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Factors Associated with Increased Aqueous Flare in Psoriasis

Fumiki Okamoto,*
Yoshihiro Umebayasi,† Fujio Ohtsuka† and Sachiko Hommura‡

*Department of Ophthalmology, University Hospital of Tsukuba, Tsukuba, Japan; Departments of †Dermatology, and ‡Ophthalmology, Institute of Clinical Medicine, University of Tsukuba, Tsukuba, Japan

Purpose: To evaluate the changes in aqueous flare in psoriasis patients and to identify the factors that influence the level of aqueous flare.

Methods: We examined the 68 eyes of 34 psoriasis patients and the 68 eyes of 34 healthy subjects with a laser flare-cell meter. Complete dermatologic and ophthalmic examinations were performed on the psoriasis patients.

Results: Flare was significantly higher in psoriasis patients than in normal controls ($P <$ .0001). The factors that increased flare significantly were age and Psoriasis Area and Severity Index. Flare was not significantly associated with sex, psoriasis type, duration of disease, and cyclosporin therapy. A flare increase was significantly correlated with serum total protein and immunoglobulin (Ig) A, but not with albumin, IgG, and IgM.

Conclusions: Psoriasis patients, even without ocular symptoms, had slight damage to the blood–aqueous barrier. Multiple linear regression analysis showed that flare had the strongest correlation with the severity of psoriasis. **Jpn J Ophthalmol 2001;45:172–176** © 2001 Japanese Ophthalmological Society

Key Words: Aqueous flare, IgA, PASI score, psoriasis.

Introduction

Psoriasis is a chronic systemic disease that is manifested by recurrent inflammation and is characterized by circumscribed erythematous, scaly surfaced plaques of various sizes. The etiology of psoriasis is still unknown. In psoriasis vulgaris, an HLA class I Cw6 specificity has been recognized serologically as the most commonly associated antigen.[1] Ophthalmologically, psoriasis is manifested as conjunctivitis, keratitis, cataract, uveitis, and trichiasis.[2] A certain percentage of psoriasis patients have uveitis, which is one of the most important ocular complications.[3,4]

Recently, the aqueous flare level was measured for 3 months in patients with psoriatic uveitis using a laser flare-cell meter.[5] It was reported that the flare level increased even when the psoriasis patient did not have a uveitis attack or any ocular symptoms.

We have used a laser flare-cell meter to evaluate the aqueous flare level in patients with psoriasis who did not have ocular symptoms, in order to determine the blood–aqueous barrier (BAB) function quantitatively.

Materials and Methods

During a 2-month period in 1995, 30 patients (16 men and 14 women, mean age = 35.8 ± 12.0 years; age range, 20–64 years), suffering from psoriasis, were examined at our hospital using a laser flare-cell meter. Some of these 30 patients had been diagnosed with psoriasis 10 or more years earlier. Five patients with primary or secondary glaucoma and cataract were excluded from the study. For controls, 34 subjects (16 men and 18 women, mean age = 35.1 ± 12.1 years; age range, 18–73 years) were examined. None of these eyes showed abnormalities in intraocular

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Correspondence and reprint requests to: Fumiki OKAMOTO, MD, Department of Ophthalmology, University Hospital of Tsukuba, 2-1-1 Amakubo, Tsukuba-shi, Ibaragi-ken, 305-8575, Japan

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pressure, slit-lamp, and fundus findings. Informed consent was obtained from all participants in the study.

The measurements with a laser flare-cell meter (FC-1000; Kowa) were performed in both eyes 30–60 minutes after dilatation of the pupil with 0.5% tropicamide and 5% phenylephrine hydrochloride. The measurements were made by the same ophthalmologist in a masked fashion. For each eye, five measurements were taken and averaged. The flare value (average of both eyes) was expressed as photon count per millisecond (pc/ms).

