IFNAR1 and IFNAR2 polymorphisms in patients with Behçet's disease

Sirs,

Behçet's disease (BD) is an idiopathic systemic inflammatory disease characterized by a T helper 1 (Th 1) polarization. We and others have reported that patients with BD have higher levels of interferon (IFN)-alpha compared to healthy control subjects (1, 2), while human recombinant IFN-alpha2a has been successfully used in the treatment of Behçet's patients for a long time (3). Interferon alpha receptor (IFNAR) is consisted of two receptor chains, IFNAR1 and IFNAR2 which are encoded by two different genes located on chromosome 21q (4). Up to now, several polymorphisms involving both IFNAR1 and IFNAR2 have been identified and shown to be related with the predisposition to some infectious diseases (6-8). Two of these polymorphisms induce amino acid substitutions in the mature proteins [IFNAR1 (G/C in SNP 18417) and IFNAR2 (G/T in SNP 11876)] and are disclosed to confer susceptibility to multiple sclerosis characterized Th1 polarization (9).

The aim of this study was to investigate the role of two polymorphisms in the IFNAR1 (G/C in SNP 18417) and IFNAR2 (G/T in SNP 11876) genes in BD susceptibility in a group of 118 patients (median age 23 years; range 13 years; 94 male, 24 female) and 96 controls (median age 23 years; range 20 years; 78 male, 18 female). Real-Time Polymerase Chain Reaction (Real-time PCR) was used for this purpose. Comparisons of the allele, genotype and genotype combination of patients and healthy controls were performed by using Chi-Square test or Fisher's exact test, which was appropriated. The consistency of the genotype frequencies with the Hardy-Weinberg equilibrium was also determined. The calculations of odds Ratios (OR) together with their confidence intervals (CI) were performed by using a calculator, which is available at the website: http://www.hutchon.net/ConfidORselect.htm. A *p*-value of <0.05 was considered as indicating a significant difference.

There was no association between BD patients and healthy controls with regard to allelic frequencies and genotypic distributions (Table I). However, as compared with healthy controls, BD patients had significantly higher frequencies of the -18417GG/-11876GG and -18417CC/-11876GT genotype combinations (15.2% *vs*. 6.3%, OR=2.696, 95% CI=1.009 to 7.206, *p*=0.041 and 7.6% *vs*. 1.0%, OR=7.835, 95% CI=0.961 to 63.858, p=0.037) (Table II). We did not find any association between BD patients with mucocutaneous and systemic involvement (ocular, articular, vascular or neurologic), and healthy controls by means of allelic frequencies, genotypic distributions, and genotype combinations. Our results indicate that Turkish BD patients have higher frequency of some genotypic combinations of IFNAR1 (G/C in SNP 18417) and IFNAR2 (G/T in SNP 11876) polymorphisms compared with healthy control subjects. We concluded that IFNAR1 (G/C in SNP 18417) and IFNAR2 (G/T in SNP 11876) polymorphisms jointly, but not individually, may confer susceptibility to BD in Turkish population. In the light of the above mentioned findings of the present study, we suggest that polymorphisms relating either IFNAR1 (G/C in SNP 18417) or IFNAR2 (G/T in SNP 11876) might be involved in the pathogenesis of BD either by increasing the susceptibility to infections or elevated IFN-alpha levels for which is responsible for the Th1 type polarisation.

Table I. Genotype and allele distribution of the IFNAR1 and IFNAR2 polymorphisms in patients with Behçet's disease and healthy controls.

Polymorphisms	Patients no. (%)*	Controls no. (%)*	χ^2	*p*	OR	95% CI
IFNAR1-18417						
Genotypes						
GC	42 (35.6)	35 (37.6)	0.094	0.760	0.915	0.521-1.609
CC	9 (7.6)	3 (3.2)	1.878	0.171	2.477	0.651-9.423
GG	67 (56.8)	55 (59.1)	0.119	0.730	0.907	0.523-1.574
Alleles						
G	176 (74.6)	145 (78.0)	0.653	0.419	0.829	0.526-1.305
C	60 (25.4)	41 (22.0)				
IFNAR2-11876						
Genotypes						
GT	47 (41.6)	48 (50.0)	1.480	0.224	0.712	0.411-1.231
TT	45 (39.8)	38 (39.6)	0.001	0.972	1.010	0.579-1.761
GG	21 (18.6)	10 (10.4)	2.741	0.098	1.963	0.874-4.405
Alleles						
G	89 (39.4)	68 (35.4)	0.695	0.404	1.184	0.795-1.764
T	137 (60.6)	124 (64.4)				

*no. values of patients and controls are 118 *vs*. 93 and 113 *vs*. 96, respectively, for IFNAR1-18417 and IFNAR2-11876 polymorphisms.

Table II. Genotype combination distribution of IFNAR1 18417 and IFNAR2 11876 polymorphisms in patients with Behçet's disease and healthy controls.

Polymorphisms 18417–11876	Patients no. (%)*	Controls no. (%)*	χ^2	*p*	OR	95% CI
GG/TT	22 (21.0)	17 (17.7)	0.337	0.561	1.231	0.609-2.490
GG/GT	25 (23.8)	33 (34.4)	2.727	0.099	0.596	0.322-1.104
GG/GG	16 (15.2)	6 (6.3)	4.156	0.041	2.696	1.009-7.206
GC/TT	17 (16.2)	16 (16.7)	0.008	0.927	0.965	0.457-2.038
GC/GT	12 (11.4)	19 (19.8)	2.689	0.101	0.522	0.238-1.144
GC/GG	3 (2.9)	2 (2.1)	0.124	0.725	1.382	0.226-8.455
CC/TT	–	2 (2.1)	2.209	0.137	0	0-NaN
CC/GT	8 (7.6)	1 (1.0)	5.072	0.037	7.835	0.961-63.858
CC/GG	2 (1.9)	–	1.847	0.174	∞	NaN-∞

*The calculations of frequency of genotype combinations were performed in 105 patients and 96 controls.

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