

Increased Platelet Aggregation in Psoriasis

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Platelet aggregation was measured in fasting platelet-rich plasma in 25 psoriatics, 6 of whom were diabetic, 50 normal controls, and 24 diabetics. The aggregating agents employed to induce platelet aggregation included ADP, epinephrine and collagen. Platelet aggregation was significantly increased in psoriatics compared with normal controls. An additive effect was observed when diabetes was associated with psoriasis, with platelet aggregation being further increased by ADP. Platelet aggregability was re-evaluated in 7 psoriatics after they presented with clearing of the rash. The increased platelet aggregation with ADP and epinephrine was significantly reduced when the skin lesions had cleared. *Key words: Platelet; Hyperaggregability; Psoriasis; Diabetes.* (Received October 6, 1984.)

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Psoriasis is a widespread disorder which is not limited to the skin. It affects joints, blood vessels, and perhaps the liver and other organs (1). McDonald & Calabresi (2) observed that the psoriatic patient suffers an abnormally high incidence of occlusive vascular diseases such as coronary thrombosis, thrombophlebitis, cerebrovascular accident, and pulmonary embolism. They also observed that the psoriatic patient attended by certain predisposing factors to these vascular disorders is at a greater risk of manifesting them than the non-predisposed psoriatic patient. This observation motivated us to investigate platelet aggregation in psoriatic patients, because of the potential importance of abnormal platelet behavior in the genesis of occlusive vascular disease (3). Psoriatic patients examined included those with diabetes mellitus.

PATIENTS AND METHODS

The patient population consisted of 25 patients (17 male and 8 female, 15–76 years, mean 50.9 years) with vulgaris-type psoriasis involving 10–40% of their body surface. Among these, 6 patients (2 male

and 4 female, 54–72 years, mean 61.2 years) had type II diabetes mellitus (4); they did not require insulin therapy. Blood specimens were obtained before initiating treatment for psoriasis. In 7 patients who were hospitalized in the dermatology ward, blood specimens were obtained again after clearing of the rash. The therapy used for these patients consisted of topical tar, topical anthralin and UVB irradiation. The control groups consisted of 50 healthy male volunteers (23–44 years, mean 35.0 years) and 24 nonpsoriatic patients with type II diabetes (18 male and 6 female, 27–82 years, mean 57.9 years). Neither controls nor psoriatics had taken aspirin or other anticoagulants for at least 2 weeks prior to the study.

Venous blood was drawn in the morning after an overnight fast using 3.8% sodium citrate (1.0 ml to 9.0 ml blood). Platelet-rich plasma (PRP) was obtained by centrifugation at 100 g at 26°C for 10 min. The platelet concentration in PRP was adjusted from 200 000 to 350 000/mm³. Platelet aggregation was determined by the method of Born (5) using a Bio-Data Aggregation Profiler, model PAP-3A. Percentage aggregation was determined assuming that platelet-poor plasma represented 100% and PRP 0%. The agents employed to induce platelet aggregation included adenosin-5'-diphosphate (ADP) (Sigma Chemical Co.), epinephrine (Nakarai Chemical Ltd.) and collagen (Hormone Chemie). Final concentrations of these agents in PRP were 1.0 µM, 0.2 µg/ml and 0.5 µg/ml, respectively. Aggregation study was started 90 min after the collection of the blood sample. The maximum percentage of aggregation (MPA) within 150 sec after addition of aggregating agent to PRP was calculated.

RESULTS

As shown in Table I, all MPA values in the psoriatics showed, independent of their association with diabetes, significantly higher values than those of normal controls. The values of ADP-induced MPA in psoriatics with diabetes were significantly higher than those in non-diabetic psoriatics ($p < 0.05$) and diabetic controls ($p < 0.01$). The values of MPA induced by ADP and collagen in the diabetic controls were also significantly higher than those of normal controls ($p < 0.01$, $p < 0.05$). No significant difference in MPA values was found between diabetic controls and non-diabetic psoriatics.

In 7 psoriatics who were hospitalized, MPA was re-evaluated after the treatment when lesional skin had cleared. The value (mean \pm SD) of ADP-induced MPA in 7 patients fell from 67.7 \pm 22.2 to 35.0 \pm 14.9 ($p < 0.05$) after the treatment. Similarly, the value of epinephrine-induced MPA fell from 48.6 \pm 35.9 to 26.9 \pm 17.2 ($p < 0.05$). No significant difference was found between the values of collagen-induced MPA before and after the treatment.

The individual values of ADP and epinephrine-induced MPA before and after the treatment in 7 patients are depicted in Fig. 1.

Table I. Maximum percentage of platelet aggregation (MPA) with aggregating agents in normal controls, diabetic controls, psoriatics with diabetes, and psoriatics without diabetes

Values were means \pm SD; numbers of subjects in parentheses

Aggregating agents (final concentration in PRP)	Controls		Psoriatics	
	Normal	Diabetic (n=24)	With diabetes (n=6)	Without diabetes (n=19)
ADP (1.0 µM)	30.6 \pm 13.8 (n=30)	42.7 \pm 18.6**	69.0 \pm 14.3 ^{a,b} **	47.0 \pm 20.0**
Epinephrine (0.2 µg/ml)	24.5 \pm 23.5 (n=50)	29.5 \pm 23.7	48.5 \pm 31.4*	37.5 \pm 25.7*
Collagen (0.5 µg/ml)	13.7 \pm 21.7 (n=50)	26.7 \pm 25.2*	48.8 \pm 37.7**	37.7 \pm 31.8***

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. normal controls. ^a $p < 0.05$ vs. psoriatics without diabetes. ^b $p < 0.01$ vs. diabetic controls.

