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ANTIDEOXYRIBONUCLEASE B TITERS IN PSORIASIS

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Abstract. Psoriatic patients were examined for serologic evidence of streptococcal infections by using antideoxyribonuclease B (ADB), which has been shown to be a more sensitive screening tool than antistreptolysin O (ASO) for detecting such evidence in other clinical circumstances. Antistreptococcal antibody titers (ASO and ADB) of 71 patients with psoriasis vulgaris, 7 with guttate psoriasis, and 6 with erythrodermic psoriasis were compared with ASO and ADB antibody titers of 25 nonpsoriatic dermatologic patients hospitalized at the same time and of an adult group that was used as a control for the test itself. Thirty-six of 71 patients with psoriasis vulgaris had elevated titers of ADB or ASO or both, and ADB was more frequently elevated than ASO (41% vs. 15%). Compared with control values the ADB titers were significantly higher in patients with psoriasis vulgaris ($P<0.02$) and patients with guttate psoriasis ($P<0.05$). The ASO titers were significantly higher in patients with psoriasis vulgaris than in controls ($P<0.04$). Within the group with psoriasis vulgaris, ADB titers were significantly higher than ASO titers ($P<0.01$). Among patients with psoriasis vulgaris, histories of sudden flares of psoriasis and early recurrences of psoriasis after previous successful hospital treatment, family histories of psoriasis, and histories of potential streptococcal infections were more frequent in those with elevated antistreptococcal antibodies.

Key words: Psoriasis; Anti-DNAse B; Streptococcus; Antistreptolysin O

The coincidence of streptococcal infections, particularly of the pharynx, and psoriasis has been known for some time (11, 15, 17). This association has been stressed in guttate psoriasis (10) but has also been noted in psoriasis vulgaris. Our means for investigating this association have been clinical history, bacteriological cultures, and serologic markers of streptococcal infections. Antistreptolysin O titers (ASO) have been the only serologic marker employed in most previous studies. ASO titers, however, while generally as reliable as antideoxyribonuclease B (ADB) titers in detecting pharyngeal infections, are less sensitive indicators than ADB titers of skin infections (2, 6). The use of both ASO and ADB titers detects a much higher percentage of patients who have had significant streptococcal infections than the use of ASO alone.

As our knowledge of immunologic factors in psoriasis expands, it is important to screen our patients with as sensitive a group of indicators as we can in order to record the incidence of exposure to streptococcal antigens. In particular, we believe that the skin may be an important portal of exposure to such antigens in psoriatic patients and that screening by ASO titers alone may have failed to detect many such exposures in previous studies. Therefore, we have used this relatively new and more sensitive serologic tool (ADB), in conjunction with ASO titers, to examine a group of patients hospitalized with psoriasis, giving special attention to morphologic variants of psoriasis. Our results confirm that serologic evidence of streptococcal infections is relatively frequent in psoriasis vulgaris and in guttate psoriasis and that ADB is an important screening tool for detecting such evidence. No direct etiologic or temporal correlations can be made from this study of single titer determinations, but further investigation of antistreptococcal antibodies of psoriatic patients is indicated.

METHODS

Patients studied were hospitalized between February and June 1979. Serum was drawn early during hospitalization, and ASO and ADB titers were measured by microtitration tests using reagents from Beckman Instruments. This technique is available in commercial kit form and yields reproducible results. The normal values, as published by the manufacturer, are 0 to 85 U of ASO and ADB in an adult population. It is difficult and somewhat arbitrary to determine what level of antibody, on a single specimen, is high enough to be considered abnormal. Klein and associates (7, 8) studied adult normal subjects who had no evidence of recent streptococcal infections and, using this technique of antibody measurement, found that more than 98% of the subjects had ASO and ADB titers that were less than or equal to 170 U. On the basis

Table I. *Antistreptolysin O (ASO) titers and antideoxyribonuclease B (ADB) titers in patients with psoriasis and in controls*

