

CONCISE COMMUNICATION

Case of atopic dermatitis concurrent with idiopathic thrombocytopenic purpura, whose serum thymus and activation-regulated chemokine level remained undetectable

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ABSTRACT

We report a 9-year-old Japanese female patient with atopic dermatitis associated with idiopathic thrombocytopenic purpura. She demonstrated high serum immunoglobulin (Ig)E and IgE specific to several environmental allergens, but extremely low serum thymus and activation-regulated chemokine (TARC) levels regardless of the disease progression. This case suggests platelets as the main source of serum TARC.

Key words: atopic dermatitis, biomarker, idiopathic thrombocytopenic purpura, platelet, thymus and activation-regulated chemokine.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by the predominant infiltration of T-helper (Th)2 cells in lesional skin. Recently, it has been demonstrated that serum thymus and activation-regulated chemokine (TARC) levels are elevated in AD patients compared with patients with psoriasis or healthy control subjects, and that immunoreactive TARC is detected in the lesional skin of AD.¹ Furthermore, serum TARC levels in AD patients correlate with their Scoring Atopic Dermatitis index; thus, they already serve as a reliable biomarker reflecting the disease progression of AD in daily clinical practise, especially in Japan.^{2,3} TARC, a member of CC chemokine family, is a potent and selective chemoattractant for Th2 cells via CC chemokine receptor 4. Various cell types, including keratinocytes, dendritic cells, endothelial cells and platelets, have been suggested to produce TARC.^{1,4,5} We report here a unique case of AD who is associated with idiopathic thrombocytopenic purpura (ITP) and shows normal or undetectable serum TARC levels regardless of the disease progression.

CASE REPORT

A 9-year-old Japanese girl with a past medical history of allergic rhinitis and food allergies presented with persistent itchy eruptions. Her mother reported that itchy eruptions appeared when she was 1 year old. On physical examination, there was dry skin on the whole body, crusting and numerous fine erythematous macules and papules on the trunk (Fig. 1), and lichenified erythematous plaques on the neck, cubital fossae (Fig. 2) and popliteal fossae.

The main laboratory data were 1566 IU/mL serum IgE level (normal range, <170 IU/mL), 8.1% eosinophil percentage of leukocytes (normal range, 0–10), $41 \times 10^3/\mu\text{L}$ platelet count (normal range 150–350) and less than 125 pg/mL serum TARC level (normal range, <743 pg/mL). Allergen-specific immunoglobulin (Ig)E antibody scoring was class 6 for house dust mite and cedar pollen, class 4 for orchardgrass, class 3 for cypress pollen, cat and *Malassezia*, class 2 for dog, *Candida* and *Aspergillus*, and class 1 for milk and sesame.

Based on these clinical and laboratory findings, her diagnosis was AD and her Eczema Area and Severity Index (EASI) was 10.8 (range, 0–72). Because her platelet count was abnormally low, she consulted a hematologist and was diagnosed with ITP. There was no other laboratory data indicating immunodeficiency or autoimmune disease.

Topical steroid and an oral non-sedating antihistamine that were prescribed on the diagnosis of AD improved her skin condition, although it sometimes became worse in summer or in winter. Her clinical course including EASI and serum TARC level are shown in Table 1. The serum TARC levels were consistently undetectable irrespective of her disease progression.

DISCUSSION

This case that showed typical clinical manifestation of AD, increased level of serum IgE and thrombocytopenia must be differentiated from the mild variant of Wiskott–Aldrich syndrome (WAS). WAS is a rare X-linked recessive disease characterized by the clinical triad of thrombocytopenia, eczema and recurrent infections (classic WAS). The mild variant of WAS is also known as X-linked thrombocytopenia that

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Figure 1. Crusting pigmented erythematous macules and papules on the back.

