HLA-DR and DQ Antigens in Iraqi Patients with Behçet's Disease

Dr. Ikbal Kh. AL-Joofy*. Ph.D.
Dr. Raad AL-Muslih*. Ph.D.
Dr. Khalida M. AL-Mousawy.** Ph.D.
Dr. Mokaram M.AL- Waiz.** Ph.D.
Dr. Amera Jabir Omar*** M.Sc.

Summary:

Background: *Behçet's disease (BD) is a multisystemic in inflammatory disorder, disease onset is believed to be triggered by many factors with a particular genetic background. The aim of this study is to investigate the possible correlation between HLA-DR & DQ antigens and onset of this mysterious disease.*
Method: *By using microlymphocytoxicity test, the frequencies of 18 HLA-DR & DQ antigens were calculated in 65 patient with BD compared with 32 patients control with recurrent oral ulcers (ROU) & 115 healthy control.*
Results: *Significant increased trend of HLA-DR52, DR53 and DQ3 antigens ($P<0.001$), and significant reduced frequencies of DQ4 antigen ($P<0.01$) in patient with BD as compared to H.C. group, on the other hand significant decreased DR1 antigen in patient with BD ($P<0.005$) as compared with patients with ROU.*
Conclusion: *Higher frequency of DR52, DR53 & DQ3, these alleles could in one way or another play a crucial role in susceptibility to BD. Whereas DR1 DQ4 phenotypes decrease the risk to develop, this disease.*
Key words: *Behçet's disease, HLA- typing HLA-DR and DQ.*

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Introduction

Behçets disease is a multisystemic inflammatory disorder characterized by oral ophthae, ocular & skin lesions, genital ulceration, and occasional involvement of other tissues and organs including joints and the central nervous system[1,2,3].

Although its etiology and pathogenesis remain mysterious, disease onset is believed to be triggered by the involvement of some external factors in individuals with a particular genetic background[3,4]. Oral ulceration are common to all types of BD, it is difficult to predict the clinical courses of BD based on oral ulcers only, and to differentiate from this disease. Clinical manifestations, in a sense, that this common oral disease with multifactorial etiology[5,6] could be considered as one end of the spectrum of wide clinical manifestation of BD.

* *Al-Mustansiriyah University, College of Science*
** *University of Baghdad, College of Medicine.*
*** *Forensic Medicine Institute.*

Several investigators demonstrated strong association of HLA-DR2, DR4, DR5, DR7 and DRW9 in patients with ROU, and DRw3, DRw8, DQ3, DR7, DRw52 and DQ3 in patients with BD[7,8,9,10].

To investigate the possible correlation between HLA-DR & DQ antigens in Iraqi patients with BD, the frequencies of 18 HLA-DR & DQ antigens were calculated and compared with those in patients control with ROU and those in HC, in order to asses a possible genetic basis of the disease susceptibility.

Subject & Methods

The study compares 3 groups.

1. Patients group

Sixty five patients (21F, 44M) who fulfilled the international study group (ISG) criteria(2) for diagnosis of Behçet's disease, who were attending the multidiscipline Behçet's disease clinic. From July 1999-Feb. 2001 were included in this study.

2. Patients control group

Age, sex, and ethnicity matched patients control (N=32) with only ROU were included.

3. Healthy control group

Healthy subjects who have no history or clinical evidence of BD or any chronic disease and obvious abnormalities were selected as HC. (staff and students of college of science and from blood bank donors).

Method

All subject were tested for HLA class II antigens (HLA-DR!, DR2,DR3,DR4, DR5,DRW6,DRW7,DRW8,DRW10, DRW11,DRW12,DRW14,and HLA DRW52, DR53, in addition to HLA DQW1, DQW2, DQW3, DQW4). (Biotest, Germany).

HLADR and DQ typing were performed on nylon-wool separated B cells using complement dependent microlymphocytotoxicity test that was established by Terasaki (1964) and modified furtherly by Dick et al., (1979) and Bender (1984)(11), result were considered to be positive if 80% or more of lymphocytes were killed.

Statistical analysis

The association between HLA antigens and the disease was evaluated in terms of relative risk (RR) and eitiological fraction (EF), Svejgaard et al., (1983). While the statistical differences were assessed by Chi-square test with Yate's correction (X2y).

Results

The prevalence of HLA-DR & DQ antigens in Iraqi patients with BD and in H.C. subjects is shown in Tab.1, an increased trend of DR52, DR53, and DQ3 antigens ($P<0.001$), (X2y=36.42, RR=13.75, EF=0.40), (X2y=25.78, RR=9.95, EF=0.32), (X2y=12.88, RR=3.30, EF=0.45) respectively. Tab.1.

Significant decreased ($P<0.001$) in DQ4 antigen in patients with BD as compared with HC. (X2y=7.84, RR=0.24) Tab.1.

On the other hand significant decreased ($P<0.005$) of DR1 in patient with BD as compared with patient control group (ROU); (X2y=8.40, RR=1.92, EF=0.20) Tab.2.

