Glutathione S transferase theta 1 gene (GSTT1) null genotype is associated with an increased risk for acquired aplastic anemia in children.

Abstract:
Two main factors have been implicated in the mechanism underlying the pathogenesis of acquired aplastic anemia: environmental factors and genetic susceptibility. Individuals vary in their ability to metabolize several DNA-damaging agents due to polymorphisms of biotransforming enzymes. Genetically determined differences in the expression of these enzymes could explain interindividual risks in developing acquired aplastic anemia. The aim of the study was to characterize the genetic polymorphism of biotransforming phase I (p450-cyp2E1) and phase II [microsomal epoxide hydrolase (mEh), glutathione S-transferase (GST)] enzymes in pediatric patients with acquired aplastic anemia. The GSTT1 null genotype (absence of both alleles) was associated with a significantly increased risk for acquired aplastic anemia (odds ratio, 2.8; 95% confidence interval, 0.15-5.7). In contrast, the GSTM1 null genotype or polymorphisms within the p450-cyp2E1 and mEh genes was not significantly different in patients and controls. Multivariate analysis was performed to assess whether the enzymes together or with other variables as age, gender, or response to therapy may have any significant association with the tested genotypes. In no combinations of the mentioned parameters was an association found with acquired aplastic anemia. GST
are mainly involved in metabolizing hematotoxic and mutagenic substrates such as benzene
derivatives. The GSTT1 null genotype may modulate the metabolism of exogenous pollutants or toxic
intermediates. The absence of the GSTT1 enzyme, leading to genetic susceptibility toward certain
pollutants, might determine the individual risk for development of acquired aplastic anemia in children.