

Patient Report

Atopic dermatitis and transient hypogammaglobulinemia of infancy improved simultaneously

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The serum level of IgG in an infant reduces with the decline of the maternally derived IgG antibody, reaching a nadir at 3–4 months of age, and then rises as the infant's own IgG production gradually increases.¹ Transient hypogammaglobulinemia of infancy (THI) is an extension of this physiological hypogammaglobulinemia.^{2,3} Atopic dermatitis (AD) is a common chronic eczematous dermatitis that typically begins during the first 6 months of life.⁴ In both THI and infantile AD, many affected patients experience resolution before early childhood. Atopic disease has been suggested to be one of the features of THI in a few reports. Recently, it has been reported that i.v. gammaglobulin treatment for resistant AD was clinically effective and that AD worsened on bacterial infection due to hypogammaglobulinemia.^{5–8} Although infections are not life-threatening, in some infants THI may be associated with recurrent infections.^{1–3} Various studies indicate that bacterial infection, such as *Staphylococcus aureus*, is one exacerbating factor of AD.^{4,9} Therefore an etiological relationship between AD and THI is predictable but no evidence has been produced.

In this paper we present five case studies of 4-month-old infants with AD who subsequently improved simultaneously with resolution of concomitant THI.

Case reports

The five infants had similar clinical courses: the erythema began on the cheek at 2 months of age, with subsequent extension to jaw, neck, chest and extensor aspects of the extremities. Weepy patches developed at 3 months of age. When they visited health-care centers for routine medical check-up at 4 months of age, they were recommended to consult Kyoto

City Hospital for treatment of the eczema. Until then, they had not undergone any medical treatment. Blood examinations indicated low serum gammaglobulin in the five patients (Table 1). Although treatment with hydrophobic occlusion (azulene) and topical corticosteroid (clobetasone butyrate) resulted in clearing of their dermatitis, IgG levels did not normalize before 6 months of age. Thereafter, relapses of erythema were observed in three patients. Two patients developed erosive lesions on the cheek from which *S. aureus* was cultured. Another showed non-serous red papules on cheek and *S. epidermitis* and α -*Streptococcus* sp. were detected. All patients had outgrown the typical manifestations of AD and developed mild irritant dermatitis at 12 months of age, and their serum gammaglobulin levels were normalized (Fig. 1). Based on these laboratory findings, hypogammaglobulinemia of each infant was diagnosed as THI. The patients are 18–24 months old at the time of writing and relapse of AD has not been observed.

Discussion

Many patients with AD develop bacterial, viral, or fungal skin infections that flare and complicate their disease, possibly because of disruption of the cutaneous barrier or impaired cutaneous immunity.⁴ Several reports have suggested an interaction between AD and hypogammaglobulinemia and the clinical efficacy of gammaglobulin treatment for AD. It has been reported that infection immunities, serum IgE levels, adhesion molecules, cytokine levels and CD4/CD8 counts were affected by gammaglobulin treatment.^{5–8} We presented five cases of infantile AD all of which improved, coinciding with the recovery of THI. From these observations it would appear that the immune abnormality due to THI has an influence on the pathologic condition of AD.

There are two possible hypotheses to explain the correlation between AD and THI: at first, loss of protein from the weepy skin lesion and/or gastrointestinal tract contributed to the hypogammaglobulinemia; second, AD developed and became

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Table 1 Laboratory findings of the five patients

	Case 1	Case 2	Case 3	Case 4	Case 5
WBC (/mm ³)	8400	9600	18300	10300	14700
Neu (/mm ³)	1008	2016	1830	1236	1911
Lym (/mm ³)	5376	4512	9882	6386	11920
Eo (/mm ³)	1260	2496	5673	2163	441
RBC (/mm ³)	413	397	541	432	474
Hb (g/dL)	11.4	10.5	13.2	11.1	11.9
Ht (%)	33.2	30.6	40.1	41.8	36.1
Plts (×10 ⁴ /mm ³)	41.6	36.3	55.9	41.5	67.7
Tp (g/dL)	5.0	4.3	5.1	5.1	6.0
Alb (g/dL)	3.7	3.3	3.5	3.9	4.7
α1 (%)	3.3	4.0	4.2	3.2	3.3
α2 (%)	14.3	10.5	12.5	9.8	9.8
β (%)	9.8	8.9	10.4	9.8	8.1
γ (%)	3.0	3.4	2.3	8.3	4.0
GOT (IU/L)	42	44	39	60	64
GPT (IU/L)	38	43	31	41	58
Che (IU/L)	205	123	221	156	207
Na (mEq/L)	134	141	133	141	139
K (mEq/L)	5.3	5.3	5.6	4.8	5.3
Cl (mEq/L)	99	106	101	106	103
IgG (mg/dL)	85	101	145	152	176
IgA (mg/dL)	10	8	11	11	7
IgM (mg/dL)	63	41	34	39	53
IgE (mg/dL)	41	44	681	71	22
Specific IgE	Egg white, cat	Egg white	Egg white, wheat, milk, egg yolk, soybean, cheese	Egg white, milk	Egg white
Culture of skin surface	ND	<i>S. aureus</i>	<i>S. aureus</i>	<i>S. epidermitis</i> , <i>α-Streptococcus sp</i>	ND*

