

The possible Association of HLA Class II with Bladder Cancer in Iraqi Patients

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Summary:

Fac Med Baghdad
2007; Vol.49, No.4
Received July 2006
Accepted Jun.2007

Background: - Genetic Factors have a major role in the development of bladder cancer.

Objectives: - This study was carried out to shed a light on the possible association of HLA class II antigens and BC patients and to correlate this finding with the family history.

Patients and Methodes :- Lymphocytotoxicity assay had been used to assess HLA-typing of 65 BC patients and 50 healthy controls.

Results:- comparison between BC patients and healthy controls showed several antigens deviations in their frequencies. HLA-DR1, HLA-DQ1 and HLA-DQ3 antigens were observed with increased frequencies in patients group with significant differences (P=0.000, 0.000 and 0.017 respectively). Moreover there was decrease frequency of HLA-DR7 in patients group (P=0.010). Stastical analysis showed non significant correlation of the specific HLA –Ags with family history.

Conclusions: - This finding demonstrated that HLA-DR1, DR7, DQ1 and DQ3 might play a role in BC susceptibility.

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Key Words :- Bladder Cancer BC, Human Leukocyte Antigen HLA.

Introduction:

Bladder cancer is a disease in which the lining of the urinary bladder lose the ability to regulate their growth and start dividing uncontrollably, this abnormal growth will form a tumor (1). It is a disease largely affecting the late middle and elderly ages population , also it is possible to be detected in young ages or even in children , More than 70 % of diagnosed new cases found in patients aged 65 years and above (2,3).

Crallan and associates (4) mentioned that BC was considered in USA? While ACS, 2004 (5) reported that BC is the 4th most commonly

diagnosed malignancy in USA men and the 10th in USA women.

In Iraq, according to ICR, 2000 (6) BC is the 3rd most common tumor (6.6 %) in both men and women , but individually it was reported to be 10.3% as the 2nd most common tumor in men and 3.0 % as the 8th most common in women.

Bladder cancer as with other cancers, the exact causes are still mysterious. Though accumulative knowledge showed that genetical and environmental factors had an important role in this disease development (7, 8, and 9).

Accordingly to several observations, attention has been brought to the belief that genetics factors have a major role in bladder cancer, since certain alterations shown to cause mutation that may prevent the protective mechanisms of certain proteins (10, 11).

The genetic factors importance of this disease currently based on the increased risk of cancer in relatives with the BC patient. Frequencies alteration of specific HLA-antigens have been showed in patients with bladder cancer in different areas as suggested by (12) that positive association with the antigen DR4 was reported in English Caucasoid patients . While another study reported by (13) revealed an increased frequency of HLA-DQ3 and lack any association at DR loci in Iranian patients. While the result reported by Saunders and associates that no significant alteration in DR antigens were observed in Caucasian patients (14).

Patients and Methods:-

Patients:-

The present study included 65 Arab Iraqi BC patients (21 female and 44 male) with male predominance ratio of (2.6%). The age incidence range between 37-85 years with mean age of 61 ± 11 years. The histopathological grades are shown clearly in table – 1, Compared with 50 healthy age sex matched control group.

HLA-typing:-

Microlymphocytotoxicity assay has been applied for HLA-typing as described by Terasaki and McClelland (15) and modified by Dick et al., and Bender (16, 17).

Statistical Analysis:-

Univariate analysis has been applied for the date depending on logistic regression and the results were reported as odd ratio (ORs), which represented the increased or decreased risk for BC.

Results:

A total of 65 Iraqi Arab patients with BC were typed for HLA-class II (DR&DQ) antigens. The frequency distribution of various class II HLA-Ags for the studied groups are presented in tables (2, 3). Comparison between

BC patients and healthy controls showed several antigens deviations in their frequencies for instance HLA-DR1, HLA-DQ1 and HLA-DQ3 antigens were observed with increased frequencies in patients group (60,67.7,50.8 % respectively) , Versus healthy controls (8,26,24% respectively). With p-value of (0.000, 0.000 and 0.017 respectively).while there was significant decreased frequency of HLA-DR7 in patients (0%) versus healthy control (20%) with p-value=0.010.

Regarding the correlation between the specific HLA-Ags (DR1, DR7, DQ1 and DQ3) and patient's family history, this study found a correlation between HLA-DQ1 and BC patients with positive family history (Inverse OR-2.1) though statistically not significant, as shown in table (4).

Discussion:-

In our work, there was a significant association of HLA-DR1 with BC patients (P=0.000) as compared with healthy group. This result is in agreement with that of (15), but it is at variance with some other (13, 14).

Regarding the presence of HLA-DQ Ag and its proposed association with BC , our study revealed an increased frequency of HLA-DQ1 and HLA-DQ3 was statistically significant in BC patients (p=0.000,0.0017 respectively). Compared to control group. This result is in agreement with that of (14), but there was no significant with HLA-Dr.

Interestingly, the present study failed to demonstrate a significant association of these specific HLA-Ags (DR1, DR7, DQ1 and DQ3) with family history. This might be in part, result from the limited number of investigated patients.

Table – 1:- The histopathological grading of BC. Patients.

Grade	N	%
Grade I	19	29.2
Grade II	21	32.3
Grade III	25	38.5
Total	65	100

Table – 2:- Antigen Frequency of the HLA-DR (% , OR, inverse OR, P, adjusted P, EF, PF) of the BC patients and healthy control

HLA-Ags	Healthy control		Bladder Cancer Cases		OR	Inverse OR	P	Adjusted P	EF	PF
	N	%	N	%						
HLA-DR										
1	4	8	39	60	17.3		0	0	0.565	
2	9	18	6	9.2	0.5	2.2	NS			0.096
3	12	24	22	33.8	1.6		NS		0.129	
4	19	38	28	43.1	1.2		NS		0.082	
5	2	4	0	0	0.1	6.8	NS			
6	1	2	0	0	0.3	4	NS			
7	10	20	0	0	0	34	0.001	0.01		
8	3	6	12	18.5	3.5		NS		0.133	
10	5	10	1	1.5	0.1	7.1	NS			0.084
11	4	8	0	0	0.1	12.7	0.022	NS		
14	2	4	5	7.7	2		NS		0.039	
DR-blank	29	58	17	26.2						
DR-double blank	0	0	0	0						
Total	50	100	65	100						

Table – 3 : Antigen frequency of the HLA-DQ (% ,OR, Inverse OR,P,adjusted p, EF,PF) of the BC patients and healthy control

HLA-Ags	Healthy control		Bladder Cancer Cases		OR	Inverse OR	P	Adjusted P	EF	PF
	N	%	N	%						
HLA-DQ										
1	13	26	44	67.7	6		0	0	0.563	
2	11	22	20	30.8	1.6		NS		0.113	
3	12	24	33	50.8	3.3		0	0.017	0.352	
4	8	16	4	6.2	0.3	2.9	NS			
DQ-blank	44	88	29	44.6						
Total	50	100	65	100						

Table – 5 :- Antigen frequency of the specific HLA-Ags in BC patients according to family history

HLA-Ags	Family history Bladder Cancer				OR	Inverse OR	P
	Negative		Positive				
	N	%	N	%			
HLA-DR1							
Negative	20		6				
Positive	27	57.4	12	66.7	1.5		NS
HLA-DQ1							
Negative	13		8				
Positive	34	72.3	10	55.6	0.5	2.1	NS
HLA-DQ3							
Negative	23		9				
Positive	24	51.1	9	50	1	1	NS

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