based controls and the results of this work will be summarized in the near future.

In conclusion, we described in this case report a CLL patient with a functional (heterozygous) polymorphism in the COMT gene in her malignant B cells that can be important in the pathogenesis of CLL. This finding suggests that further studies about the COMT Val158Met as a possible biomarker for CLL are needed to confirm or disprove our hypothesis. Nevertheless, considering that the current treatment options of CLL often do not provide a final deletion of malignant clone, development of novel treatment strategies are of great importance.

References


