Isolated IgA Deficiency Accompanied by Autoimmune Thyroid Disease

Toshiki Mano, Akitoshi Kawakubo and Masahiro Yamamoto

Selective immunoglobulin (Ig) A deficiency is reported to occur in 1 in 16,000 in Japan and has been reported to be complicated with various autoimmune diseases. A 49-year-old woman was diagnosed as having autoimmune thyroid disease. Her serum IgA, IgM and IgG were revealed to be 4.1, 154 and 1930 mg/dl, respectively. Severe skin eruption which occurred with 30 mg/day of methimazole (MMI) or 300 mg/day of propylthiouracil (PTU), was relieved by reducing MMI to 15 mg/day and administering anti-allergic drugs. Although the influence of IgA deficiency on autoimmunity and allergy still remains unclear, this is a report of IgA deficiency associated with autoimmune thyroid disease.

(Key words: hyperthyroidism, immunodeficiency)

Introduction

Selective immunogloblin A (IgA) deficiency was first described in 1962 (1). Subsequently, many reports have appeared in the literature (2-4). The incidence of selective IgA deficiency was shown to be from 1 in 500 to 1 in 700 in Sweden (3, 5). But this disease is rare in Japan, in about 1 in 16,000 (6).

The majority of patients with selective IgA deficiency reported in the literature have significant complications (7, 8); the most common complication is an autoimmune disease, such as rheumatoid arthritis, SLE or chronic hepatitis. However, there are few reports on selective IgA deficiency with chronic thyroiditis or Graves’ disease. Here we describe a case of selective IgA deficiency with autoimmune thyroid disease.

Case Report

A 49-year-old woman was diagnosed as having hyperthyroidism by a Physician in June 1989, and 30 mg/day of methimazole (MMI) was started on June 10. About 20 days after the start of medication, drug eruptions were noted over the entire body. MMI was changed to 300 mg/day of propylthiouracil (PTU) on July first, and administration of antihistamines was started, but the eruptions did not disappear. As she refused to take the drugs, she was referred to our hospital on July 10 to undergo subtotal resection of the thyroid gland, and was admitted to our hospital on August 3.

On admission, she complained of easy fatigability, palpitation and severe sweating. She was 140 cm tall and weighed 39 kg. She lost 5 kg over the period of one month. Her body temperature was 35.8°C, pulse rate 88/minute, and respiration rate 24/minute. The blood pressure was 114/50 mmHg.

On physical examination, she was asthenic, but conscious. The diffusely enlarged thyroid was elastic firm without tenderness. She did not show exophthalmus. The lungs were clear, and the heart sound was normal. The abdomen was soft with normal bowel sound. Finger tremor was observed and pretibial myxedema was not seen. The neurologic examination did not reveal any abnormalities. Her skin was slightly wet. Although she presented with urticaria when she was 32 years old, she had no history of asthma, atopic dermatitis, nasal or drug allergy.

The urine was normal. The blood count showed that she had slight anemia. Erythrocyte sedimentation rate was 18 mm/h. The blood chemical determination was normal, and endocrinological examination revealed the following: free T3, 17.5 pg/ml; free T4, 4.29 ng/dl; TSH, 0.10 µU/ml; thyroglobulin, 27 ng/ml. Immunochemical examination revealed the following: serum immunoglobulin G (IgG), 1930 mg/dl; serum IgM, 154 mg/dl; serum IgE, 53 mg/dl; serum IgA, 4.1 mg/dl; thyroid receptor
antibody, 56% (TRAb Smith kit); anti-thyroglobulin antibody, 1:400 (Fuji Levin serodia ATG kit); antimicrosomal antibody, 1:2560 (Fuji Levin serodia ATG kit); salivary IgA, 0.6 mg/dl; anti-DNA antibody (single strand), 3.2 U/ml (MBL, MESACUP SS DNA IgG kit) (Table 1).

An electrocardiogram was interpreted as normal. A roentgenographic examination revealed no abnormalities on chest and abdomen. We performed a biopsy of her thyroid on August 14. The specimen of the thyroid showed lymphocyte infiltration, fibrosis of the interstitial tissue, destruction of the thyroid follicle (Fig. 1), and in some areas, the epithelium of the follicle was cylindrical or cuboidal (Fig. 2).

As she had not taken any drug which affects the serum and salivary IgA, it was thought that she also had selective IgA deficiency based on her level of serum and salivary IgA. We administered again 15 mg/day of MMI from August 20. The administration of $\beta$-blocker, antihistamine and antiallergic drug was started at the same time. This time, no skin eruptions were noted. The patient became euthyroid on October 25 1989. Her serum and salivary IgA was 4.0 mg/dl and 0.7 mg/dl, respectively on October 18, 1991.

