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Association of MDR1 gene polymorphism (G2677T) with Imatinib response in Egyptian chronic myeloid leukemia patients

Lamia Ibrahim
Mansoura University, Egypt

Background: Despite the excellent efficacy results of imatinib treatment in CML patients, resistance to imatinib has emerged as a significant problem. Genetic variations in genes involved in drug transportation might influence the pharmacokinetic and metabolism of imatinib. The genotype of a patient is increasingly recognized in influencing the response to the treatment. **Aim:** To investigate the genotype frequencies of single nucleotide polymorphisms (SNPs) G2677T in CML patients undergoing imatinib treatment to determine whether different genotype pattern of these SNPs have any influence in mediating response to imatinib. **Methods:** A total of 96 CML and 90 control samples were analyzed for the human multidrug resistance gene 1 (MDR1) gene polymorphism (G2677T) using polymerase chain reaction-restriction fragment length polymorphism technique. **Results:** Genotype distribution revealed a significant lower frequency of TT genotype in CML patients and non-significant difference in the GG, GT genotype frequencies between patients and controls (P=0.004, 0.138, 0.210, respectively). GG genotype was significantly higher in chronic phase (P=0.046), while GT genotype was significantly higher in Blastic crisis phase (P=0.002). There was a significant difference in genotype frequency of G2677T among patients showing response and resistance to imatinib in chronic phase (P=0.02). TT genotype was associated with complete hematological response (P=0.01), complete cytogenetic response (P<0.001), and better molecular response with a significant association (P<0.001). GT genotype was associated with partial hematological response (P=0.01) and minor cytogenetic response (P<0.001). Optimal and suboptimal responses were observed for patients with TT genotype (P=0.003). Failure of drug response was associated with GT genotype (P=0.02); however, GG had no association with drug response. Multivariate analysis considered GT genotype as independent risk factor for resistance (P=0.037), while TT genotype as protective factor against resistance to imatinib (P= 0.008). **Conclusion:** Determination of MDR1 polymorphisms (G2677T) might be useful in response prediction to therapy with imatinib in patients with CML.

Loomy16@yahoo.com

Meningioma 1 (MN1) expression: Refined risk stratification in acute myeloid leukemia with normal cytogenetics (CN-AML)

Lamiaa Ibrahim
Mansoura Medical School, Egypt

Background: Prognostic stratification of cytogenetic normal acute myeloid leukemia (CN-AML) is an area of active research. **Aim:** The aim of this study was to determine the prognostic importance of the meningioma 1 (MN1) gene expression levels in CN-AML. **Methods:** One hundred patients with CN-AML were diagnosed and MN1 expressions were analyzed using quantitative real-time polymerase chain reaction. **Results:** High expressions were detected in 48 (48%) patients (expression range: 2.35–31.99, mean: 13.9±8.49) in comparison with 52 (52%) patients with low expression (expression range: 0.02–2.3, mean: 0.68±0.77). The course of the disease in patients with high MN1 expression was unfavorable. Patients with high MN1 expression was associated with significant low complete remission rate (62.5 vs. 8.4%, high vs. low MN1, P=0.001) and high mortality rate (75% vs. 46.1, P=0.03). AML patients with high MN1 expression tended to be refractory (37.5 vs. 19.2%, P=0.00) and relapse risk (54.1 vs. 23%, P=0.02). Multivariable analysis confirmed high MN1 expression as an independent risk factor for disease-free survival and overall survival. Conclusion: **MN1 over expression independently predicts bad clinical outcome in CN-AML patients.**

loomy16@yahoo.com