

# Frequency of streptococcal upper respiratory tract infections and HLA-Cw\*06 allele in 70 patients with guttate psoriasis from northern Poland

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## Abstract

**Introduction:** The association of guttate psoriasis with a streptococcal throat infection and HLA-Cw\*06 allele is well established in different populations. Nevertheless, only few studies on this form of disease have been performed in the Polish population.

**Aim:** To analyze the frequencies of streptococcal-induced guttate psoriasis and HLA-Cw\*06 allele in 70 patients with guttate psoriasis originating from northern Poland.

**Material and methods:** Seventy patients with guttate psoriasis and 24 healthy volunteers were enrolled into the study. Both groups were sex- and age-matched. The evidence of streptococcal infection was based on the positive throat swabs and/or elevated ASO titers. The modified method, including PCR-SSP and PCR-RFLP, was applied to HLA-Cw\*06 genotyping.

**Results:** HLA-Cw\*06 allele was confirmed in 49 (70%) out of 70 patients, which is significantly higher than in the control population (30%) ( $p = 0.001$ ). Evidence for streptococcal infection was found in 34 (48.5%) subjects with psoriasis. Twenty-seven of them (79%) carried HLA-Cw\*06 allele. In 36 individuals in whom no evidence of streptococcal infection was found, 14 (39%) did not carry HLA-Cw\*06 allele.

**Conclusions:** Our data confirm that HLA-Cw\*06 is a major, but not imperative, genetic determinant for guttate psoriasis.

**Key words:** guttate psoriasis, human leukocyte antigen, HLA-Cw\*06, *streptococcus pyogenes*.

## Introduction

Guttate psoriasis is a rare clinical presentation of the disease affecting approximately 2% of all psoriatics. The course of the disease is acute, manifesting as an eruption of small papules disseminated on the trunk and limbs. The disease is usually preceded by a throat streptococcal infection, so a role of bacterial superantigens in the pathogenesis of this variant of psoriasis has been postulated [1].

Linkage and association studies strongly suggest that HLA-Cw\*06 is the major genetic determinant in psoriasis.

This allele significantly confers the risk of guttate psoriasis [2, 3].

Up to date, only few reports of guttate psoriasis have been published, including one study which has been performed in the population from northern Poland [4–8].

## Aim

The aim of the presented study was to analyze the frequency of upper respiratory tract infections caused by *Streptococcus pyogenes* and HLA-Cw\*06 allele status in patients with guttate psoriasis.

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## Material and methods

### Study group

Seventy unrelated patients aged 6 to 77 (mean age: 28.5 years) were enrolled to the analysis (43 females and 27 males). Details of the personal and family history of psoriasis were collected from all the patients (Table 1).

Fifty-two (74%) patients have declared the relationship between an upper respiratory tract infection, which preceded guttate psoriasis for mean 21 days and eruption of guttate psoriasis. Eighteen (26%) of patients were treated with oral antistreptococcal antibiotics prescribed by the physician (mean time of the treatment  $\pm$  10 days).

Diagnosis of the streptococcal upper respiratory tract infection was based on the positive culturing for *Streptococcus pyogenes* and/or increased antistreptolysin O titer in the blood sample.

### Control group

Twenty four healthy (14 women and 10 men; mean age: 33.3 years), unrelated volunteers were enrolled into the study. Based on the physical examination, personal and family negative history of psoriasis, the disease was excluded in all controls.

The study was approved by the Local Bioethics Committee for Scientific Researches, Medical University of Gdansk, Poland. Written consent to participation in the study was obtained.

### HLA-Cw\*06 genotyping

HLA-Cw\*06 typing was performed in the study and the control group. Biological material for genetic analysis was obtained from the epithelium of the mucous membranes of the mouth or peripheral blood. The modified method, including PCR – SSP (sequence specific primers)

and PCR – RFLP (restriction fragment length polymorphism), was applied [9].

Genomic DNA was extracted either from 0.5 ml samples of peripheral blood by modified non-enzymatic method by Lahiri and Nurnberger [10] or from oral epithelial swabs with the use of ‘Sherlock AX’ set. The purity and concentration of DNA were determined in a spectrophotometer (NanoDrop® ND-1000).

HLA-Cw\*06 molecular typing was performed in three stages. In the first stage PCR with sequence-specific primers (PCR-SSP) was used to specifically amplify HLA-Cw\*06.

In the second stage, all Cw\*06-positive samples underwent PCR and restriction fragment length polymorphism analysis (PCR-RFLP) for detection of patients heterozygous for this allele. The 618-bp PCR product was cleaved into fragments of 348, 196 and 74 bp for homozygotes, whereas for heterozygotes, an additional product of 270 bp was seen.

As a final step, samples homozygous for Cw\*06 were screened for nonspecific digestion by PCR-SSP using a degenerated reverse primer specific for Cw\*07 and Cw\*18, under identical conditions to those in the first stage PCR-SSP analysis. All genotypes were visualized by silver staining after separation in 13% polyacrylamide gels.

### Bacteriology

To detect  $\beta$ -hemolytic group A streptococci, the biological material from oral mucosa was placed on the culture medium and incubated in 35–37°C for 24 h. The bacterial colonies which gave complete hemolysis were Gram-stained to search Gram-positive bacteria. For final *Streptococcus pyogenes* differentiation from *Staphylococcus aureus*, the 3% H<sub>2</sub>O<sub>2</sub> test was performed – *Streptococcus pyogenes* gave a negative reaction and *Staphylococcus aureus* – positive.

