Original article

Family history of psoriasis and recent infectious disease are risk factors for the first episode of acute guttate psoriasis

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Abstract

Background Psoriasis is a heterogeneous disease in its clinical expression. Both genetic and environmental factors are thought to contribute to the pathogenesis. The association of guttate psoriasis with streptococcal pharyngitis is well accepted. The association of other risk factors is less well-defined.

Objectives The aim of this study was to estimate the risk for guttate psoriasis with recent infections and to explore other potential risk factors like family history of psoriasis.

Patients and methods This was a case-control study. Cases were patients with the first diagnosis ever of acute guttate psoriasis. Controls were patients newly diagnosed as having dermatologic conditions other than psoriasis and seen in the same outpatient services as the cases. Inclusion of cases and controls was restricted to patients up to 18 years of age. A total 35 cases (median age, 8 years) and 150 controls (median age, 12½ years) were included in the analysis.

Results A significant difference was observed for a family history of psoriasis. 45.7% of patients with guttate psoriasis gave a family history of psoriasis in their first-degree relatives. The risk of psoriasis was also increased in subjects who reported a history of a recent infectious episode. The analysis by individual diagnosis pointed to acute pharyngitis as the disease with the strongest association. Twenty-seven patients (77.1%) gave a history of sore throat preceding the onset of guttate psoriasis. All of them had a throat swab performed, of these 20 had normal flora cultured. Only 6 had a positive culture and in these cases Lancefield group C ß-hemolytic streptococci were isolated. ASO titer was raised in 21 (60%) patients of guttate psoriasis.

Conclusion The study confirmed that recent pharyngeal infection is a risk factor for guttate psoriasis. It also documented the strong association between guttate psoriasis and a family history of psoriasis

Key words Guttate psoriasis, streptococcal pharyngitis, ASO titer

Introduction

Psoriasis is a chronic scaly and inflammatory skin disorder, the pathogenesis of which remains elusive, but genetic and environmental factors are thought to contribute. The disease process comprises immune-mediated cutaneous inflammation and keratinocyte hyperproliferation, and many biochemical and immunological abnormalities have been identified.[1] Psoriasis is a heterogeneous disease and various clinical subtypes can be differentiated. Guttate psoriasis is characterized by the eruption of small erythematous and scaling lesions over large areas of the skin surface 1-2

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weeks after an episode of acute tonsillitis or pharyngitis.[2] It represents a manifestation of psoriasis of an early age at onset and as such is more frequent than other varieties in children and young adults. It may arise on its own (acute guttate psoriasis) or may complicate existing, often quite limited, chronic plaque psoriasis (guttate flare of chronic plaque psoriasis). If left untreated, guttate psoriasis may clear spontaneously or may develop into chronic plaque psoriasis. It may recur, although the risk is not well-defined.[3] Acute guttate psoriasis is associated with infections by *Streptococcus pyogenes*, and cross-reaction between skin and streptococcal antigens have been reported.

The role of superantigens in the pathogenesis of psoriasis is a well-established and attractive hypothesis.[4] Superantigens include viral and bacterial proteins that can stimulate T-cells to proliferate without prior intracellular processing by an antigen-presenting cell.

The aim of our case-control study was to provide a quantitative estimate of the risk for guttate psoriasis associated a recent streptococcal throat infection.

Patients and methods

Our case-control study was conducted at dermatology department, Rawalpindi General Hospital, Rawalpindi, from Dec. 2002 to Dec. 2003.

Entry criteria for cases were the first ever diagnosis of acute guttate psoriasis with no previous diagnosis of psoriasis. Guttate psoriasis was defined as the abrupt appearance of drop-like, round or oval orange-brown asymptomatic papules covered with scales and scattered over the body. Controls were patients who were diagnosed for the first time in their life as having dermatologic conditions other than psoriasis. They were recruited in the same outpatient services. Inclusion of cases and controls was restricted to patients up to 18 years of age. A standardized interview was used to assess the disease onset in cases and controls. A total 35 cases of guttate psoriasis, satisfying entry criteria, and 150 controls were recruited.

