

Influence of the polymorphisms *CASP3* IVS1-15G>T and *CASP8* -652 6N ins/del, associated with apoptosis, in the squamous cells carcinoma oropharyngeal risk

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Abstract

The oropharyngeal (OP) squamous cell carcinoma (SCC) can result from apoptosis abnormality in cells that DNA cannot be repaired. It is known that the ability to promote apoptosis in damaged cells is variable in humans, once polymorphic genes produce many proteins involved in the process. Proteins like *CASP3* and *CASP8* are important in apoptosis. Polymorphisms *CASP3* IVS1-15G>T and *CASP8* -652 6N ins/del are associated to occurrence of different tumors, but their functions in development and clinical-pathological manifestations of OPSCC are unknown. Therefore, the objectives of this study are clearing these points. One hundred ninety four patients with OPSCC and 194 blood donors from HEMOCENTRO of UNICAMP were studied. The genotypes were analyzed by real time polymerase chain reaction in peripheral blood DNA. We observed that the polymorphisms do not change the risk of OPSCC occurrence, but the polymorphism *CASP8* -652 6N ins/del was associated with clinical aspects (sex and skin color) and tumor differentiation grade, in our sample.

Key words: oropharyngeal squamous cell carcinoma, genetic polymorphism, risk

Introduction

It is known that individuals with smoke and drink habits for many years have more susceptibility to development oropharyngeal (OP) squamous cell carcinoma (SCC) (1). The polymorphisms *CASP3* IVS1-15G>T and *CASP8* -652 6N ins/del were associated with risk of occurrence of different tumors (2, 3). The variant alleles of referred polymorphisms were associated with less production of respective proteins (3, 4). The roles of these polymorphisms in OPSCC development, and in the clinical manifestations and in tumor biologic aspects are unknown, which justified our study.

Results and Discussion

The genotypes of 194 patients with OPSCC and 194 controls were performed by real time polymerase chain reaction with DNA from peripheral blood of individuals. The differences between groups were analyzed by chi-square or Fisher's exact tests and by multiple logistic regressions. Similar frequencies of genotypes *CASP3* IVS1-15G>T and *CASP8* -652 6N ins/del were observed in patients and controls. Considering only the patients, the wild-type genotype *CASP8* ins/ins was more common in women than men (80,0% vs. 45,3%; $P= 0,01$). The frequency of the *CASP8* ins/ins or ins/del genotypes was higher in individuals with non-white skin color than white individuals (87,5% vs. 68,5%; $P= 0,03$). In addition, the wild-type genotype *CASP8* ins/ins also was more common in patients with tumor histological grade undifferentiated or poorly differentiated than well

or moderately differentiated tumors (75,0% vs. 40,9%; $P= 0.003$).

Conclusions

Our results suggest that the *CASP8* -652 6N ins/del polymorphism is an important inherited factor to identify groups of patients that deserved periodic medical attention for OPSCC treatment.

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