Correspondence

Severe atopic dermatitis associated with transient hypogammaglobulinemia of infancy

Atopic dermatitis (AD) is a common chronic inflammatory skin disease, which, in infants, is usually treated with topical steroids and dietary restriction. However, these treatments are often ineffective. In infants, as the expression of maternally derived IgG decreases, serum IgG levels reduce, resulting in physiological hypogammaglobulinemia. These levels reach a nadir at the age of 3–4 months and subsequently increase when infant IgG production commences. Transient hypogammaglobulinemia in infancy (THI) is an extension of this physiological hypogammaglobulinemia.[1] We report two cases of severe AD associated with THI, both of which improved after the serum IgG levels increased.

Case 1 was a 6-month-old boy that developed erythema on both cheeks at two months of age (Fig. 1a), which subsequently spread throughout the body. He was treated with herbal medicine only at another clinic; however, the erythema progressed to scaling and eczema. Therefore, the boy was admitted to our hospital and was treated with topical and intravenous corticosteroids.

Case 2 was a 4-month-old girl that developed erythroderma with severe eczema on the face and body and was treated with emollient only for two months at a pediatric clinic. However, the eczema progressed, and she developed phlegmon in the middle finger of the left hand. Thus, she was referred to our hospital, where she was administered topical corticosteroids, intravenous antibiotics, and corticosteroids. As IgE antibodies specific to certain food allergens were elevated in both patients (Table 1), the implicated foods were subsequently avoided. Both patients were diagnosed with AD according to the Japanese guidelines for the management of AD.[2]

Both patients shared common clinical features, had a similar clinical course, and hypogammaglobulinemia but had no family history of allergy (Table 1). Their eruptions resolved during hospitalization but relapsed after discharge, despite the application of topical corticosteroids. At 10 months of age, their erythema and eczema began to resolve as their serum IgG levels increased. At 16 months of age, the eczema had completely resolved without corticosteroid treatment (Fig. 1b), and the serum IgG levels reached their normal limits. Currently, both children are healthy and being treated with only a topical emollient.

Several studies have reported that hypogammaglobulinemia is associated with severe AD,[3] but the precise relationship between these two conditions is unclear. Recent studies have shown that regulatory T-cell (Treg) levels increase in THI patients, and the suppressive effects of Treg cells on B lymphocytes may be associated with the decreased immunoglobulin production.[4,5] Interestingly, in both our patients, symptoms resolved with increased serum IgG levels at 16 months of age, and we attribute this to the resolution of THI. A recent study demonstrated that 72% of THI children normalized IgG values within 24 months of age,[6] and hence, resolution at 16 months is not improbable.

Based on our observations, we hypothesize that in our patients, primary hypogammaglobulinemia with associated

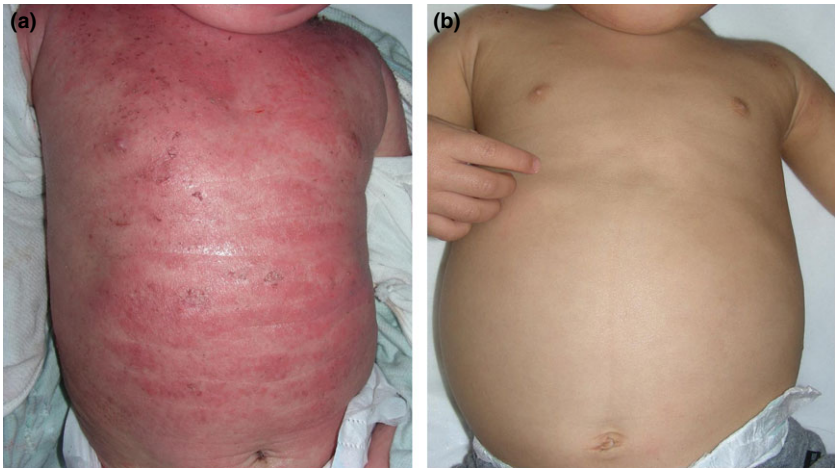


Figure 1 Clinical features of the patient (case 1). (a) Clinical features at the age of 6 months. Erythema with scaling and eczema was noted. (b) Clinical features at the age of 16 months. No eczema or erythema was noted

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Table 1 Laboratory data of the two patients

Case 1								
Age (months)	6		8		10		19	
WBC (10^3cell/μl)	27.7	(7.0–15.0)	90	(7.0–15.0)	81	(7.0–15.0)	96	(7.0–11.0)
CRP (mg/dl)	0.01	(< 0.3)	0	(< 0.3)	0.05	(< 0.3)	0.1	(< 0.3)
TP (g/dl)	2.9	(5.8–7.3)	5.4	(5.8–7.3)	4.9	(5.8–7.3)	6.2	(6.3–8.0)
Alb (g/dl)	1.2	(3.9–4.9)	3.8	(3.9–4.9)	3.9	(3.9–4.9)	3.8	(3.9–4.9)
IgG (mg/dl)	50	(440–1033)	203	(440–1033)	329	(440–1033)	667	(665–1343)
IgA (mg/dl)	21	(7–29)	26	(7–29)	39	(7–29)	43	(12–49)
IgM (IU/ml)	51	(29–126)	75	(37–146)	78	(37–146)	104	(40–195)
IgE (IU/ml)	218	(< 20)	ND		87.4	(< 20)	190	(< 30)
RAST (score): egg, 5; wheat, 1								
Case 2								
Age (months)	5		8		10		18	
WBC (10^3cell/μl)	179	(7.0–15.0)	153	(7.0–15.0)	137	(7.0–15.0)	97	(7.0–11.0)
CRP (mg/dl)	0.01	(< 0.3)	ND		ND		0.03	(< 0.3)
TP (g/dl)	5.4	(5.8–7.3)	6.8	(5.8–7.3)	7.0	(5.8–7.3)	7.3	(6.3–8.0)
Alb (g/dl)	3.0	(3.9–4.9)	4.7	(3.9–4.9)	4.9	(3.9–4.9)	ND	
IgG (mg/dl)	122	(440–1033)	227	(440–1033)	300	(440–1033)	569	(649–1306)
IgA (mg/dl)	7	(7–29)	5	(7–29)	10	(7–29)	26	(22–103)
IgM (IU/ml)	76	(28–152)	78	(37–186)	104	(37–186)	159	(58–309)
IgE (IU/ml)	ND		188	(< 20)	ND		99	(< 30)
RAST (score): egg, 3; milk, 3; cheese, 3; wheat, 3; soy, 3								

Alb, albumin; CRP, C-reactive protein; ND, not done; (), reference value; TP, total protein; WBC, white blood cell count; RAST, Radioallergosorbent test.

THI induced AD. Cutaneous pathogenic microbes can exacerbate atopic eczema in patients with hypogammaglobulinemia, and features of AD are noted in other primary immunodeficiency syndromes, including Wiskott–Aldrich syndrome.[7] Thus, patients with THI-associated AD should be administered high-dose topical or oral corticosteroids, antibiotics, and intravenous immunoglobulin (IVIG).[8] A recent study showed that IVIG therapy for AD in children improved clinical features and reduced IgE levels,[9] suggesting that IVIG therapy is suitable for THI-associated AD, because IVIG is effective for stopping the vicious circle of infection-immunodeficiency, as well as for treating AD symptoms.[10]

In conclusion, THI-associated AD seems to differ from typical AD in terms of the prognosis being more favorable, despite the occurrence of severe eczema with infection due to hypogammaglobulinemia, and serum IgG levels may be a good marker for THI.

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