DOI: 10.1002/cia2.12037

WILEY Journal of Cutaneous Immunology and Allergy

LETTER TO THE EDITOR

# Transient hypogammaglobulinemia of infancy with no evidence of immunodeficiency other than atopic dermatitis: A case report and review of literature

*Dear Editor,*

Transient hypogammaglobulinemia of infancy (THI) is a type of primary immunodeficiency (PID) characterized by accentuation and prolongation of physiologic hypogammaglobulinemia. Recurrent infections, a major manifestation of THI, usually occur in infants diagnosed as THI.[1] Skin manifestations, including severe atopic dermatitis (AD), are important signs of PID. However, reports describing THI-associated AD are limited.[2–4] We report a case of an infant with THI and severe AD, with no history of infections. Additionally, we review previous reports of THI-associated AD to clarify the diagnostic features of underlying THI in cases without history of infections.

A 4-month-old boy was referred to our hospital with a 10 week history of severe eczematous lesions. He had no history of recurrent or severe infections, or familial AD or PID. His serum IgG level was 100 mg/dL (normal range: 300-960 mg/dL). Other immunoglobulins (IgA, IgM, and IgE), leukocyte fractions, and albumin levels were within normal ranges. He was treated with topical corticosteroids but showed a poor response, with repeated relapses over the next 3 months. Consequently, a diagnosis of AD was made. At 7 months of age, his serum IgG level (238 mg/dL) was increased and the skin lesions were improved. At 10 months, the serum IgG level (373 mg/dL) was spontaneously normalized, and relapses of eczema have not been observed thereafter, even without topical corticosteroid therapy.

In this case, the absence of history of infections allowed the incorrect diagnosis of typical AD because the underlying THI was overlooked. However, this risk has not been discussed in the previous reports. Literature regarding THI-associated AD is limited; as there have been documented only 13 cases involving the description of the clinical course of this condition (Table 1).[2–4] Past history of infections was described only in case 11. The rarity of reports

**TABLE 1** Previous reports of transient hypogammaglobulinemia of infancy associated with atopic dermatitis

| No | Age of AD onset (months) | Age evaluated (months) | IgG (mg/dL) | IgE (IU/mL) | Outgrow of AD (months) |
|---|---|---|---|---|---|
| 1 | 2 | 4 | 85 | 41 | 12[a] |
| 2 | 2 | 4 | 101 | 44 | 12[a] |
| 3 | 2 | 4 | 145 | 681 | 12[a] |
| 4 | 2 | 4 | 152 | 71 | 12[a] |
| 5 | 2 | 4 | 176 | 22 | 12[a] |
| 6 | 2 | 6 | 50 | 218 | 19[a] |
| 7 | 2 | 5 | 122 | N.D. | 18[a] |
| 8 | 3 | 6 | 87 | 2246 | N.D. |
| 9 | 2 | 5 | 197 | 309 | N.D. |
| 10 | 4 | 6 | 115 | 2135 | N.D. |
| 11 | 3 | 5 | 164 | 856 | N.D. |
| 12 | 1 | 7 | 70 | 11 492 | N.D. |
| 13 | 3 | 11 | 225 | 12 706 | N.D. |
| Present case | 1.5 | 4 | 100 | <20 | 10[a] |

AD, atopic dermatitis; N.D., not described.[2–4]

[a]The normalization of serum IgG level and resolution of atopic dermatitis occurred simultaneously.

Journal of Cutaneous Immunology and Allergy —WILEY— 175

suggests that a history of infections may be an infrequent presentation among patients with THI-associated AD. Therefore, there may be more undiagnosed cases of THI-associated AD.

We aimed to report the clinical findings of our patient to help detect such cases. Herein, we observed three features that are atypical for AD. First, our patient developed AD at 6 weeks of age; however, symptoms of AD generally appear after the age of 4 months.[5] Moreover, 13 of the 14 patients in Table 1 developed AD by the age of 4 months. Second, the lack of family history of AD should be noted. In general, 60%-70% of cases have a family history of AD.[6,7] In contrast, only three cases (case 9 and 12 from Table 1 and the present case) had positive family histories. Third, the normal IgE level is notable. High IgE levels are observed in approximately 80% of patients with typical AD;[5] therefore, we expected the IgE level to be a good marker to distinguish THI-associated AD from typical AD. However, no significant IgE level trends are shown in Table 1. Further studies are warranted to provide clues for guiding the diagnosis of THI in cases without a history of infections.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## INFORMED CONSENT

Written informed consent was obtained from the patient's parents.

## ORCID

*Tomoyuki Minowa* http://orcid.org/0000-0002-8353-036X

Tomoyuki Minowa
Yasuyuki Sumikawa
Tokimasa Hida
Hisashi Uhara

*Department of Dermatology, Sapporo Medical University School of Medicine, Sapporo, Japan*

**Correspondence**
*Yasuyuki Sumikawa, Department of Dermatology, Sapporo Medical University School of Medicine, Sapporo, Japan.*
*Email: y.sumikawa@sapmed.ac.jp*

## REFERENCES

1. Dorsey MJ, Orange JS. Impaired specific antibody response and increased B-cell population in transient hypogammaglobulinemia of infancy. Ann Allergy Asthma Immunol. 2006;97(5):590–5.
2. Yasuno T, Yamasaki A, Maeda Y, Fujiki A, Yagyu S. Atopic dermatitis and transient hypogammaglobulinemia of infancy improved simultaneously. Pediatr Int. 2007;49(3):406–8.
3. Sumikawa Y, Kato J, Kan Y, Sato S, Yamashita T. Severe atopic dermatitis associated with transient hypogammaglobulinemia of infancy. Int J Dermatol. 2015;54(5):e185–7.
4. Breslin ME, Lin JH, Roberts R, Lim KJ, Stiehm ER. Transient hypogammaglobulinemia and severe atopic dermatitis: open-label treatment with immunoglobulin in a case series. Allergy Rhinol. 2016;7(2):69–73.
5. Katayama I, Aihara M, Ohya Y, et al. Japanese guidelines for atopic dermatitis 2017. Allergol Int. 2017;66(2):230–47.
6. Uehara M, Kimura C. Descendant family history of atopic dermatitis. Acta Derm Venereol. 1993;73(1):62–3.
7. Wen HJ, Chen PC, Chiang TL, et al. Predicting risk for early infantile atopic dermatitis by hereditary and environmental factors. Br J Dermatol. 2009;161(5):1166–72.