

ORIGINAL ARTICLE

Recovery of platelet factor 4 (PF-4) and beta-thromboglobulin (beta-TG) plasma concentrations during remission in patients suffering from atopic dermatitis

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Abstract

Our previous study has for the first time demonstrated that atopic dermatitis (AD) patients show enhanced plasma concentrations of PF4 and beta-TG. In addition, it has been suggested that chemokines may be the markers of AD severity. The aim of this study was to determine whether enhanced platelet activation in active AD withdraws when the disease reaches the clinical remission stage. Plasma PF-4 and beta-TG concentrations were studied in 10 AD patients and in 23 healthy controls. Patients were examined twice: first, during the active period, and next, during the clinical remission lasting for at least 6 months. Plasma PF-4 and beta-TG concentrations in patients upon AD remission were significantly lower as compared to active AD and did not differ significantly from the healthy subjects. Enhanced platelet activation is a transient phenomenon accompanying active AD and disappears during clinical remission. As with earlier data, the findings point to platelet activity in AD increasing during flare, falling following therapy and normalizing upon remission.

Keywords: *Platelet activation, platelet factor 4, beta-thromboglobulin, atopic dermatitis*

Introduction

Apart from the critical role in hemostasis, blood platelets are implicated in inflammatory reactions and immune response. Platelet activation leads to the release of multiple chemokines from alpha-granules, including platelet factor 4 (PF-4) and beta-thromboglobulin (beta-TG) [1, 2].

It has been suggested that platelets play an important role in different skin diseases, including atopic dermatitis (AD) [3–7]. AD is a chronic relapsing inflammatory skin disease frequently accompanying so-called atopic triad disorders, such as asthma and allergic rhinitis, marked, however, by some differences in plasma concentrations of platelet-derived chemokines [8, 9].

Following animal model analysis, it was suggested that the increased PF-4 expression might play an important role in the etiology of allergic dermatitis [10]. Moreover, eosinophils from AD patients

increased significantly the migratory response towards PF-4 [11].

We were the first to establish earlier that plasma PF-4 and beta-TG concentrations were increased in patients with active AD [12]. Such results were then confirmed by Tamagawa-Mineoka et al. [13]. As AD may be associated with increased plasma PF-4 and beta-TG concentrations during the active period of the disease, we wanted to recognize any possible occurrence of such a phenomenon with the disease reaching the clinical remission phase.

Materials and methods

The study group comprised a total of 18 AD patients who were then examined twice. Eighteen AD patients were first examined during the active phase of the disease, manifested by the flares of eczema. The characteristics of the patients were presented earlier [12]. Briefly, all patients suffering from

moderate AD at the time of the study were classified according to the criteria by Rajka and Lageland [14]. None of them suffered from the concomitant inhalatory allergy. All the subjects showed positive results from a skin prick test to three or more different common airborne allergens and positive serum specific IgE for the relevant allergens.

Ten patients (four men/six women; average age 28 years, range: 21–38 years) who had previously showed active skin lesions and enhanced platelet activation were classified for the second stage of the study performed when clinical remission was reached. All patients were in remission and had been medication free (except emollients) for at least 6 months. Their skin involvement was characterized as follows: without (erythema, excoriations, exudation), only minor lichenification (two cases) or none at all, and only mild pruritus. None of the patients showed any acute flare after more than 6 months. The remaining eight patients, participating in the previous stage, failed to reach the remission phase.

The control group consisted of 23 healthy subjects (eight women and 15 men) with an average age of 26 years (range: 18–40 years) [12].

Statistical analysis

The data is presented as median and range. Mann-Whitney test was employed to assess differences between the patients and healthy controls. The Wilcoxon's paired test was employed to compare the AD groups. *P* values below 0.05 were considered significant.

PF-4 and beta-TG measurement

Blood was obtained in the morning (7.00 a.m. to 8.00 a.m.; in the fasting state) after 25-minute rest at slight or no stasis from the antecubital vein into CTAD tubes (Becton Dickinson, Plymouth, UK) and then placed instantly in ice/water bath for 20 minutes. The tubes were then centrifuged at 2500 g for 30 minutes at 4°C, and the top third the volumes of the resultant plasma supernatants were collected. Plasma concentrations of PF-4 and beta-TG were measured by enzyme-linked immunosorbent assay (ELISA), using commercial Asserachrom® (Diagnostica Stago, Asnieres, France).

Results

Plasma PF-4 and beta-TG concentrations were significantly higher in active AD patients compared to AD patients upon remission and to the healthy subjects. Furthermore, PF-4 and beta-TG plasma concentration values during the remission period were similar to that of the healthy controls (Figures 1 and 2). Individual changes in plasma PF-4 and beta-TG concentrations in AD patients during the active

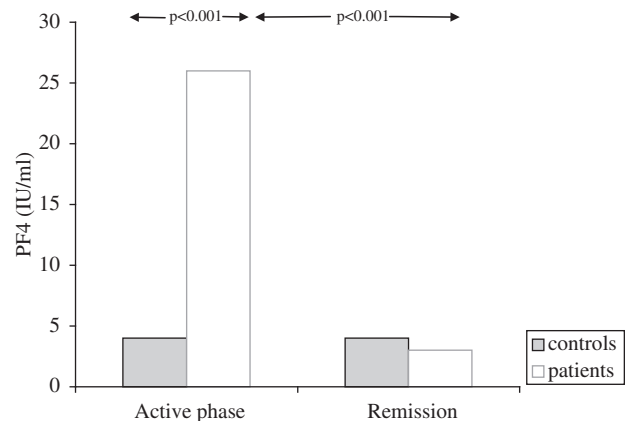


Figure 1. Plasma PF-4 concentration in AD patients during the active and remission phase ($n = 10$) and in controls ($n = 23$).