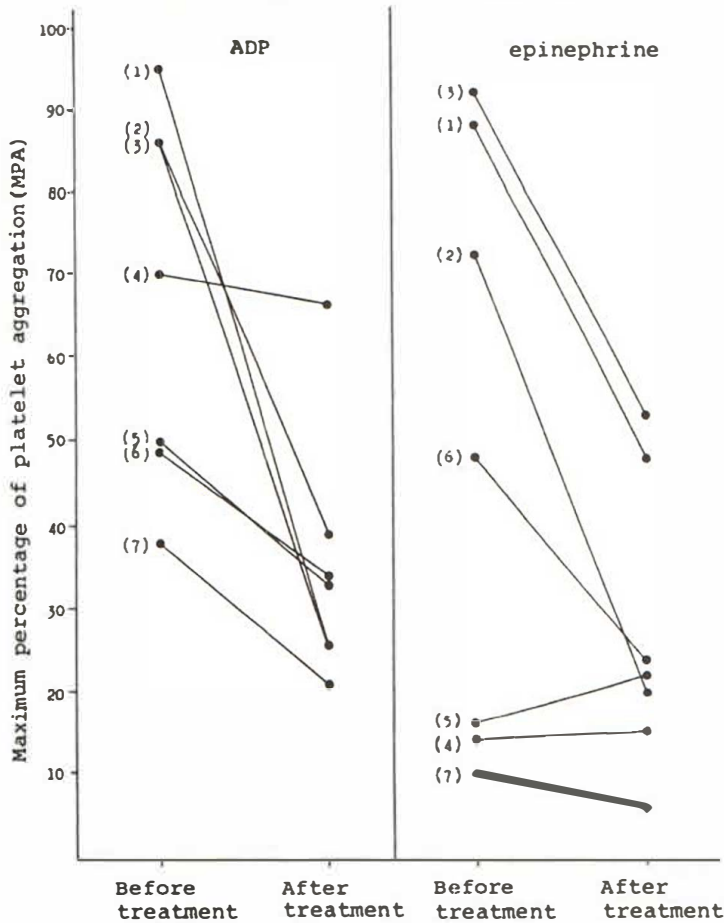


Fig. 1. Platelet aggregation with ADP and epinephrine before and after treatment in 7 psoriatic patients. Numbers in parentheses represent subject numbers.

DISCUSSION

Recently Wolf et al. (6) studied platelet aggregability in 11 psoriatic patients. They reported, in contrast to our results, platelet aggregability within normal range. This disagreement may be due to differences in the experimental methods. In their study, normal control levels of MPA to ADP, epinephrine and collagen were 82%, 80% and 75%, respectively. With conventional aggregometers, these values are near maximum ones, and therefore thought to be not suitable for the detection of further increased platelet aggregability. In the present study, we adjusted normal control levels of MPA to below those in their study. Thus, the difference in platelet function among the studied groups became more evident.

Arachidonic acid (AA) and its metabolites are known to play a key role in the regulatory mechanism of platelet aggregation (7). Concerning AA metabolism in psoriasis, several abnormalities have been observed in the psoriatic epidermis (8). Hammarström et al. (9) noted that the cellular concentrations of free AA and 12-hydroxyeicosatetraenoic acid (HETE) in involved psoriatic skin were 2500% and 8100% greater respectively than those in uninvolved psoriatic skin. Treatment of the lesional area reduced the level of free AA and 12-HETE in comparison to a non-treated lesional area (10). AA is in itself a potential agent triggering aggregation of platelets and at low concentrations enhances the effects of

other platelet aggregating agents (11). 12-HETE also plays an important role in producing irreversible aggregation of the platelets (12). These observations raise the possibility that platelet hyperaggregability in psoriasis may be related to an altered AA metabolism in the lesional psoriatic areas. However, information concerning AA metabolism in this disorder is still lacking.

The present study demonstrated that platelets from psoriatics presenting with diabetes had a greater sensitivity to ADP than those from non-diabetic psoriatics. It is well acknowledged that diabetic-derived platelets evidence enhanced aggregation (13), and several factors have been postulated to account for this phenomenon (14). Thus, the association of diabetes with psoriasis may culminate in an additive effect, further increasing platelet aggregation.

Wolf et al. (6) observed a significant elevation in whole blood viscosity in psoriatic patients and suggested that this may contribute to the higher incidence of occlusive vascular disease occurring in these patients. In this study, we observed that the platelets of the psoriatic patient had an increased sensitivity to aggregating agents, which seemed to be further accelerated when diabetes, a predisposing factor to the vascular disease, was present. In view of the important role of platelets in occlusive vascular disease (3), enhanced platelet aggregability may be also involved in the genesis of the higher incidence of occlusive vascular disease in the psoriatic patient.

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