	Non-psoriatic controls		Psoriasis vulgaris		Erythrodermic psoriasis		Guttate psoriasis	
Units	ASO (%)	ADB (%)	ASO (%)	ADB (%)	ASO (%)	ADB (%)	ASO (%)	ADB (%)
>1000	1[a] (4)	...	...	1[b] (1)				
960	1 (4)	...	...	1 (1)				
680	...	...	...	4 (6)				
480	...	1 (4)	1 (1)	2 (3)	...	...	1 (14)	1 (14)
340	...	1 (4)	4 (6)	10 (14)	...	...	...	1 (14)
240	1 (4)	3 (12)	6 (9)	11 (15)	1 (17)	...	2 (29)	1 (14)
170	4 (16)	3 (12)	14 (20)	19 (27)	...	2 (33)	1 (14)	2 (29)
120	1 (4)	4 (16)	13 (18)	9 (13)	1 (17)	...	...	2 (29)
85	3 (12)	3 (12)	8 (11)	2 (3)	1 (17)	...	1 (14)	
60	3 (12)	2 (8)	12 (17)	3 (4)	...	1 (17)	...	
0	11 (44)	8 (32)	13 (18)	9 (13)	3 (50)	3 (50)	2 (29)	
Total 7 (100)	25 (100)	25 (100)	71 (100)	71 (100)	6 (100)	6 (100)	6 (100)	7 (100)

[a] 1360.
[b] 1920.

of their work, we selected the normal range for this study as ≤170 U for ASO and for ADB. Titers were expressed in serum dilutions from 0 to 1920 U. Throat cultures for β-hemolytic streptococcus were obtained from 37 of the 71 patients with psoriasis vulgaris.

The 84 psoriatic patients were divided into three groups on the basis of the morphologic appearance of their lesions: (1) 71 patients with psoriasis vulgaris—common, discrete, erythematous plaques with silvery scale, (2) 7 patients with guttate psoriasis—lesions less than 1 cm in diameter, and (3) 6 patients with erythrodermic psoriasis—all or nearly all of the skin involved with diffuse erythema and exfoliative scaling.

A control group of 25 non-psoriatic patients was randomly selected from hospitalized patients on the dermatology service. Their diagnoses included atopic dermatitis (4 patients), generalized dermatitis (3 patients), urticaria (2 patients), Sézary's syndrome (2 patients), and one patient each with granuloma annulare, Hailey-Hailey disease, parapsoriasis, stasis ulcers, pityriasis rubra pilaris, mycosis fungoides, erythema multiforme, vasculitis, dyshidrotic eczema, intertrigo, ulcerated necrobiosis lipoidica, herpes zoster, erythema nodosum, and pyoderma gangrenosum. Some of these patients had pyodermatous lesions, but in no case could streptococcus be cultured from the skin. Throat cultures were obtained from 7 of the 25 control patients, and all results were negative.

Charts of psoriatic patients were reviewed, and most patients were interviewed, with special reference to family history of psoriasis, recent history of significant throat or skin infection, spondylitis or peripheral inflammatory arthritis with negative rheumatoid factor, history of sudden precipitous flare of their psoriasis in the 6 weeks before admission, and previous hospitalization for treatment of psoriasis within the past 6 months.

RESULTS

The group with psoriasis vulgaris had significantly higher ADB titers than ASO titers ($P<0.01$), whereas the other three groups showed no signifi-

Table II. *Values of antistreptolysin O (ASO) and antideoxyribonuclease B (ADB) titers in psoriasis*

	Non-psoriatic controls (25pats.)[a]		Psoriasis vulgaris (71pats.)[b]		Erythrodermic psoriasis (6 pats.)[c]		Guttate psoriasis (7pats.)[d]	
Titer	No.	%	No.	%	No.	%	No.	%
Elevated ASO and ADB	1	4	4	6	0	0	2	29
Elevated ASO alone	2	8	7	10	1	17	1	14
Elevated ADB alone	4	16	25	35	0	0	1	14
Elevated ASO or ADB (or both)	7	28	36	51	1	17	4	57
Normal ASO and ADB	18	72	35	49	5	83	3	43

Mean age (yr): [a] 48, [b] 49, [c] 60, [d] 36.

Table III. *Comparison of patients with psoriasis vulgaris who have elevated and normal antistreptococcal antibody*

	With elevated antibody (36 pats.)[b]		With normal antibody (35 pats.)[c]	
	No.	%	No.	%
Family history of psoriasis[a]	18	53	9	30
Sore throat or pyoderma	9	25	4	11
Seronegative arthritis	10	28	7	20
Sudden flare-up	7	19	3	9
Hospitalization in past 6 mos.	6	17	2	6

[a] Information on family history unavailable for some patients.
[b] Mean age 43 years.
[c] Mean age 55 years.

cant difference (Table I, paired *t*-test using logarithms of the values). The group with psoriasis vulgaris had ASO titers and ADB titers that were significantly greater than those found in the non-psoriatic patients ($P<0.04$, two-sample *t*-test). Patients with guttate psoriasis had significantly higher ADB titers than had the non-psoriatic patients ($P<0.05$). Patients with psoriasis vulgaris and those with guttate psoriasis had significantly higher titers of ADB than had the patients with erythrodermic psoriasis ($P<0.02$).