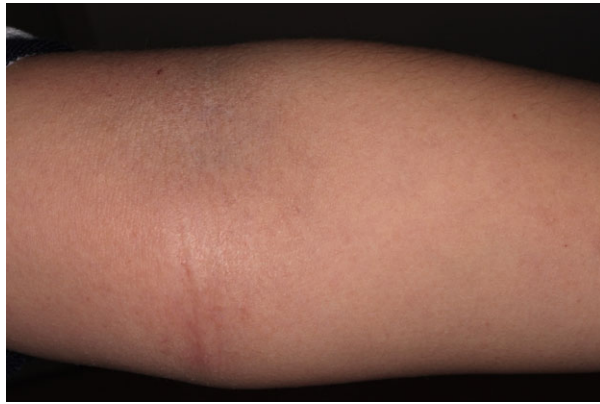


Figure 2. Lichenified erythematous plaques on the cubital fossa.

presents congenital thrombocytopenia and mild eczema. The underlying mutation is in the gene for the WAS protein (WASP) on the X-chromosome at Xp11.22. Being X-linked and potentially lethal, it would be expected to almost invariably affect males and more than 90% of affected patients are male, although affected females have been reported. In this case, careful examination revealed the increased mean platelet volume and number of immature platelets and detected antiplatelet IgG, which support the diagnosis of ITP. Moreover, the gene analysis could not detect any mutations in the known genes responsible for several cases of congenital thrombocytopenia including WAS. Consequently, we diagnosed her AD associated with chronic ITP.⁶

As shown in Table 1, it is notable in this case that, whereas the EASI score fluctuated along with exacerbation and remission, the serum TARC level was consistently within normal range and sometimes undetectable. It is possible that her serum TARC level was low because the disease severity was moderate even at the initial visit. However, it has been reported that the serum TARC levels of children were shown to be higher than those of adults in control groups as well as AD patients; the cut-off values of serum TARC in children

Table 1. Clinical course of the present case including EASI and serum TARC level

	June/ 201X	Oct.	Feb./ 201X + 1	June	Oct.
TARC (pg/mL)	<125	155	<125	116	<100
normal range between 2 and 15 years old: <743 pg/mL					
Plt ($\times 10^3/\mu\text{L}$)	41	76	76	74	70
IPF (%)	ND	13.3	9.7	8.9	12.1
IgE (IU/mL)	1566	ND	1080	ND	933
EASI	10.8	3.8	2.6	2.0	0.6

The serum TARC level was consistently within normal range irrespective of her disease progression. EASI, Eczema Area and Severity Index; Ig, immunoglobulin; IPF, immature platelet fraction; ND, not done; Plt, platelets; TARC, thymus and activation-regulated chemokine.

(>2 years old) and adults (>15 years old) were 743 and 450 pg/mL, respectively.⁷ Therefore, her serum TARC level was low even compared with that of the control group.

It has been already demonstrated that platelets from AD patients contain high levels of TARC.⁵ TARC levels in the serum samples were significantly higher than those in the plasma samples; the mean values of TARC in AD patients were 3225.9 pg/mL in serum and 253.2 pg/mL in plasma, whereas in control subjects they were 240.5 pg/mL in serum and 35.2 pg/mL in plasma. They found that this difference was caused by the release of a significant amount of TARC from platelets during clotting. The serum TARC levels of the present case fluctuated under 200 pg/mL, equal to the plasma TARC levels of AD patients. It was assumed that the reason of the low serum TARC level in this case was the reduction of platelet numbers due to ITP.

There is increasing evidence that TARC is involved in the development of various allergic disorders. Although TARC in the stratum corneum of the most severe acute AD lesions was correlated with serum TARC level,⁸ the cellular source of TARC in AD lesional skin is still controversial. Acute severe AD lesions should show parakeratosis and prominent spongiosis histologically, then stratum corneum obtained from these lesions by tape-stripping could contain TARC in tissue fluid, probably derived from T cells, dendritic cells and platelets as well as from keratinocytes. Furthermore, some studies demonstrated immunohistochemically TARC in epidermal keratinocytes and in vascular endothelial cells, T cells and dendritic cells in the dermis,¹ whereas the others demonstrated TARC specifically in microvascular endothelial cells of the dermis but not in epidermal cells.⁴ This controversy may be caused by the intermingled TARC from platelets in the skin, whose source cannot be identified immunohistochemically.

A recent study has demonstrated that in a murine model of chronic hapten-induced dermatitis resembling the features of AD, depletion of blood platelets greatly reduces the degree of skin inflammation as determined by ear thickness and leukocyte infiltration into inflamed ear skin.⁹ Thus, the disease severity of the present case, which was relatively mild even

when aggravated, may be because of the reduction of platelets due to ITP, although it is difficult to show platelets involved in the pathogenesis of AD lesional skin immunohistochemically.

Finally, we reported a case of AD associated with ITP that demonstrated high serum IgE and IgE specific to several environmental allergens but extremely low serum TARC level, which suggests platelets as the main source of serum TARC.

CONFLICT OF INTEREST: None declared.

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