The severity of psoriasis was estimated by the Psoriasis Area and Severity Index (PASI score), which is commonly used to evaluate the severity and efficacy of treatment of psoriasis in many dermatological studies. For calculating the PASI score, four main body areas are assessed: the head, the trunk, the upper extremities, and the lower extremities. The area of psoriatic involvement of these four main areas are given a numerical value, and the severity of the psoriatic lesions are assessed on a scale of 0–4. To calculate the PASI score, the sum of the severity ratings is multiplied by the numerical value of the involved areas and by the various percentages of the four body areas.[6] The PASI score varies in steps of 0.1 unit from 0.0 to 72.0. The higher PASI scores correspond to more severe disease. We had PASI scores examined by a dermatologist.

Serum total protein, albumin, immunoglobulin (Ig) G, A, and M levels were measured using standard techniques in psoriasis patients.

The difference in the flare value between psoriatic eyes and control eyes was statistically analyzed using the Student unpaired *t*-test. The relationship between the flare values and six variables of the patient with psoriasis was also evaluated using the same test. The six variables were: (1) sex; (2) age (≥40 and <40 years); (3) psoriasis type (psoriasis vulgaris or psoriasis arthropathica or pustulosa); (4) PASI score (≥10.0 and <10.0); (5) duration of disease (≥10 and <10 years); and (6) cyclosporin treatment history (yes or no). The correlation of the flare values to these six variables was analyzed by multiple linear regression. The relationship between the flare value and the serum protein content of psoriasis patients (Tp, Alb, IgG, IgA, and IgM) was evaluated using a simple regression analysis.

Results

None of the psoriasis patients was found to have anterior uveitis or cells in the anterior chamber by slit-lamp examination. The mean flare value in the psoriasis group (4.05 ± 0.75 pc/ms) was significantly higher than the value in the control group (3.13 ± 0.64 pc/ms; $P < .0001$; Figure 1).

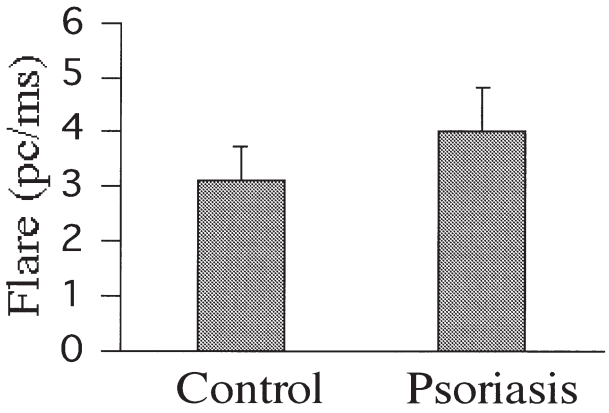

Figure l. Flare values in two groups. Mean flare value is significantly higher in psoriasis group than in control group. Columns show mean values and error bars are SD. *$P < .000l$ by Student unpaired *t*-test. pc/ms: Photon count per millisecond.

The flare value was higher in patients older than 40 years, and with PASI scores greater than 10.0 (Table 1). Flare values were not significantly different in men and women, in patients undergoing or not undergoing cyclosporin therapy, duration of disease and psoriasis type (Table 1).

In the multiple regression analysis, an increased flare value significantly correlated with the PASI score ($r = 0.56$, $P < .01$; Figure 2A) and age ($r = 0.45$, $P < .01$; Figure 2B). However, flare value did not correlate with sex ($r = -0.01$, P = NS), psoriasis type ($r = 0.04$, P = NS), duration of disease ($r = 0.17$, P = NS), or cyclosporin therapy ($r = 0.01$, P = NS).

There was a significant linear correlation between flare value and serum total protein ($r = 0.47$, $P < .05$; Figure 3A) and IgA ($r = 0.56$, $P < .01$; Figure 3B). A significant linear correlation was not found between flare value and albumin ($r = -0.15$, P = NS), IgG ($r = 0.26$, P = NS), or IgM ($r = -0.09$, P = NS).

