CELLULAR PRION POLYMORPHISMS ASSOCIATION WITH CARDIOTOXICITY SUSCEPTIBILITY TO DOXORUBICIN

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Doxorubicin is applied in cancer treatment but it has a potential cardiotoxic effect that increases mortality and decreases cured patients life quality. Cellular prion protein is highly expressed in myocardium and has a repetitive octapeptide region involved with protection against oxidative stress. This region is a polymorphic site where 10% of the human population has 4 octarepeats and the remaining individuals present 5 octarepeats. Another polymorphism is present at codon 129, which regulates protein function. Since doxorubicin´s cardiotoxicity is dependent on the concentration of free radicals in the myocardial cells, polymorphisms at PrPc could predispose to cardiac damage. We analyzed 172 patients treated with doxorubicin and out of treatment for more than 3 years, by ecodopplercardiography for evaluation of the cardiac function and by DHPLC for the PrP^c gene polymorphisms analysis. Ejection fraction was altered (<55%) in 17.5% of patients and the octarepeat polymorphism was present in 9.3% of them. A significant correlation was found between the presence of the octarepeat deletion associated to the homozygosis for methionine at codon 129 and altered ejection fraction. A higher number of patients need to be evaluated to determine if PrPc gene polymorphisms may be related to the sensitivity to doxorubicin-induced cardiotoxicity.

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