In the group with psoriasis vulgaris, 36 (51%) of 71 patients had elevated ASO or elevated ADB titers (or both) as compared with 7 (28%) of 25 in the non-psoriatic group (Table II). The increased sensitivity of ADB titers is reflected in the group with psoriasis vulgaris, in which 29 (41%) of 71 ADB titers were elevated, compared with 11 (15%) of 71 ASO titers. The small size of the groups with erythrodermic and guttate psoriasis made comparison impractical.

Family histories of psoriasis, histories of sore throats or pyoderma, seronegative arthritis, histories of sudden flares of disease, and histories of frequent recurrences of disease were all more frequent in the group with elevated antistreptococcal titers (Table III). The mean age of patients with elevated titers was lower than those without elevated titers (43 vs. 55 years).

Throat cultures were negative in 36 patients with psoriasis vulgaris (17 in patients without elevated antistreptococcal antibodies and 19 in patients with elevated antistreptococcal antibody titers). Only one patient with psoriasis vulgaris had a positive throat culture at hospitalization, and one other patient had a documented streptococcal pharyngitis 2 months earlier, which was associated with a flare of her psoriasis vulgaris. Both of these patients had elevated ADB titers (680 U) and normal ASO titers. Only 2 of 6 patients with guttate psoriasis had a positive throat culture at hospitalization. One of these patients had an elevation of only the ASO titer, and the other patient had elevation of both ASO and ADB titers. None of the patients with erythrodermic psoriasis had positive throat cultures.

DISCUSSION

Streptococci are grouped on the basis of the immunologic reaction of their cell wall and are further classified as to hemolysis produced on blood agar plates. Group A β-hemolytic streptococcus is the primary group involved in human infections. These organisms secrete at least 20 antigens, including toxins and enzymes (3, 12). Antibodies directed against these antigens are useful markers of recent infection(s). A person's immunologic response to infection varies with (1) age of the host, (2) site of infection, (3) duration of stimulus, and (4) whether the patient has previously been exposed to organisms with cross-reacting antigens. Antibodies to streptolysin O were the first markers employed clinically. Recently, other antibodies to streptococcal antigens, including antideoxyribonuclease B (ADB) and antihyaluronidase, have been found to be valuable in detecting patients who have had streptococcal infections (2, 6).

The coincidence of psoriasis and streptococcal infections, usually of the upper respiratory tract, has been recognized for some time (11, 15, 17). The most direct evidence for this association has

been histories and serologic indicators of recent streptococcal infection. In 1947, Norrlind (11), in a random sample of 66 patients with psoriasis, found that 36 (54.5%) had elevated streptococcal O agglutination tests. In a series of patients with other dermatologic conditions (including mycoses, prurigo, infected dermatitis, and pyodermas), he found 42 (26%) of 161 patients with elevated titers. In a control group of patients from the venereal disease clinic, 7.35% had elevated titers. The titers being measured may have been less specific than present-day ASO titers.

In 1964, Whyte & Baughman (15) found elevated ASO titers in 17 (85%) of 20 patients with guttate psoriasis. Cohen Tervaert and Esseveld (4) investigated psoriasis vulgaris. They divided 200 patients with psoriasis into three groups: group 1, acute guttate psoriasis with average ASO titers of 525 U; group 2, chronic psoriasis with acute disseminated psoriasis, with average ASO titers of 340 U; and group 3, psoriasis at typical sites of predilection on a chronic basis, with average ASO titers of 196. U. Svejgaard et al. (13) measured ASO titers and antistreptococcal hyaluronidase titers and found them to be elevated in 51 of 156 patients with psoriasis vulgaris.

In the present study, the populations were compared on the basis of the actual value of the titers, and these data are the basis for our findings of elevated ASO titers and ADB titers in patients with psoriasis vulgaris and of elevated ADB titers in patients with guttate psoriasis in comparison with both the non-psoriatic control group and the group with erythrodermic psoriasis. Actual values were also used to compare ASO and ADB titers within each group, and only the group with psoriasis vulgaris had ADB titers that were significantly greater than the corresponding ASO titers.

The non-psoriatic control group used in this study was matched with respect to age, time of antibody measurement, and inpatient treatment status. This group seemed to be the most appropriate comparison group for investigating whether antibody titers in psoriatic patients were higher than in a general population of dermatologic patients. The controls were not matched as to degree of epidermal alteration, such as percentage of surface area involved.