Discussion

Psoriasis is one of the most common dermatologic disorders in clinica1 practice, and is reported to be associated with some ophthalmological complications, of which, iridocyclitis may be the most significant. Iridocyclitis has been reported to be a complication in 3.09–7.1% of psoriasis cases.[3,4] The characteristics of uveitis in psoriatic patients are: bilateral acute ante-

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Table 1. Flare Values in Psoriasis Patients

Variables	Categories	No. of Patients	Flare Values (Mean ± SD)	Range	*P Value
Sex	Female	16	4.18 ± 0.70	3.0–5.5	.31
	Male	14	3.90 ± 0.75	2.7–5.0	
Age (years)	≤40	20	3.77 ± 0.62	2.7–4.6	<.005
	>40	10	4.60 ± 0.60	3.7–5.5	
Psoriasis type	Vulgaris arthropathica/pustulosa	26	4.09 ± 0.78	2.0–5.5	.16
		4	3.50 ± 0.75	2.8–4.4	
PASI score†	≤10.0	19	3.74 ± 0.64	2.7–5.0	<.005
	>10.0	11	4.57 ± 0.54	3.6–5.5	
Duration of disease (years)	≤10	20	3.95 ± 0.83	2.7–5.5	.31
	>10	10	4.24 ± 0.39	3.7–4.9	
Cyclosporin therapy	Yes	10	4.06 ± 0.61	3.0–5.0	.94
	No	20	4.04 ± 0.79	2.7–5.5	

*Student unpaired *t*-test.
†PASI: Psoriasis Area and Severity Index.

rior uveitis, HLA-B27 negative, frequent recurrence. Systemic corticosteroid administration is not effective but cyclosporine treatment is.[5,7]

We have compared the aqueous flare value of psoriatic patients with that of normal controls. Under normal conditions, the protein concentration of aqueous humor is 5–50 mg/mL protein equivalent.[8–10] This corresponds to approximately 1.3–8.7 pc/ms.[11] In our study, the flare value in the psoriasis group was 4.05 ± 0.75 pc/ms, and in the control group was 3.13 ± 0.64 pc/ms. Although the flare values of the two groups were almost normal, statistical analysis showed that the difference between the two groups was significant. We calibrated the laser flare-cell meter and both groups were measured during a 2-month period by an ophthalmologist who did not know whether the subject was normal or had psoriasis. Therefore, the methods used in our study were well-controlled.

Although we acknowledge that the mean flare value in the psoriatic group is within the normal range, this result suggests that the BAB may have been damaged due to subclinical inflammation in the anterior segment, even in psoriatic patients without clinical iridocyclitis.

There was no significant difference in the flare values between the patients with psoriasis vulgaris and arthropathica or pustulosa. However, the number of patients may be too few to analyze the differences in flare values among psoriasis types. In fact, this study

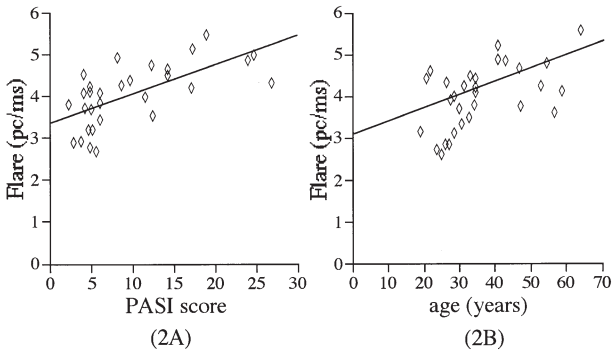

Figure 2. Regression line of flare values as function of Psoriasis Area and Severity Index (PASI) score (**A**) and age (**B**). Flare values correlated significantly with PASI score ($r = 0.56$, $P < .01$) and age ($r = 0.45$, $P < .001$). pc/ms: Photon count per millisecond.

