Short Communication

Fcγ Receptor Ila Polymorphism in Patients with Brucellosis

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(Received January 9, 2007. Accepted February 28, 2007)

SUMMARY: Recent evidence suggests that certain Fc gamma receptor (FcγR) alleles are genetic risk factors for infectious diseases. In this study, we evaluated FcγRIIa polymorphism in patients with brucellosis. In a case-control study, the frequency of two alleles and three genotypes for FcγRIIa were measured by PCR in 150 patients with brucellosis and 125 healthy controls. The H131 and R131 alleles were found in 133 (44.3%) and 167 patients (47.6%), respectively. The frequencies for the three genotypes (a/a, a/r, r/r) were 10 (6.7%), 113 (75.3%) and 27 (18%), respectively. There was no significant difference in the distribution of FcγRIIa genotypes and the two allelic forms between the patients and controls. Our study indicates that FcγRIIa polymorphism is not decisive for the acquisition of brucellosis.

Our knowledge of the role of human FC receptors for IgG (FcγR) has increased considerably in the last several years. These receptors vary in their affinity for IgG, their preferences for IgG subclasses, their cell-type-specific expression patterns, and the intracellular signals that they elicit. Additional FcγR heterogeneity is introduced by the presence of phagocyte biologic activity, providing a basis for inherited predisposition to disease (1). FcγRII (CD32) represents the widely expressed class of FcγR, encoded by three genes (FcγRIIa, Iib, and Iic). The FcγRIIa molecule occurs in two codominantly expressed allelic forms, Ia-R131 and H131. The Ia-H131 genotype exhibits a higher ability to bind complexed IgG2 and IgG3 (2). Several studies have identified polymorphisms of FcγRIIa as genetic factors for autoimmune disorders and certain infectious diseases (3-5).

Brucellosis is one of the most common zoonotic infectious diseases and has a wide spectrum of clinical presentations, from a subclinical to an acute or relapsing chronic illness. These variations could be, in part, due to the genetic factors affecting host immunity. Genetic studies in various animals have shown that resistance to intracellular pathogens is polygenic; however, single genes are recognized to have a major effect on immune-mediated resistance (6). Natural resistance to Brucella infection has been reported in swine and cattle, and macrophages from innately resistant cattle were better able to control the intracellular replication of B. abortus (7). To date, there are no published studies on FcγRIIa polymorphism in brucellosis. The purpose of this study was to determine the relationship between polymorphism of FcγRIIa and the acquisition of brucellosis.

The study was performed at Sina Hospital, Hamedan, Iran. We prospectively studied 150 consecutive patients with brucellosis who had been referred to the outpatient department or the infectious diseases unit of the hospital during a 10-month period, between June 1, 2004 and March 30, 2005. Demographic and clinical data were obtained for these patients. The diagnosis of brucellosis was based on clinical suspicion along with one of the following criteria: (i) isolation of Brucella from blood, bone marrow, or other tissues; (ii) a positive standard tube agglutination test (serum antibody titer of 1:160 or higher); and (iii) positive brucella enzyme-linked immunosorbent assay (ELISA). We also selected 125 sex-matched healthy persons from the patients’ families as a control group. Demographic information on these healthy participants was obtained. All subjects were evaluated for coexisting disorders and interfering factors, and patients with known autoimmune diseases, myocardial infarction, diabetes mellitus, chronic obstructive pulmonary disease, and those with a history of surgery or acute infections other than brucellosis in the preceding 4 weeks were excluded from the study. The study protocol was approved by Hamedan University of Medical Sciences, and informed consent was obtained from all participants; this study conforming to the provisions of the declaration of Helsinki. For each individual enrolled in the study, a sample of venous blood was collected in EDTA. DNA was extracted from the blood by the salt-out technique and stored at a final concentration of 200 μg/ml until genotyping (8). FcγRIIa genotyping was performed for all patients and controls by the polymerase chain reaction (PCR)-based allotyping method with allele-specific primers (PCR ARMS method) (9). Data analysis involved the Fishertest, which was performed using the statistical software SPSS version 11, and P ≤ 0.05 was considered statistically significant.

During the study period, a total of 150 patients with brucellosis were included. Ninety were males and 60 were females. The controls included 125 healthy subjects (67 males and 58 females). No significant differences were observed in the demographic characteristics of patients and controls. The most common symptoms and signs of brucellosis were fever (72.5%), sweating (73.2%), arthralgia (69.9%), low back pain (69.4%), myalgia (57.7%), headache (42.2%), weight loss (28.6%), arthritis (12.3%), depression (6.8%), and delirium (2%). The frequencies of the H131 and R131 alleles and genotypes of FcγRIIa are shown in Table 1. No significant differences were seen in the frequency of the two alleles between the subjects with brucellosis and the controls (44.3 versus 47.6% for H131 and 55.7 versus 52.4% for R131, respectively). Similarly, the distribution of the FcγRIIa genotypes was not significantly different between the patients and the controls. Thus, we concluded that there is no association.

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between polymorphism of FcRIIa and susceptibility to brucellosis. Several studies have recently been carried out by our coworkers to determine the influence of genetic polymorphism of immunologic molecules on the susceptibility to brucellosis. The findings suggest that genetic polymorphisms in Toll-like receptor-4, L-selectin, interleukin-4 promoter, interleukin-1 receptor antagonist, transforming growth factor-beta 1, and the promoter region of the CD14 gene may each contribute to the development of brucellosis (10-15).

Our information on immunity to brucellosis and the role of FCγRIIa in infectious diseases enhances our theory of an existing relationship between FCγRIIa and brucellosis. FCγRIIa is expressed on the surface of lymphocytes and monocyte/macrophages, and the molecule provides an important link between humoral and cellular immune systems (16). Nevertheless, our study indicates that FCγRIIa polymorphism is not decisive in the acquisition of brucellosis in the Iranian population. Thus, further studies are needed to determine the role of other receptors for IgG in brucellosis.

REFERENCES

### Table 1. FcγRIIa allele and genotype frequencies in brucellosis patients and controls

<table>
<thead>
<tr>
<th>FcγRIIa polymorphism</th>
<th>Brucellosis (n = 150)</th>
<th>Controls (n = 125)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Allele</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H131</td>
<td>133 (44.3)</td>
<td>119 (47.6)</td>
<td>NS</td>
</tr>
<tr>
<td>R131</td>
<td>167 (55.7)</td>
<td>131 (52.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Genotype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a/a</td>
<td>10 (6.7)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>a/r</td>
<td>113 (75.3)</td>
<td>119 (95.2)</td>
<td>NS</td>
</tr>
<tr>
<td>r/r</td>
<td>27 (18)</td>
<td>6 (4.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, no significant.

Today, 14, 215-221.