The evaluation of ASO titers in 70 patients was performed with the use of Quantia ASO reagents and ARCHITECT®, Abbott.

### Statistical analysis

Fischer’s exact test was applied. Value of  $p < 0.05$  was considered statistically significant.

### Results

HLA-Cw\*06 allele was detected in 49 (70%) patients, which is significantly higher than in the control population ( $n = 7, 30%$ ) ( $p = 0.001$ ).

The laboratory evidence of the streptococcal upper respiratory tract infection was found in 34 of the 70 (48.5%) patients. The elevated titer of ASO ( $> 200$  IU/ml) was observed in 30 individuals and the obtained values were between 270 and 1450 IU/ml (the average titer 214 IU/ml). *Streptococcus pyogenes* was isolated from the throat in 9 (26%) of 34 patients.

**Table 1.** Epidemiological data obtained from all the subjects from the study group

Parameter	Number of cases (%)
Age [years]:	
< 40	56 (80)
> 40	14 (20)
Gender:	
Male	27 (38.6)
Female	43 (61.4)
First clinical manifestation of psoriasis:	
Guttate psoriasis	34 (48.5)
Plaque psoriasis	36 (21.5)
Recent upper respiratory tract infection (anamnesis):	
Yes	18 (26)
No	52 (74)

Twenty-seven out of 34 patients with streptococcal induced psoriasis (79%) carried HLA-Cw\*06 allele. Among 36 subjects in whom no evidence of streptococcal infection was found, 22 (61%) were HLA-Cw\*06 positive and 14 (39%) were HLA-Cw\*06 negative (Table 2).

## Discussion

Clinical observations suggest a strong correlation between streptococcal upper respiratory tract infections and guttate psoriasis, however this relationship has not been confirmed in 100% of affected individuals [4–6, 11–15].

Recent epidemiological studies have confirmed that the incidence of psoriasis strongly correlates with geographical distribution and mortality due to systemic streptococcal infections observed during the global epidemics, what may emphasize the role of superantigens in the pathogenesis of the disease [16].

The occurrence of streptococcal-induced guttate psoriasis varies in different cohorts (58%, 62%, 88%, 93% and 97%) [4–6, 12–15].

The aim of the presented study was to analyze the frequency of throat streptococcal infections in patients with guttate psoriasis from northern Poland. In the study group, an upper respiratory tract infection preceding the guttate eruption has been self-reported by most of individuals. However, the evidence of confirmed streptococcal infection was confirmed in approximately 50% of patients.

A relatively low incidence of laboratory proved streptococcal infections is in concordance with the results of Fry *et al.* and Mallbris *et al.* who reported streptococcal throat infection in 56% and 55% of patients, respectively [6, 12].

The low incidence of *Streptococcus pyogenes* in our population does not rule out its role in the pathogenesis of guttate psoriasis. The values may differ depending on when the examination was performed in relation to the disease onset (7 weeks in our group). The high percentage of negative results of microbiological investigations in our study group could have been also caused by the treatment with oral antibiotics which were used by 25% of patients.

It is suggested that streptococcal organisms may be capable of becoming intracellular in the epithelial cells of the tonsils and being a persistent source of superantigens [6, 17]. This mechanism may impair streptococci identification.

There have been only few reports considering the frequency of HLA-Cw\*06 allele in patients with guttate psoriasis. The results of recent analyses have confirmed the incidence of HLA-Cw\*06 in 73%, 74%, 86% and 100% of patients with guttate psoriasis [4, 6, 13, 18, 19].

The high frequencies of HLA-Cw\*06 in all reported populations may confirm the special role of this molecule in the pathogenesis of guttate psoriasis. Most of the au-

**Table 2.** HLA-Cw\*06 allele incidence in correlation with *Streptococcus pyogenes* throat infection

<i>Streptococcus pyogenes</i> bacteriological status	Total	HLA-Cw*06 +	HLA-Cw*06 –
<i>Streptococcus pyogenes</i> (+)	34	27 (79%)	7 (21%)
<i>Streptococcus pyogenes</i> (–)	36	22 (61%)	14 (39%)

thors postulate the role of HLA-Cw\*06 in the induction of guttate psoriasis provoked by streptococcal infection [9]. It has been proved that HLA-Cw\*06 molecule is involved in the presentation of bacterial antigens (streptococcal M protein) and autoantigens (keratin 17) to lymphocyte T (subpopulation CD8+) [20, 21]. Skin homing lymphocytes from individuals HLA-Cw\*06 positive with active psoriasis have a stronger response to keratin 17 and streptococcal M protein than T cells derived from patients HLA-Cw\*06 negative.

Up to date only one study on incidence of HLA-Cw\*06 allele in patients with guttate psoriasis has been performed in the population of northern Poland [8].

The frequency of HLA-Cw\*06 allele in the present study group was 70% vs. 30% in controls ( $p = 0.001$ ). Seven out of 34 (21%) patients with streptococcal induced guttate psoriasis did not carry HLA-Cw\*06 allele, which is concordant with other studies [6, 13].

## Conclusions

Our data confirm that HLA-Cw\*06 is a high, but not imperative, risk factor for streptococcal induced guttate psoriasis.

## Conflict of interest

The authors declare no conflict of interest.

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