Human Leukocytes Antigen Association with Brain Astrocytic Tumors Detected by Genomic DNA Typing

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Background: Malignant astrocytomas are the most common brain tumors in adults with an increased incidence of glioblastoma multiform particularly in older age groups. Human Leukocyte Antigen (HLA)is a human immuno genetic marker and its loss is considered important for tumor growth, metastasis, and may allow tumor to escape immunosurvilliance. It is known that HLA alleles control a variety of immune functions and influence the susceptibility to more than 40 diseases including brain astrocytomas.
Aim: This study is designed to investigate the association between HLA alleles and development of malignant brain astrocytomas.

Study Design: Blood and tumor biopsies from eighty-three malignant astrocytomas grades II-IV were taken from each patient to be used for HLA-genotyping by PCR-Sequence Specific Priming (PCR-SSP). Data was analyzed using several statistical tests, odds ratio (OR), relative risk (RR) and Corrected Cumulative Risk Value (CCRV) to calculate allelic combinations of high risk, predisposing and neutrals allele groups. Confidence Interval was performed for normal sample distribution, Hardy Weinberg Equilibrium and Chi-square test for expected probability and significance. Wilcoxon Rank test and means were used for comparison with median values and for calculation of standard errors respectively.

Results: The results showed that there is a significant association between HLA-A alleles and brain astrocytomas (high risk group of alleles). This association was markedly decreased in patients by 6 folds (frequency in patients 60% and in control 93%, OR=5.07,p<0.01). A consistent association between HLA-B alleles and brain astrocytomas was also observed (frequency in patients 93% and in controls 70%, OR=4.24,p<0.01). HLA-DRB loci showed a significant decrease in the frequencies of high risk group alleles (frequency in patients 53% and in controls 93%, OR=8.76,p<0.01). The HLA-A, B, DRB1 risk group alleles was striking in certain HLA combinations such as HLA-A*03012 which was in linkage disequilibrium with HLA- B*3804 contributing to increased risk of brain astrocytomas (CCRV= 15.34).

Conclusion: Results indicates that the loss of single HLA-A,-B, and -DRB1 alleles and/or their combinations and estimated haplotypes showed strong association with the susceptibility (HLA-B) or protection (HLA-A) to brain astrocytomas. The results may suggest that some single HLA alleles or combination are associated with a significant increased risk for brain astrocytomas.