Alb, albumin; Eo, eosinophils; Che, cholinesterase; GOT, glutamate oxaloacetate; GPT, glutamate pyruvate transaminase; Hb, hemoglobin; Ht, hematocrit; Plts, platelets; ND, not done; Lym, lymphocytes; Neu, neutrophil; RBC, red blood cells; Tp, total protein; WBC, white blood cells.

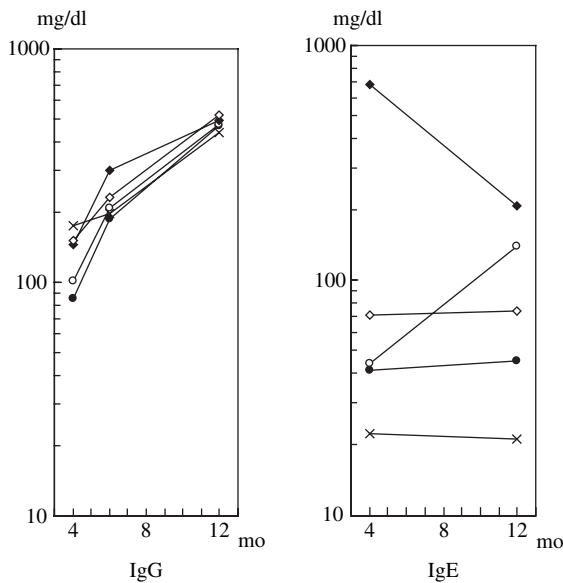


Fig. 1 Change in serum IgG and IgE concentrations of five patients. Serum IgG levels were normalized at 12 months of age. No trend was seen in IgE levels. (●), Case 1; (○), case 2; (■), case 3; (□), case 4; (+), case 5.

exacerbated by secondary infection or fluctuations of inflammatory cytokines and CD4/CD8 counts due to hypogammaglobulinemia of THI. As a serious complication of severe infantile AD with intense erosive inflammation, life-threatening hypoproteinaemia has been described and the main route of protein loss was considered to be through the skin.¹⁰ Walker *et al.* reported that 12 of 15 THI patients had symptoms of either atopic disease or food allergy/intolerance, and suggested in view of this preponderance that subclinical protein loss from the bowel due to allergic inflammation may be a contributing factor to the development of THI.³ In the present study all five infants had mild weepy patches with low exudations that were not considered to cause protein loss. All of them were fed on supplementary breast milk and weaning foods without dietary restriction and none of them developed food intolerance, growth retardation or diarrhea. It is suggested that there was no significant protein loss from the gastrointestinal tract. Thus hypogammaglobulinemia in the present patients was concluded to be a result of production failure attributed to THI rather than protein loss from skin and/or intestine. In contrast, there were patients with hypoalbuminemia (case 2) and hyponatremia (case 1, 3), and serum gammaglobulin levels were still low despite improvement of the damaged serous skin, but the

serum gammaglobulin levels increased in comparison with the first medical examinations. In view of these facts, the presence of protein loss from skin and/or intestine was undeniable.

In all of the present patients, AD improved at 6 months of age but serum IgG levels were still low, and in three cases weepy patches flared up again. In two of these three infants, *S. aureus* was detected in the exudates of weepy patches. It suggests that bacterial infection exacerbates AD. After IgG levels were normalized at 12 months of age, the recurrences did not occur. Hypogammaglobulinemia of the present patients was considered a possible reason for exacerbation of AD, regardless of whether hypogammaglobulinemia was from primary THI or protein loss. Although it is unclear whether primary THI is involved in the genesis of AD, the fact that all of the present patients developed it around the same age and had similar conditions suggests the reasonable possibility of a relationship between THI and the genesis of AD.

Our current cases presented several interesting problems, that is, whether THI was strongly associated with AD, whether THI played a role in the development of AD and whether it was universal that AD and THI improved simultaneously. Further investigation is necessary to clarify these problems.

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