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SHORT COMMUNICATION

New insights into HLA class I association to Behçet's syndrome in Iranian Azari patients

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Abstract Behçet's syndrome (BS) is a chronic recurrent inflammatory disorder characterized by oral and genital ulcers and ocular inflammation. BS has a complex genetic etiology. To evaluate the influence of human leukocyte antigen (HLA) class I in BS susceptibility in Iranian Azari population, we studied 290 BS patients and 300 healthy controls. As expected, a high frequency of HLA-B5 was found. Remarkably, HLA-B35 frequency was higher in the patient than control group, and the frequency of HLA-B51, HLA-B52, and HLA-BW4 was significantly elevated. Thus, HLA-B5 and HLA-B35 seem to confer susceptibility to BD in Iranian Azari patients.

Keywords HLA antigens · Behçet's syndrome · HLA typing

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Introduction

Behçet's syndrome (BS) is a chronic inflammation disease characterized by recurrent oral and genital ulcers, relapsing uveitis, mucocutaneous, articular, neurologic, urogenital, vascular, intestinal, and pulmonary manifestations [1]. BS has been reported worldwide, but has a peculiar geographic distribution with the highest prevalence in countries along the ancient silk route [2]. Etiology and pathogenesis are unclear but it probably occurs because of environmental trigger in genetically susceptible subjects [3].

The role of human leukocyte antigen (HLA) has been the focus of extensive research in BS. It is associated with the B51 subtype of HLA-B5 gene, especially the B*5101 allele and has been confirmed in many ethnic groups [4]. The primary purpose of this study was to investigate the importance of HLA-B5, B51, and B52 in the genetic susceptibility to BS in an Iranian Azari population but association with other HLA class I was also analyzed.

Patients and methods

In a retrospective cohort (case–control) study, 290 Iranian Azari patients with BS (61.2 % male, 38.8 % female), aged between 16 and 87 years (average: 34.39 ± 1.1 years), were chosen from outpatient of Imam Reza Medical Research andTraining Hospital, Tabriz, Iran by referral from requests to rheumatologists during a period of 4 years (from January 2009 through July 2012). The study was conducted observing the ethical guidelines approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran.

The diagnosis of Behçet's syndrome was based on the criteria of the International Study Group Criteria (ISG)

Table 1 Clinical manifestations in 290 patients with Behçet's syndrome

Clinical manifestations	Positive (%)
Oral ulcer	100
Genital ulcer	64.0
Skin lesion	72.4
CNS disease	10.6
Ocular disease Uveitis	52.9
Gastrointestinal disease	21.1
Arthritis	20.6

Results are given as percentage of positive patients

(Table 1). Briefly, this required the presence of recurrent oral ulceration along with two of the following: recurrent genital ulceration, eye lesion (anterior or posterior uveitis), skin lesions (erythema nodosum, pseudofolliculitis, or papulopustular lesions), and a positive pathergy test [3]. Patients with incomplete disease were excluded from study and HLA typing was performed on patients of Iranian Azeri origin. The control group consisted of 300 healthy individuals. All relevant clinical manifestations that developed since the onset of BS were recorded on a standard form.

Peripheral blood lymphocytes were separated on a Ficoll–Hypaque density gradient. HLA tissue typing was performed by the standard two stages National Institute of Health micro-lymphocytotoxicity technique. The unrelated normal controls group consisted of 300 healthy voluntary blood donors to the Blood Transfusion, of whom all had HLA-A and HLA-B typing. Comparisons of HLA frequencies between patients and controls were performed using the Pearson Chi-squared test, with continuity correction, or the Fisher's exact test when appropriate.

Results

No statistically significant differences were found in HLA-A frequencies between patients and controls. In contrast, HLA-B5 was found in 61.9 % of the patients compared to 1.3 % of controls; [Odds Ratio (OR) = 123.350 with CI: 20.961–1412.123, $p < 0.001$]. HLA-B35 was represented among Iranian Azeri patients with BS, being found in 65.4 % of the patients compared to 21.5 % of controls (OR = 6.901 with CI: 3.514–13.666, $p < 0.005$). An increased frequency was observed for HLA-B51 (OR = 15.048 with CI: 5.168–47.597, $p < 0.001$) in the BS group compared to the control group. We also observed an increased frequency of HLA-B52 (OR = 20.490 with CI: 6.099–79.267, $p < 0.001$) and HLA-CW4 (OR = 2.309 with CI: 1.202–4.454, exact p value = 0.007), in patients with BS compared with controls.

Discussion

The purpose of this study was to examine the association between HLA susceptibility and BS in Iranian Azari patients. Indeed, HLA association with BS in Iranian Azari patients presents some specific characteristics. HLA-B35 was present in 65.4 % of patients (no other data are available in other ethnic groups). However, the predisposing effect of HLA-B5, B51, and B52 in our patients was the same as that observed in patients of the other ethnic group origin [5, 6]. More unexpected was our observation of a predisposing effect of HLA-BW4 for the disease. Instead, HLA-B7 (OR = 0.813 with CI: 0.347–1.901, exact p value = 0.512) (13.5 vs. 16.1 %) and B27 (OR = 0.510 with CI: 0.202–1.265, exact p value = 0.095) (9.7 vs. 17.4 %) were negatively associated with the disease in contrast to other ethnic groups [7, 8]. To the best of our knowledge, this is the first report on genetic background in Iranian Azari Behçet patients showing a significantly increased frequency of HLA-B5, HLA-B35, HLA-51, HLA-B52, and HLA-BW4. Our findings showed that there is no association between HLA-B7, HLA-B27 and Iranian Azari patient in comparison with other ethnic groups.

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Conflict of interest Fatemeh Zare Shahneh, Fatemeh Hamzavi, Babak Bayazi, Ali Bandehagh and Behzad Baradaran declare that they have no conflict of interest.

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