

IgE antithyroid microsomal antibodies in a patient with chronic urticaria

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Until recently, the majority of patients with chronic urticaria (CU) have been determined to be idiopathic. Despite the absence of an obvious etiology, it is widely accepted that mast cell degranulation followed by perivascular cellular infiltration underlies the characteristic manifestations of this condition. Recently, there have been several reports of an increased frequency of thyroid autoimmunity in patients with CU.^{1,2} It has been suggested that the affected patients may have an underlying autoimmune process directed both at thyroid antigens and at antigens involved in mast cell degranulation.^{3,4} However, the presence of antithyroid antibodies that may directly activate mast cells has not been demonstrated. We hereby describe a case of CU associated with the presence of IgE antithyroid antibody. This heretofore

Abbreviations used

CU: Chronic urticaria
TPO: Thyroid peroxidase

unrecognized finding may provide a possible explanation for the underlying pathogenic mechanism in some subjects with CU associated with thyroid autoimmunity.

CASE REPORT

A 26-year-old white woman was referred to our clinic for evaluation of prolonged intractable urticaria. The patient's medical history had been uneventful except for drug eruption, which occurred after taking amoxicillin 6 years before her present illness. Two months before her first visit, the patient began to have recurrent episodes of urticarial eruption, arthralgia, and sore throat. Penicillin VK was prescribed, and by the ninth day her urticaria flared up and did not abate. Daily flares of urticaria resistant to antihistamines were associated with exacerbation of arthralgia and were aggravated by exercise. Physical examination was unremarkable except for several urticarial lesions that were intensely pruritic and evidence of dermographism. Of note, thyroid size and texture were normal. Chest x-ray film and sinus computed tomography scans were normal. Skin prick test responses and RAST results for inhalant and

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food allergens were negative. Laboratory work-up revealed normal blood count with no eosinophilia. Blood chemistry, including electrolyte values and liver and renal function tests, were within normal limits. Complement levels (CH_{50} , C_3 , and C_4), were also normal. Serologic markers for recent exposure to EBV and hepatitis B and C were not detected. Serum IgA, IgG, and IgM levels were within normal limits, although IgE was found to be elevated (450 IU/mL). No antinuclear antibodies were detected. Antithyroid microsomal antibodies (antithyroid peroxidase [anti-TPO] antibody; DPC, Los Angeles, Calif) were found to be significantly elevated. Free thyroxine index, triiodothyronine, and thyroid-stimulating hormone levels were normal.

The concomitant findings of a high IgE level in the absence of a history of atopic diseases and antithyroid antibody led us to further investigate the possibility that IgE may be directed against the thyroid microsomal antigen (TPO). We have used the same ELISA kit to detect antimicrosomal antibody mentioned above, except that horseradish peroxidase-labeled mouse monoclonal anti-human IgE antibody (instead of anti-IgG) was used as a second antibody. In this system the patient's serum revealed an OD of 0.670, whereas OD in sera obtained from 8 atopic nonurticarial patients with high levels of IgE (>500 IU/mL) was 0.033 ± 0.004 , and in 10 healthy age- and sex-matched volunteers OD was 0.020 ± 0.004 . In 5 other patients with CU who were found to have antimicrosomal antibody without elevated levels of IgE (<250 IU/mL), OD was found to be 0.023 ± 0.003 .

The patient began a course of low-dose levothyroxine (50 to 100 $\mu\text{g/day}$), which was ineffective in improving the urticaria and therefore discontinued after 6 weeks.

DISCUSSION

The histopathologic findings in skin biopsy specimens of urticarial lesions obtained from patients with CU have been suggested to be compatible with the view that CU may be an autoimmune phenomenon, whereas transient urticaria has exogenous triggers.³ More recently it has been reported that a large fraction of patients with CU have antibody directed to Fc ϵ RI that is functional, and about 10% have anti-IgE antibodies.⁴ Several lines of evidence suggest a relationship between thyroid autoimmunity and the allergic response. Association has been reported between thyroid autoimmunity and CU,^{1,2}

immune complexes in some thyroid tissues from subjects with Graves' disease contain IgE, and mRNA levels for IL-4, a switch factor for IgE production, were found to be elevated in thyroid tissue from patients with Graves' disease with high titers of TPO autoantibodies.⁵ However, the pathophysiologic mechanism or mechanisms responsible for the skin lesions seen in these patients remains unknown. It has been suggested that the autoantibodies serve only as a marker of autoimmunity and that the proinflammatory cytokines that are involved in this condition decrease mast cell threshold to endogenous or exogenous stimulants.³ We hereby propose that in certain patients specific IgE autoantibodies may sensitize mast cells, which on encountering the specific circulating antigen (released as a result of thyroid damage), will degranulate. The suggested allergic mechanism that underlies the urticaria in this patient, may explain the lack of effectiveness of levothyroxine, which has been found to be beneficial in treating patients with CU with IgG anti-TPO antibody.³

Evidence for low concentration of TPO autoantibodies of the IgE class, in addition to the well-recognized IgG antibodies, has recently been reported in patients with autoimmune thyroid diseases.⁵ However, no pathophysiologic role has been attributed to these antibodies because of their low concentration. Thus the association between CU and thyroid autoimmunity in patients with high titers of specific IgE autoantibodies should be further investigated. However, as specified above, IgE anti-TPO antibodies were detected in 1 of 6 patients with CU. It may therefore be concluded that this finding is the exception and not the rule.

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Correction

In the June issue, in the article by Bar-Sela et al (Bar-Sela S, Reshef T, Mekori YA. IgE antithyroid microsomal antibodies in a patient with chronic urticaria. 1999;103:1216-7) the last 3 references were omitted.

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