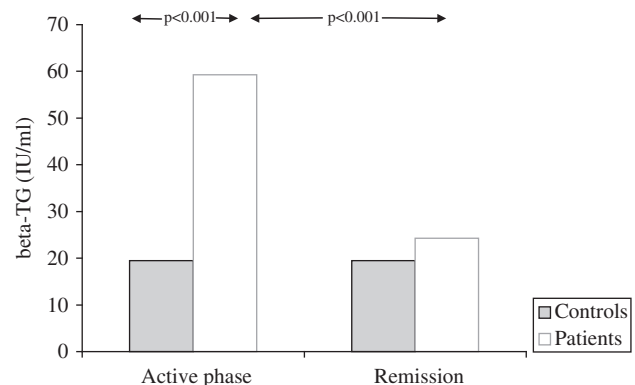


Figure 2. Plasma beta-TG concentration in AD patients during the active and remission phase ($n = 10$) and in the controls ($n = 23$).

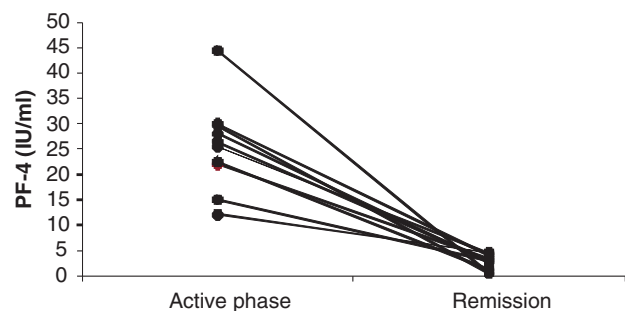


Figure 3. Changes in plasma PF-4 concentration in AD patients during the active phase in comparison to the remission phase of the disease (significant decrease of PF-4).

phase of the disease, compared to the remission phase are shown in Figures 3 and 4.

Discussion

Previously, we and others described that plasma PF-4 and beta-TG concentrations are increased in patients with active AD, suggesting that platelets may

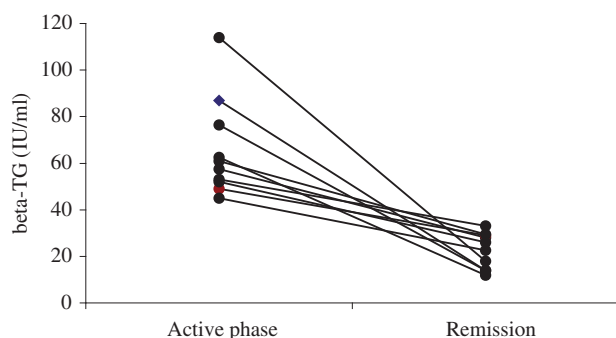


Figure 4. Changes in plasma beta-TG concentration in AD patients during the active phase in comparison to the remission phase of the disease (significant decrease of beta-TG).

be involved in pathogenesis of the disease [12, 13]. In addition, plasma concentrations of the chemokines were correlated with the disease severity assessed according to SCORAD index [13]. However, no correlation was found between plasma PF-4 and beta-TG concentrations and peripheral eosinophil count, serum total IgE and lactate dehydrogenase concentration [13].

In the present study, we found significantly lower plasma PF-4 and beta-TG concentrations in AD patients during remission as compared to the active phase of the disease. In addition, these values did not differ significantly from those of the healthy subjects.

Tamagawa-Mineoka et al. observed a significant decrease in plasma concentrations of the chemokines in six AD patients after therapy [13]. However, these values were mostly higher than in the normal controls.

On the contrary, the clinical remission of AD symptoms is accompanied by the recovery of PF-4 and beta-TG values that are not any different from those of the controls. Therefore, we suggest that elevated plasma PF-4 and beta-TG concentrations characterize the active phase of AD as well as platelet activation behaving dynamically during the clinical course of the disease. Increased platelet activation is a transient and reversible phenomenon accompanying AD occurring during the active period and withdraws upon remission of the disease.

This result, along with our earlier reports as well as data delivered by others on plasma PF-4 and beta-TG concentrations, indicates that platelet activation in atopic dermatitis may increase during the flare, fall after therapy, and normalize upon remission. Platelet activity may be dependent on the severity and activity of the disease. Our results may confirm that blood

platelets are involved in the pathomechanism of skin lesions in atopic dermatitis.

Acknowledgements

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