Table 1. Laboratory Findings

<table>
<thead>
<tr>
<th>CBC</th>
<th>Blood Chemistry</th>
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<tr>
<td>RBC 4.55 x 10^12/mm^3</td>
<td>T-P 7.2 mg/dl</td>
</tr>
<tr>
<td>WBC 5,700/mm^3</td>
<td>GTO 23 IU/dl</td>
</tr>
<tr>
<td>Hb 10.9 g/dl</td>
<td>GPT 20 IU/dl</td>
</tr>
<tr>
<td>Ht 32.5%</td>
<td>AIP 194 IU/dl</td>
</tr>
<tr>
<td>plt 342 x 10^3/mm^3</td>
<td>LDH 234 IU/dl</td>
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<tr>
<td>Neutrophil 44%</td>
<td>Amyl 85 IU/l</td>
</tr>
<tr>
<td>Lymphocyte 69%</td>
<td>CK 26 IU/l</td>
</tr>
<tr>
<td>Eosinophil 4%</td>
<td>Cr 0.7 mg/dl</td>
</tr>
<tr>
<td></td>
<td>BUN 14 mg/dl</td>
</tr>
<tr>
<td></td>
<td>U.A 5.0 mg/dl</td>
</tr>
<tr>
<td></td>
<td>Na 141 mEq/l</td>
</tr>
<tr>
<td></td>
<td>K 3.6 mEq/l</td>
</tr>
<tr>
<td></td>
<td>Cl 107 mEq/l</td>
</tr>
<tr>
<td></td>
<td>Ca 8.9 mg/dl</td>
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<tr>
<td></td>
<td>P 4.1 mg/dl</td>
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</table>

Endocrinological examination

FT3 17.5 pg/ml
FT4 4.29 ng/dl
TSH <0.10 $\mu$U/ml
Tg 27 ng/ml

Immunological Study

S-IgG 1,930 mg/dl
S-IgM 154 mg/dl
S-IgE 53 mg/dl
S-IgA 4.1 mg/dl
C3 80 mg/dl
C4 17 mg/dl
Salivary IgA 0.6 mg/dl
TRAb 56%
TGPA ×400
MCQA ×2560
anti-DNAAb(ss) 3.2 U/ml
RF <2.0 U/ml
ANA (-)
Anti ENA Ab (-)
Anti lymphocyte Ab (-)
Anti plt. Ab (-)
Anti gastric-wall cell Ab (-)
Anti mitochondria Ab (-)
HLA
A3
B44
B51

Fig. 1. The specimen of the thyroid showed lymphocyte infiltration, fibrosis of the interstitial tissue and destruction of the thyroid follicle (HE Stain. ×200).

Fig. 2. The specimen of the thyroid showed that the epithelium of the follicle was cylindrical or cuboidal (HE Stain. ×400).
Discussion

IgA deficiency is reported to accompany some autoimmune diseases. Kanou et al reported that 16 selective IgA deficiency cases out of 107 were associated with autoimmune diseases (6). In this report, only one case showed isolated IgA deficiency accompanied by chronic thyroiditis. We found one paper reporting selective IgA deficiency accompanied by Graves' disease (9). From our experience IgA abnormality was not found among 93 cases of Graves' disease and 75 cases of chronic thyroiditis.

The present patient was diagnosed as having thyrotoxicosis because of her thyrotoxic sign and serum T3 and T4 levels. The specimen of the thyroid showed lymphocyte infiltration, fibrosis of the interstitial tissue and destruction of thyroid follicle, and in some areas, the epithelium of the follicle was cylindrical or cuboidal. The diagnosis of chronic thyroiditis can not be definite because the patient had already been treated by antithyroid drug when the thyroid gland specimen was obtained. As the period of antithyroid drug treatment was relatively short, we thought that the histological changes were perhaps due to the thyroid disease itself. Since the TRAb level was high, this patient may have Graves' disease. After we reduced the dose of MMI to 15 mg/day, and started administration of β-blocker, antihistamines and antiallergic drug at the same time, the patient escaped the skin eruptions.

Douglas et al suggested that subjects with immunodeficiency may be predisposed to autoimmune disorders (10). In fact, Taylor and Norman reported a case showing transient IgA deficiency followed by atopic dermatitis (11). We think that, in the present case, these is a possibility that the state of agammaglobulinemia had some influence on the immune system, which causes the allergic disease, autoimmune disease and drug allergy. Although the influence of IgA deficiency on the incidence of autoimmune disease still remains unclear, the present case may suggest a close relationship between IgA deficiency and allergic reaction or autoimmunity.

References