Discussion

In this study a significant increased ($P<0.001$) trend of HLA DR52, DR53 and DQ3 antigens, and significant decreased ($P<0.01$) of DQ4 antigen in Iraqi patients with BD as compared with HC. Tab.1, and significant decreased ($P<0.005$) of DR1 in BD as compared with ROU Tab.2, which is the first time to be reported in Iraq since many studies have been carried out in this field abroad. Association between HLA-B5 (subtype B51) with BD has been proved by investigators in a few countries (12,13,14). However different results of association between HLA class II antigens and BD are reported, this association can be found in British, (DR7), Japanese (DR52, DQ3) south Korrean (DR3, DR8) and Italian (DR7)(7,14,15).

The HLA antigens are essential for immune recognition by T-lymphocytes which are only able to bind to antigens when are associated with those molecules. The different classes of HLA antigens are involved in the restriction of different T-cell types or subsets.

T-lymphocytes subsets perform different function but the division is not absolute, one thing that they have in common is that they recognize, through their T-cell receptor complex (CD3, CD4 or CD8, TCR), CD4 positive cells produced molecules, lymphokins that stimulate & support the production of immune system cells(16).

The possession by an individual of a number of different MHC class I & II molecules probably ensures that at least one of the molecules will able to bind a peptide produced from an infectious agent, HLA-DR1 positively may confer resistance against onset of BD(17). The polymorphisim will protect the species since it is likely that at least some members of the species will be able to respond to a particular pathogen(18).

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Table 1: Frequencies of HLA-DR and DQ antigens in Iraqi patients with Behçet's Disease and in healthy control subjects

Antigens	Patients with BD (N=65)		Healthy control (N=115)		X^2_y	P	RR	EF
	No.	%	No.	%				
HLA-DR1	27	41.5	31	26.96	3.40	N.S.	1.92	0.20
DR2	26	40	32	27.83	2.89	N.S.	1.73	0.17
DR3	18	27.7	28	24.34	-	N.S.	-	-
DR4	16	24.6	30	26.10	-	N.S.	-	-
DR5	5	7.7	9	7.83	-	N.S.	-	-
DR6	8	12.3	11	9.57	-	N.S.	-	-
DR7	16	24.6	31	26.96	-	N.S.	-	-
DR8	11	16.9	10	8.69	-	N.S.	-	-
DR10	8	12.3	2	1.74	-	N.S.	-	-
DR11	5	7.7	8	6.96	-	N.S.	-	-
DR12	8	12.3	1	0.87	-	N.S.	-	-
DR14	14	21.5	9	7.83	5.83	<0.025	3.2	0.15
DR52	28	43	6	5.22	36.42	<0.001	13.75	0.40
DR53	23	35.4	6	5.22	25.78	<0.01	9.95	0.32
Blank	2	3.1	13	11.3	-	N.S.	-	-
HLA-DQ1	35	53.9	55	47.83	-	N.S.	-	-
DQ2	30	46.2	62	53.91	-	N.S.	-	-
DQ3	42	64.6	41	35.65	12.88	<0.001	3.30	0.45
DQ4	5	7.7	30	26.10	7.84	<0.01	0.24	-
Blank	24	36.9	50	43.5	-	N.S.	-	-

N.S. = not significant, RR= relative risk
X^2_y= Chi-square with Yate's correction
EF=Etiological Fraction, P= Probability

Table 2: Comparisons in frequencies of HLA-DR and DQ antigens between patients with Behçet's Disease and patient control subjects

Antigens	Patients with BD (N=65)		Healthy control (N=32)		X^2_y	P	RR	EF
	No.	%	No.	%				
HLA-DR1	27	41.5	31	27.0	8.40	<0.005	1.92	0.20
DR2	26	40	12	37.5	-	N.S.	-	-
DR3	18	27.7	4	12.5	-	N.S.	-	-
DR4	16	24.6	3	9.4	-	N.S.	-	-
DR5	5	7.7	6	18.8	-	N.S.	-	-
DR6	8	12.3	0.0	0.0	-	N.S.	-	-
DR7	16	24.6	9	28.1	-	N.S.	-	-
DR8	11	16.9	7	21.9	-	N.S.	-	-
DR10	8	12.3	8	25	-	N.S.	-	-
DR11	5	7.7	4	12.5	-	N.S.	-	-
DR12	8	12.3	7	21.9	-	N.S.	-	-
DR14	14	21.5	8	25	-	N.S.	-	-
DR52	28	43	17	53.1	-	N.S.	-	-
DR53	23	35.4	10	31.3	-	N.S.	-	-
Blank	2	3.1	3	9.4	-	N.S.	-	-
HLA-DQ1	35	53.9	18	56.3	-	N.S.	-	-
DQ2	30	46.2	8	25	-	N.S.	-	-
DQ3	42	64.6	17	53.1	-	N.S.	-	-
DQ4	5	7.7	1	3.1	-	N.S.	-	-
Blank	24	36.9	18	56.3	-	N.S.	-	-

N.S. = not significant, RR= relative risk
X^2_y= Chi-square with Yate's correction
EF=Etiological Fraction, P= Probability