

Onset of Graves' Thyrotoxicosis after an Attack of Allergic Rhinitis

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ABSTRACT

We previously reported that allergic rhinitis was an aggravating factor for Graves' disease and that thyrotoxicosis relapsed 2 months after an allergic attack. In this paper, we report a patient who showed onset of Graves' thyrotoxicosis after an attack of allergic rhinitis. The patient, a 30-year-old woman, was initially diagnosed with subclinical autoimmune thyroiditis. Interestingly, the patient showed weak activity of thyroid-stimulating antibody (TSAb), while TSH-binding inhibitory immunoglobulin (TBII) was negative and her thyroid function tests, including TSH, were completely normal. The patient developed severe allergic rhinitis in response to Japanese cedar pollen lasting from February until April in 1995 with an increase in serum antigen-specific immunoglobulin E and peripheral blood eosinophils. Two months later, she developed thyrotoxicosis in association with increase in TSAb and TBII. These findings suggest that allergic rhinitis not only aggravates Graves' disease but also induces the clinical onset of Graves' thyrotoxicosis.

INTRODUCTION

WE PREVIOUSLY FOUND that parturition aggravates or induces the onset of Graves' thyrotoxicosis; however, little is known about other aggravating factors in Graves' disease (1,2). Recently we found that Graves' disease was aggravated after an attack of allergic rhinitis, possibly due to the overproduction of Th2-derived cytokines, such as interleukin (IL)-4, IL-5, IL-6, and IL-10 (3). In this paper, we report a prospective study on a patient with clinical onset of Graves' thyrotoxicosis after an attack of allergic rhinitis and propose that allergic rhinitis is another factor that may induce Graves' thyrotoxicosis.

METHODS

Commercially available kits were used to measure the serum concentrations of free T₄ (FT₄, Eiken Immunochemical Laboratory, Tokyo, Japan), free T₃ (FT₃, Ortho-Clinical Diagnostics, Tokyo, Japan), and TSH (Daiichi Radioisotope Laboratories, Tokyo, Japan) (4). Normal ranges of FT₄, FT₃, and TSH were 0.8–1.4 ng/dL

(10.3–18.0 pmol/L), 2.4–4.6 pg/mL (3.7–7.2 pmol/L), and 0.6–3.7 mU/L. Antithyroid microsomal antibody (MCAb) was measured with a commercially available particle agglutination kit (Fuji Rebio, Tokyo, Japan). A reciprocal titer of 1:100 or more was considered as positive. Serum levels of TSH-binding inhibitory immunoglobulin (TBII) were measured by a radioreceptor assay with a commercial kit (Cosmic Corp., Tokyo, Japan). The results are expressed as percent inhibition of binding of labeled TSH (1). Normal value is less than 12%. Serum thyroid stimulating antibody (TSAb) activity was measured as an activity to stimulate cAMP increase in FRTL-5 cells, as described previously (1). TSAb activities were expressed as the percent cAMP increase induced by the test sample compared to that induced by normal pooled serum. Values above 140% were considered positive. The sensitivity of this assay is 0.1 mU/L for bovine TSH.

Allergic rhinitis was diagnosed by the presence of rhinorrhea, sneezing, nasal congestion, and/or pruritus of the nose and eyes. Serum immunoglobulin E (IgE) in response to Japanese cedar pollen was measured by radioallergosorbent test (Pharmacia, Uppsala, Sweden). Values greater than 0.7 unit allergen (UA)/mL were considered positive.

CASE AND RESULTS

A 30-year-old woman consulted an obstetrician because of sterility for 6 years and various screening tests were performed. The patient demonstrated normal levels of thyroid hormones (FT₄, 1.1 ng/dL; FT₃, 2.8 pg/mL) and TSH (0.6 mU/L), but had positive MCAb (1:320). Thereafter, she was referred to our clinic for further evaluation on June 28, 1994 and was diagnosed with subclinical autoimmune thyroiditis (5). Her thyroid gland was not enlarged and she did not have ophthalmopathy. Interestingly, she showed weak TSAb activity (201%) (Fig. 1).

The patient developed severe allergic rhinitis in response to Japanese cedar pollen from February to April in 1995 because the cedar pollen count in 1995 was the highest it had been for the past 10 years. Due to general fatigue, the patient consulted our hospital on May 9, 1995. Serum IgE in response to Japanese cedar pollen increased from 10.1 unit allergen (UA)/mL to 29.7 UA/mL and peripheral blood eosinophils increased from 91/mm³ to 207/mm³ (Fig. 1). Thyroid hormones were high (FT₄, 2.0 ng/dL; FT₃, 7.3 pg/mL), TSH was suppressed (less than 0.04 mU/L) and TBII became positive (36%) in association with increase in TSAb activity (449%) (Fig. 1). Then she was diagnosed with Graves' thyrotoxicosis and treated with methimazole starting June 20, 1995. The thyroid gland did not enlarge during the observation period.

DISCUSSION

In Japan and European countries, Graves' disease is mainly treated with antithyroid drugs and some patients easily attain remission, while others do not. Differences underlying these responses to medication are mostly unknown, but if a patient has aggravating factors, the disease may be resistant to drug therapy. Parturition is classified as an aggravating factor (2).

