

HLA- DRB Genotyping of Brain Astrocytomas among Iraqi Patients

Nidhal Abdul mohymen PhD, Amara Hadi PhD.

Abstract

Background: The major histocompatibility complex (MHC) refers to as human leukocyte antigen (HLA). The loss of HLA antigens by neoplastic cells is considerably important for tumor growth and metastasis and expression of certain certain HLA alleles may predispose to have certain types of tumors.

Objective: To investigate the genetic susceptibility of HLA-DRB1, DRB3, DRB4 and. DRB5 alleles to brain astrocytomas in Iraqi patients.

Methods: HLA-DRB1, DRB3, DRB4 and, DRB5 allele polymorphisms were typed by polymerase chain- reaction with sequence-specific primers (PCR-SSP) in 30 unrelated patients astrocytomas and 17 unrelated normal control subjects. The association was measured by appropriate statistical tests.

Results: Allele frequency (AF) of HLA-DRB1*10011 and DRB1*10012 was

significantly decreased in brain astrocytomas patients than that in normal controls (0.53 vs 0.93) the odds ratio 8.76). There was no association between patients and controls in the rested HLA-DRB1 alleles.

Conclusion: HLA-DRB1*10011 and DRB1*10012 alleles were less common in the patients with brain astrocytomas than in the healthy controls. Individuals carrying HLA-DRB1* 10011 and DRB1*10012 alleles might be considered as protective markers. These protective alleles; might have a role in the degree of malignancy of the tumors and its histological type.

Keywords: PCR-SSP, brain astrocytomas, HLA-DRB

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Introduction

Astrocytic tumors comprise a wide range of neoplasms that differ in their location within the central nervous system (CNS). The majority of tumors had either heterogeneous or positive expression of HLA class I heavy chain (HLA-HC), and β 2 microglobulin⁽¹⁾. The loss of HLA antigens by neoplastic cells is considered important for tumor growth and metastasis⁽²⁻⁴⁾. Since tumor neoantigens on the surface of aberrant cells are recognized by T-cells only in the context of the HLA "self" antigens, loss of the HLA antigens may allow the tumor to escape immunosurveillance⁽⁵⁾. Defects in the expression and/or function of the human leukocyte antigen (HLA) class I antigen-processing machinery (APM) components are found in many tumor types.

These abnormalities may have a negative impact on the interactions of tumor cells with host's immune system and on the outcome of T cell-based immunotherapy⁽⁶⁾. The alleles of the HLA system controls a variety of immune functions and influence the susceptibility to more than 40 diseases, many of which have an autoimmune components^(7,8). Association of a particular HLA allele with a disease implies that the frequency of the allele is different in the patient population as compared with that of matched control population. A study done by (Angelica et al. 2005)⁽⁹⁾ showed that HLA class I antigens were lost in 50% of glioblastoma multiforme (GBM) lesions and in 20% of grade 2 astrocytoma lesions. Selective HLA-A2 antigen loss was observed in 80% of the GBM lesions and in 50% of grade 2 astrocytoma lesions stained. HLA class I antigen loss was correlated with tumor grade. HLA class II antigen expression was detected in 30% of the 44 lesions analyzed. HLA-Dr expressed by brain tumor cells selectively inhibit CD8 subset which participates in immunoreaction against brain tumors in

Dept. of Medical Microbiology. College of Medicine, Al-Nahrain University.

Address Correspondences to: Nidhal Abdul mohymen ,

Email: drinidhalmohammed@yahoo.com

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