Streptococcal infection distinguishes different types of psoriasis

P Weisenseel, B Laumbacher, P Besgen, D Ludolph-Hauser, T Herzinger, M Roecken, R Wank, J C Prinz

In order to define this predisposition better, we correlated the incidence of streptococcal infection, HLA class I antigens, family history, and age of onset in patients with chronic plaque psoriasis. Results were compared to the incidence of infection with Staphylococcus aureus that may worsen psoriasis.  

**METHODS**

HLA class I typing was performed serologically for 42 specificities (14 A, 20 B, 8 C) in 96 white patients with non-pustular chronic plaque psoriasis; there were 26 females and 70 males (mean age 48 (SD 16) years, mean duration of psoriasis 15 (SD 13) years, mean age of onset 33 (SD 18) years).

Evidence of microbial infection was assessed by nasopharyngeal swabbing and standard methods of bacteria isolation and determination of anti-streptolysin-O (ASLO) and anti-desoxyribonuclease B (ADNase-B) serum antibody titres (normal range <200 IU/ml each) resp. anti-staphylolysin titre (ASTA, normal range <2 IU/ml).

Psoriasis patients were classified according to the following definitions. Type I psoriasis: early onset (<40 years of age) and/or positive family history and/or inheritance of HLA-Cw6, -B57, or -B13. Type II psoriasis: late onset (>40 years), lack of positive family history, and lack of predisposing HLA antigens.  

Additionally, subtyping was carried out according to age of onset and HLA pattern as suggested by Szczerkowska-Dobosz et al.: type Ia/Ib, early/late onset psoriasis without the predisposing HLA antigens Cw6, B57, or B13: type Ib/Ib, early/late onset with typical psoriatic HLA antigens. The type Ia patients are identical to the type II patients classified according to Henseler and Christophers, while subgroups IIa, Ib, and IIb correspond to type I patients.

**RESULTS**

HLA typing showed a significantly increased frequency of HLA-Cw6, -B57, and -B13 in psoriasis patients compared to 367 healthy controls (p<0.001 each), confirming earlier

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**Table 1** Streptococcal and staphylococcal infection parameters in type I and II psoriasis and four psoriasis subtypes

<table>
<thead>
<tr>
<th></th>
<th>Psoriasis type (No of patients/% of total)</th>
<th>Subtypes (No of patients/% of total)</th>
<th>HLA-Cw6/-B57/-B13 (No of patients/% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type I</td>
<td>Type II</td>
<td>Ia</td>
</tr>
<tr>
<td>Total number of subjects</td>
<td>82</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASLO/ADNase-B titre &gt;200 IU and/or nasopharyngeal swabbing positive</td>
<td>32 (39%)</td>
<td>0 (0%)†</td>
<td>9 (29%)†</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASTA titre &gt;2 IU and/or nasopharyngeal swabbing positive</td>
<td>33 (40%)</td>
<td>4 (29%)</td>
<td>13 (42%)</td>
</tr>
</tbody>
</table>

* p=0.004 type I vs type II. † p=0.04 type Ia vs Ila. ‡ p=0.002 type Ib vs Ila. § p=0.006 type Iib vs Ila (two tailed Fisher’s exact test each). ¶ p=0.01 HLA positive v negative (chi-square test).
findings. Evidence of group A streptococcal infection was found exclusively in type I psoriasis patients (table 1). The difference compared to type II patients was significant (p=0.004). A dominant role of HLA antigens over the age of onset in predisposing to streptococcal infection was suggested when psoriasis subtypes were considered. Irrespective of the age of disease onset, psoriasis patients with the typical HLA antigens showed a similar prevalence of streptococcal infection (type Ib 45%, type Ib 46%), whereas signs of streptococcal infection appeared to be slightly less frequent in type Ia patients with early onset but lacking HLA-Cw6, -B57, and -B13 (29%), and they were completely missing in type IIa patients (p=0.002 type Ib vs IIa, p=0.006 type Ib vs IIa, p=0.04 type Ia vs IIa, table 1). In contrast, assessed parameters for Staphylococcus aureus (table 1) did not differ significantly between types I and II or type Ia/b and type IIa/b patients.

**Discussion**

In distinct ethnic subgroups, susceptibility to rheumatic fever has been shown to depend on the prevalence of particular HLA class I or class II alleles, resulting in a pathological immune response pattern to streptococcal antigens. The HLA class of psoriasis as a disease involving autoreactive T cells but not antibodies is thought to involve mainly HLA class I, with HLA-Cw6, -B57, and -B13 conferring the highest risk. HLA-Cw6 shows strong linkage disequilibrium with -B57 and -B13.

A former study had suggested that HLA-B13 may predispose to severe streptococcal infection. Furthermore, decreased ASLO titres had been observed in HLA-B13 positive psoriasis patients. At the time of these studies, neither HLA-Cw6 nor the psoriasis subtypes had been identified. We failed to detect significant differences in streptococcal infection when comparing patients carrying HLA-Cw6 either alone or together with -B57 and/or -B13.

In a control group of 19 healthy subjects expressing HLA-Cw6, -B57, or -B13, only two subjects showed serological evidence of streptococcal infection. This incidence of streptococcal infection was significantly lower than in type I psoriasis patients (p=0.029) or in type Ib (p=0.016) and Ib patients (p=0.038), while it did not differ significantly from psoriasis patients lacking HLA-Cw6, -B57, or -B13 (type Ia p=0.17, type IIa p=0.49) (p value determined by two tailed Fisher’s exact test). Therefore, we speculate that the predisposition to streptococcal infection in type I psoriasis is preferentially linked with HLA-Cw6 but may involve a genetic trait other than HLA-Cw6 itself. This is supported by the observation that although Cw6 confers the highest risk for psoriasis, only ~10% of Cw6 positive subjects actually develop psoriasis.

Collectively, our findings clearly show that susceptibility to streptococcal infection distinguishes two clinically and genetically defined types of psoriasis. They furthermore indicate that psoriasis patients expressing HLA-Cw6, -B57, or -B13 show a significantly higher incidence of streptococcal infection parameters, implying distinct inherited immune response patterns to streptococcal antigens as a key to understanding psoriasis pathogenesis. Accordingly, type I psoriasis as the subtype related to streptococcal infection may serve as a model disease to elucidate the mysterious pathomechanisms of post-streptococcal disorders in general.

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**Authors’ affiliations**

P Weisenseel, P Besgen, D Ludolph-Hauser, T Herzinger, M Roecken, J C Prinz, Department of Dermatology, University of Munich, Frauenlobstrasse 9-11, D-80337 Munich, Germany

B Laumbacher, R Wank, Institute for Immunology, University of Munich, Munich, Germany

Correspondence to: Professor J C Prinz, Department of Dermatology, University of Munich, Frauenlobstrasse 9-11, D-80337 Munich, Germany; joerg.prinz@lrz.uni-muenchen.de

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