Information about family history of psoriasis in blood relatives (siblings and parents), and personal medical history was obtained from cases and controls using an identical structured questionnaire. Information on any infectious disease requiring at least one medical attendance during the three months before diagnosis was collected in cases and controls. Detailed history regarding sore throat was recorded, throat swabs were taken in relevant patients and ASO titre was determined in all cases and controls. Anthropometric measures including height and weight were also obtained.

Results

The patients with guttate psoriasis consisted of 23 female (65.7%) and 12 male (34.3%) subjects. The control population consisted of 90 (60%) female and 60 (40%) male subjects. The median age at diagnosis was 8 years in cases and 12½ years in controls. The distribution of cases and controls did not show any substantial differences in the distribution of gender.

In 20 (57.1%) cases, lesions of guttate psoriasis were combined with classic plaque psoriasis. Diagnosis in the control group comprised the following: eczema 40 (26.7%), urticaria 30 (20%), scabies 50

Table 1 Demographic data of study population ad controls

	Cases	*Controls*
Age (years)		
<5	6	30
5-10	14	70
10-18	15	50
Sex (male/female)	12/23	60/90
Family history of psoriasis (parents/siblings)		
No	19	130
Yes	16	20
Recent infectious disease		
No	8	125
Yes	27	25
ASO titre		
>200 IU ml^{-1}	21	10
<200 IU ml^{-1}	14	140

(33.3%), superficial mycosis 20 (13.3%) and acne 10 (6.7%). The distribution of cases and controls according to age, sex, family history of first degree relatives and history of previous and concomitant infection is presented in **Table 1**.

A significant difference was observed for a family history of psoriasis. 16 cases (45.7%) had a family history of psoriasis whereas only 20 of the control patients (13.3%) had a family history of psoriasis. The risk of psoriasis was also increased in subjects who reported a history of a recent infectious episode. The analysis by individual diagnosis pointed to acute pharyngitis as the disease with the strongest association. Twenty-seven (77.1%) patients gave a history of sore throat preceding the onset of guttate psoriasis. All of them had a throat swab performed, of these 20 had normal flora cultured. Only 6 had a positive culture and in these cases Lancefield group C ß-hemolytic streptococci were isolated. ASO titer was raised in 21 patients (60%), while it was raised in only 10 of 150 controls (6.66%). The clinical features of cases studied are given in **Table 2**.

Discussion

This study provides the evidence that guttate psoriasis, in subjects without a previous diagnosis of psoriasis is strongly associated with a family history of psoriasis. This is in accordance with previous studies.[5, 6] To avoid recall bias in the reporting of a family history of psoriasis, the study was restricted to newly diagnosed cases and controls. It is likely that genetic factors are involved. Familial cases of guttate psoriasis have been described[5,7] and a highly significant association with HLA-Bw17 has been reported in guttate as well as in plaque psoriasis.[8] Moreover, HLA-B13 has been linked to a history of severe streptococcal infection in these patients.[9] A long held belief supported by fairly convincing clinical immunologic evidence associates guttate psoriasis with acute infection, particularly from *S. pyogenes*.[10,11] Our study suggests that recent pharyngeal infection is associated with an increase in the risk for the first episode of guttate compared with subjects not reporting such a history, as 27 out of 35 patients (77.1%) gave the history sore throat within preceding three months, the infectious agent responsible found out to be *S. pyogenes*. In studies relying on bacteriologic culture, *S. pyogenes* has been isolated in a far higher proportion of guttate psoriasis patients ranging from 20% to 97%.[12] Group A streptococci are thought to be responsible for majority of cases of streptococcal-induced pharyngitis, but strains of other serogroups, especially groups D and G, may occasionally be involved.[13] Confirmation of streptococcal infection in guttate psoriasis may be difficult because patients are often seen in the convalescent phase when antibiotics have already been prescribed[2] and throat swab cultures are more likely to be

