melanoma and other skin tumours

POLYMORPHISMS IN THE APOPTOSIS PATHWAY IN CUTANEOUS MELANOMA: RECURRENCE AND SURVIVAL

C. Oliveira, J.A. Rinck, Jr., G.J. Lourenço, A.M. Moraes, C.S.P. Lima
Department of Internal Medicine, University of Campinas, Campinas, BRAZIL

Aim: Cutaneous melanoma (CM) is notorious for its poor prognosis and resistance to conventional chemotherapy. Genes involved in the apoptosis pathway, such as P53, (tumor suppressor gene), MDM2 (p53 inhibitor), BAX (proapoptotic) and BCL2 (anti-apoptotic) are important for CM growth and survival. The aim of this study was to evaluate whether P53 Arg72Pro, MDM2 T309G, BAX G(-248)A and BCL2 C(-938)A polymorphisms, involved with inherited variations in apoptosis, are associated with relapse free survival (RFS) and overall survival (OS) of CM patients.

Methods: Our analysis included 234 consecutive CM patients at diagnosis seen at our University Hospital from December 1989 to November 2013. Genomic DNA from peripheral blood of patients was analyzed by polymerase chain reaction followed by enzymatic digestion for discrimination of pertinent genotypes. RFS and OS were calculated using the univariate Kaplan-Meier estimate probabilities, and differences between survival curves were analysed by the log-rank test. RFS was defined as the time to beginning of treatment until the date of the first relapse. OS was calculated from date of first diagnosis until the date of death or last follow-up.

Results: The median period of observation of patients in study was 50 months (9-192) for RFS and 58 months (range: 9-285) for OS. We observed at 120 months of segment, that the RFS was higher in patients with BCL2 CC + CA plus MDM2 TT + TG than patients with BCL2 AA plus MDM2 GG genotypes (54% versus 37%, P = 0.01). The OS in CM patients with the BAX GA + AA was higher than in those with the GG genotypes (100% versus 80%, P = 0.01). Moreover, the OS was also higher in patients with BAX GA + AA plus BCL2 CC + CA combined genotype than in those with BAX GG plus BCL2 AA (100% versus 78%, P = 0.02) and BAX GA + AA plus MDM2 TT + TG than BAX GG plus MDM2 GG (100% versus 71%, P = 0.001).

Conclusions: The data suggest, for the first time, that BAX G(-248)A polymorphism may independent or jointly with BCL2 C(-938)A and MDM2 T309G polymorphisms modulate RFS and OS in CM patients. Additional studies will provide some promising guidance for clinical management and tailored or personalized therapeutics in treating for CM.

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