Recently, we found that most patients with Graves' disease who were euthyroid under antithyroid maintenance therapy showed recurrence of thyrotoxicosis 2 months after an attack of allergic rhinitis (3). In this case, we were able to examine thyroid hormones and thyroid autoantibodies before the onset of thyrotoxicosis and 2 months after an attack of allergic rhinitis and found that allergic rhinitis induced the clinical onset of Graves' thyrotoxicosis. Moreover, TSAb was detected before the clinical onset of Graves' thyrotoxicosis. This is compatible with our previous study showing that patients who developed Graves' thyrotoxicosis after delivery had positive TSAb in early pregnancy (1). We have started to examine thyroid hormones and thyroid autoantibodies at the time of an attack of allergic rhinitis and 2 months later.

Allergic rhinitis is the most common symptom of type I hypersensitivity that is induced by many environmental allergens, especially in response to Japanese cedar (*Cryptomeria japonica*) pollen in Japan (6). In type I allergy, the great majority of allergen-specific T cell clones behaved like Type 2 Th cells (Th2) cells (7). Th2 cells produce IL-4, IL-5, IL-6, and IL-10, stimulating production of eosinophils, and IgE and IgG₁ antibodies (8). TSAb be-

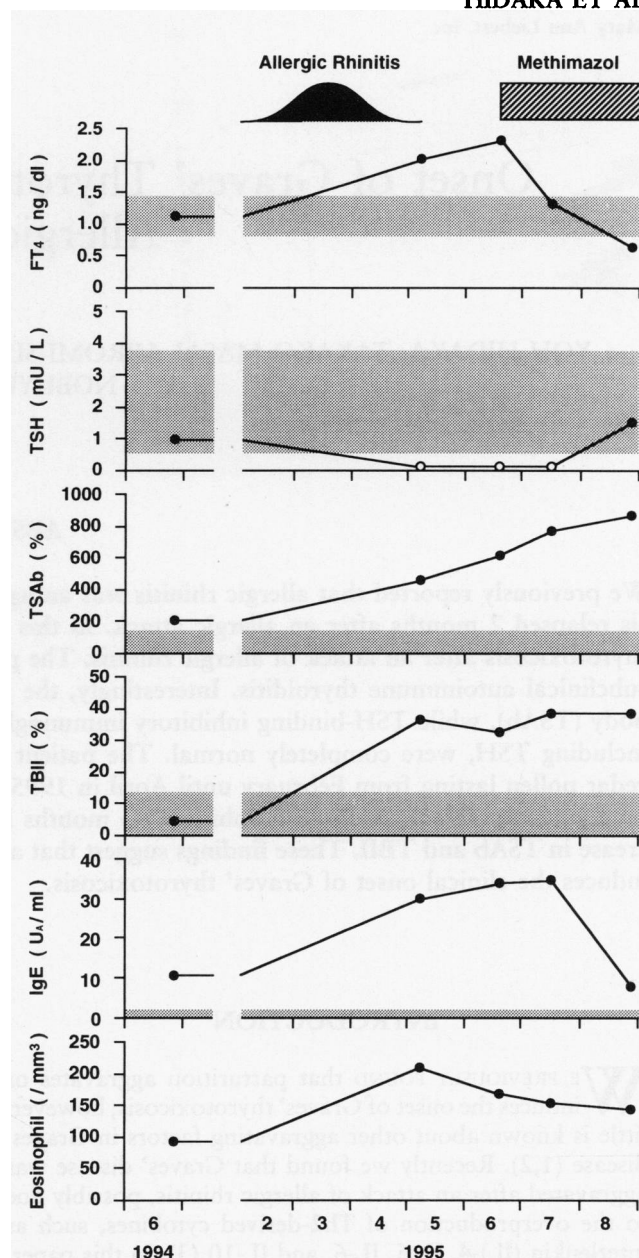


FIG. 1. Clinical course of a patient who developed Graves' thyrotoxicosis after an attack of allergic rhinitis. Serial changes in serum free T₄ (FT₄), TSH, thyroid-stimulating antibody (TSAb), TSH-binding inhibitory immunoglobulin (TBII), and immunoglobulin E (IgE) in response to Japanese cedar pollen and peripheral blood eosinophil count are shown. Normal ranges are expressed as the shaded area. Normal ranges of FT₄, TSH, TSAb, TBII, and IgE in response to Japanese cedar pollen are 0.8–1.4 ng/dL (10.3–18.0 pmol/L), 0.6–3.7 mU/L, less than 140%, less than 12%, and less than 0.7 unit allergen (UA)/mL, respectively. Open circles indicate less than 0.04 mU/L of TSH.

longs to IgG₁ subclass (9), suggesting Th2 cells may help to produce TSAb.

As in this case, the onset of Graves' thyrotoxicosis after an attack of allergic rhinitis could be predicted by measuring MCAb and then TSAb, just as in the prediction of postpartum Graves' thyrotoxicosis (1).

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