Table 2 Clinical features of guttate psoriasis

Subject	*Age (years)*	*Sex*	*Family History*	*History of sore throat*	*Throat swab culture*	*ASO titre* (IU ml $^{-1}$)[b]
1	1	m	No	Yes	n/d[c]	<200
2	7	f	Yes	Yes	normal[e]	800
3	9	m	Yes	Yes	normal	400
4	9	f	No	Yes	normal	300
5	8	f	No	Yes	normal	250
6	2	f	No	No	normal	<200
7	14	f	Yes	Yes	Gp C	400
8	7	m	No	No	n/d	250
9	17	f	Yes	Yes	normal	300
10	13	f	Yes	Yes	normal	400
11	18	f	Yes	Yes	normal	<200
12	12	f	No	Yes	normal	500
13	10	m	Yes	Yes	Gp C	1200
14	9	f	No	Yes	normal	800
15	2	f	No	Yes	normal	600
16	5	m	Yes	Yes	normal	<200
17	3	f	Yes	No	n/d	<200
18	7	f	Yes	Yes	n/d	<200
19	13	m	Yes	Yes	Gp C[g]	1600
20	10	f	No	Yes	normal	300
21	6	f	No	Yes	n/d	<200
22	8	m	No	Yes	normal	1500
23	11	m	No	No	n/d	<200
24	15	f	No	Yes	normal	500
25	3	f	Yes	Yes	Gp C	800
26	7	f	Yes	No	normal	400
27	5	f	Yes	Yes	normal	<200
28	14	m	No	Yes	normal	<200
29	16	f	No	Yes	normal	300
30	17	m	No	Yes	Gp C	800
31	10	f	Yes	No	normal	400
32	6	f	No	Yes	Gp C	1200
33	7	m	No	No	n/d	<200
34	11	f	Yes	Yes	normal	800
35	3	m	No	No	n/d	<200

[a] Preceding onset pf psoriasis. [b] Normal antistreptolysin O titre is <200 IU ml^{-1}. [c] n/d = not done. [d] GP = guttate psoriasis. [e] Normal = normal flora isolated. [f] CPP = chronic plaque psoriasis. [g] Lancefield group C ß-hemolytic streptococcus isolated. [h] Anti-DNase B

negative. Approximately 20% of group A streptococcal infected individuals do not respond by so that a negative titer alone streptococcal infection.[14]

Sixty per cent of subjects in this study had raised ASO titers at presentation while only six of 27 patients investigated with a throat swab had a positive streptococcal throat culture. There are limited data available on the results of investigation into the association between streptococcal infection and guttate psoriasis; serological evidence of streptococcal infection was found in 19 of 33 (58%) with acute guttate psoriasis in one study.[2] In another study Mallon *et al.*[15] 27twenty seven of 29 patients (93%) had raised ASO titer. In our

study, 60% of patients with guttate psoriasis had raised ASO titer and 17.1% had positive culture of *S pyogenes*. It is unlikely that these are mere chance associations. There is evidence that an immunologic mechanism is involved in the triggering of guttate psoriasis by streptococcal infection. Stimulation of T-cells by streptococcal superantigens has been suggested[11,16,17,18] They bind directly to the major histocompatibility complex class II molecule on the antigen presenting cell and stimulate T cells that express certain T-cell receptors. This leads to polyclonal T-cell activation with release of immune cytokines such as interleukin-2, which are important in the pathogenesis of psoriasis.[19] It is possible that streptococci contain antigenic substances recognized by psoriatic T-cells. Aiba *et al*.[20] and Baker *et al*.[21] reported the altered responses of peripheral blood mononuclear cells (PBLs) from psoriatic patients to streptococcal antigen *in vitro*. Furthermore, Baker *et al*.[22] have reported the presence of streptococcal antigen-specific T-cells in guttate psoriasis lesions. Gabriel *et al*.[23] confirmed the auto-immune components in guttate psoriasis, due to cross reactions between skin and streptococcal antigens.

Keeping these studies in mind, and the strong association documented in our study, between guttate psoriasis and recent acute pharyngitis, it is important to search for and eliminate microbial infections in the treatment of psoriasis. In view of this many dermatologists have recommended using antibiotics for psoriasis particularly guttate type. Some dermatologists have also recommended tonsillectomy for psoriasis in patients with recurrent streptococcal pharyngitis. There is, currently, no firm evidence on which to base any recommendations for the routine management of acute guttate psoriasis. Furthermore, it is not clear whether any intervention can effectively, prolong the duration of remission or prevent progression to chronic plaque psoriasis. More studies are needed with greater numbers of patients so that risk associations of psoriasis can be determined accurately, and optimal method for achieving clearance of psoriasis can be determined.

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