The use of single isolated titers does not generate data that enable one to discern temporal relationships between streptococcal infections and the clinical expression of psoriasis in individual patients or the immune response of psoriatic patients to such infections. For this, serial antibody determinations are required, and increasing antibody titers must be demonstrated in order for a recent infection to be diagnosed. However, this study clearly shows that psoriatic patients have elevated titers when compared with controls, and this does reflect exposure to streptococcal antigens at some point in the past. We postulate that the presence of elevated antibody titers might be explained by (1) the more frequent exposure to streptococcal antigens through an altered epidermal barrier in psoriatic skin, (2) an altered immune response to such exposures which is unique to psoriatic patients, or (3) a combination of both of these. Future investigation of antistreptococcal antibodies in psoriatic patients using serial antibody determinations and control populations with matched degrees of epidermal alteration may furnish data on these questions. Culture data from the skin and pharynx of future patients may further supplement these data. However, cultures may be subject to sampling error and may not always reflect an immunologically significant exposure.

Patients with psoriasis vulgaris who had elevated titers were compared with those who did not (Table III). The increased incidence of a family history of psoriasis may reflect an inherited tendency to psoriasis and streptococcal infections, such as that searched for by other investigators in HLA studies. The histories of clinical infections are remarkable in that, while they were more frequent in the group with elevated titers, only 7 of 36 patients with psoriasis vulgaris and elevated titers gave such histories. In addition, 2 patients with elevated titers had impetiginized psoriatic plaques. The difference in incidence of arthritis was small.

An interesting note was the increased number of patients, although small, who had histories of sudden flare-ups of their disease, or histories of relatively rapid and severe recurrences of their disease after previous successful hospital treatment. Both of these findings may merit consideration of streptococcal-associated disease in future patients. However, 2 patients without elevated titers recounted similar histories, and many patients with elevated titers did not have such histories.

Our study confirms that serologic evidence of streptococcal infections is relatively frequent in

psoriatic patients. The association between such infections and psoriasis has been further investigated by others in recent years. Svejgaard et al. (13), in studying HLA typing of 51 of 156 patients who had psoriasis vulgaris and elevated ASO or antistreptococcal hyaluronidase (or both) titers, were unable to demonstrate that HLA antigens in this group were dissimilar from the HLA antigens in the group with normal titers. Other investigators, however, have shown an association between HLA-B13 and a history of streptococcal infections and ASO titer levels in psoriatic patients (1, 9). Subsequent studies also have shown an increased incidence of HLA-B17 in patients with guttate psoriasis (16). Tauber et al. (14) have shown no cross reaction between streptococcal antigens and HLA determinants.

Gross et al. (5) found altered cellular immune response to streptococcal antigens which they believed paralleled the humoral response to group A streptococcal antigens in guttate psoriasis. These authors, as well as others, commented on the common epidemiologic, clinical, immunologic, and genetic characteristics that exist between guttate psoriasis and the other non-suppurative sequelae of group A streptococcal infections (for example, rheumatic fever and poststreptococcal glomerulonephritis). Whether streptococcal antigens have a role in the etiology of psoriasis, either through humoral or cellular mechanisms or both, is not clear. Psoriasis is a multifactorial disease, and we may be able to define subsets of patients in whom immune mechanisms may play a crucial part. Streptococcus may be one of many antigens that make an etiologic contribution. The use of more sensitive serologic indicators of previous streptococcal infections, such as ADB, enables us to examine these patients more critically.

CONCLUSION

The ASO and ADB titers as indicators of previous streptococcal infections were examined in psoriatic patients. More psoriatic patients than non-psoriatic patients had high titers of ASO and ADB. The difference was especially marked in regard to ADB, which appears to be a more sensitive indicator of exposure to streptococcal antigens. ADB titers were significantly elevated in patients with psoriasis vulgaris and patients with guttate psoriasis. The group with erythrodermic psoriasis did not have significantly elevated titers. Somewhat more than 50% of patients with psoriasis vulgaris had elevated antistreptococcal antibody titers (either ASO or ADB or both).

ADB is a more sensitive indicator of streptococcal skin infections than is ASO. The potential implications of the association of streptococcal infections and psoriasis are still speculative, but this association is re-emphasized by the use of this more sensitive indicator (ADB), in conjunction with ASO, in studying these patients. Further evaluation of antistreptococcal antibodies in psoriatic patients is indicated.

Among the patients with psoriasis vulgaris, histories of sudden flaring of disease or recurrence difficult to control, or both, were more frequent in those with elevated titers of antistreptococcal antibodies.

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