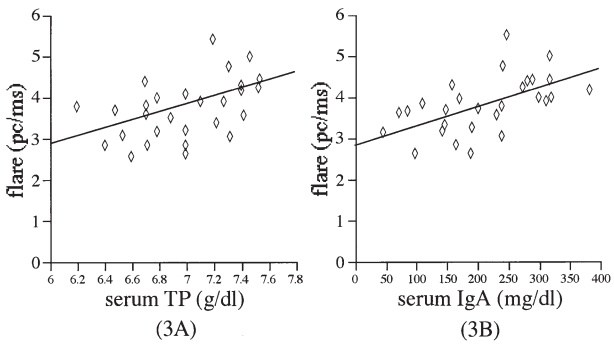

Figure 3. Regression line of flare values as function of serum total protein (TP) (**A**) and serum immunoglobulin A (IgA) (**B**). There was significant linear correlation between flare value and serum TP ($r = 0.47$, $P < .05$) and IgA ($r = 0.56$, $P < .01$).

included only one psoriasis arthropathica and three psoriasis pustulosa patients. It has been reported that patients with psoriasis arthropathica have uveitis more frequently than the patients with the other type of psoriasis.[3] Moreover, the skin lesions tend to be more severe in pustulosa patients than in vulgaris patients. We, therefore, assumed that the flare values in arthropathica or pustulosa patients would be higher than those in vulgaris patients.

The flare values of the psoriatic patients with and without cyclosporin administration were not significantly different. We treat psoriatic patients with PASI scores higher than 20.0. In this study the treatment group was comprised of patients who were currently being treated or previously had been treated. Therefore, the PASI score in this group of patients was more than 20.0 at one time.

There was no difference between the patients in this study who were diagnosed as having psoriasis more than 10 years previously and those diagnosed more recently. These results would lead us to conclude that the flare values of psoriasis patients are not affected by the previous severity and duration of the disease and that the damage to the BAB may be reversible.

There was a significant linear correlation between the flare value and age in patients with psoriasis. However, psoriasis may not have a direct influence on the flare increase by age because the flare value is well correlated with age in normal eyes.[12]

The PASI scores correlated significantly with the flare values. In most psoriatic patients, there seemed to be a correlation between the severity of the skin lesions and the severity of the uveitis. We performed a stepwise multiple regression analysis to determine which factors were most responsible for the flare value and found that the PASI score related to it more significantly than the other factors such as age, sex, type of psoriasis, duration of disease, and cyclosporin treatment. Therefore, periodic flare measurements and observations of skin severity in psoriatic patients may play an important role in the early detection of anterior uveitis.

In this study, we demonstrated that the flare values were significantly correlated with serum IgA but not serum albumin. Until recently, many quantitative estimations of serum Ig in psoriasis patients have been published.[13–15] Although these results are conflicting, IgA is usually increased in psoriasis. One of the reports estimated the serum IgA, IgG, and IgM quantitively in 60 patients with psoriasis, and compared all the data to a large control group.[10] The findings were as follows: the level of serum IgA and IgG were higher in psoriasis than in controls, especially IgA. In addition, a comparison between serum IgA and the extent of the skin lesions showed that IgA was significantly higher in the generalized psoriasis group than in the group with few lesions. Immunologically, in psoriatic patients, there was a deposition of C3, IgA and IgM in vessel walls and dermal-epidermal junctions in biopsy specimens.[16] The immune response could occur in the ocular tissues due to the systemic involvement of psoriasis. If there are immune complex depositions in the vascular rich ciliary tissues, it may activate complements and attract inflammatory cells. Consequently, damage could occur in ciliary epithelial cells and iridial endothelial cells so that the BAB is disturbed.

This study demonstrated that a BAB breakdown may exist in psoriatic patients without ocular symptoms. Moreover, higher aqueous flare values were mostly related to the severity of psoriasis in comparison to the other factors. Therefore, even if psoriatic patients do not complain of ocular symptoms, the ophthalmic examination should include flare measurements.

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