

Association between Chronic Urticaria and Thyroid Autoimmunity: A Prospective Study Involving 99 Patients

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Key Words

Chronic urticaria · Thyroid autoimmunity

Abstract

Background: The association between chronic urticaria and thyroid autoimmunity has been a subject of debate. However, this link was suggested in studies searching thyroid microsomal antibodies (TMA), which are less sensitive and less specific than anti-thyroperoxidase antibodies, moreover these studies did not measure anti-TSH receptor antibodies, nor did they use a control group. As a consequence, the results of these studies are difficult to interpret. **Objective:** The aim of this study was to determine whether chronic urticaria is statistically associated with thyroid autoimmunity. **Methods:** In a prospective case-control study, we compared the frequency of thyroid autoantibodies in 45 patients with chronic urticaria and in 30 healthy adult volunteers; we also compared the frequency of chronic urticaria in 32 patients with thyroid diseases with thyroid autoantibodies and in 22 patients with thyroid diseases without thyroid autoantibodies. Thyroid autoantibodies and thyroid hormones were measured in all the subjects; antinuclear antibodies, rheumatoid factors, complement, IgE were assessed and routine laboratory tests were done in patients with chronic urticaria. Fisher’s exact statistics were used to test our hypothesis. **Results:** The frequency

of thyroid autoantibodies was significantly higher in patients with chronic urticaria than in healthy controls (26.7%/3.3%; $p < 0.01$). All the patients with thyroid autoantibodies had thyroid hormone concentrations within the normal limits. The frequency of chronic urticaria was not significantly different (12.5%/9.1%; $p = 0.7$) in patients with thyroid diseases with or without thyroid antibodies. The rest of the biological investigations revealed only 1 patient with connective tissue disease. **Conclusion:** This study shows a significant association between chronic urticaria and thyroid autoimmunity, and that tests to detect thyroid autoantibodies are relevant in patients with chronic urticaria, whereas extensive laboratory tests are not.

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Urticaria is a frequent dermatosis observed in 15–25% of the general population, and 25% of them suffer from chronic urticaria [1, 2]. The possible lethal risk of laryngeal angioedema, and the influence of chronic urticaria on the quality of life [3] make this disease a true public health concern. Its causes are numerous and oral antihistamines are the mainstay of drug treatment [4]. However, antihistamines are not always effective: 20% of treated patients exhibit symptoms 10 years after disease onset [5].

Previous reports showed that thyroid autoantibodies, such as antithyroglobulin (anti-TG) or antithyroperoxi-

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dase (anti-TPO) antibodies, could be found in some patients with chronic urticaria [6–11]. In one study [12], the frequency of chronic urticaria was higher in patients with thyroid diseases with thyroid antibodies than in patients without thyroid antibodies. In some instances, the treatment with thyroxine was found to be effective in chronic urticaria [13, 14]. These data suggest a relationship between chronic urticaria and/or angioedema and thyroid autoimmunity.

The aim of this study was to search for a statistical association between chronic urticaria and/or angioedema and thyroid autoimmunity. To determine whether there is a statistical association, we compared the frequency of thyroid autoantibodies in patients with chronic urticaria with those in healthy individuals. In addition, we compared the frequency of chronic urticaria and/or angioedema in two groups of patients with defined thyroid diseases, with and without thyroid autoantibodies.

Patients and Methods

Patients

We conducted a prospective case-control study during 12 months, from December 2000 to December 2001; 129 outpatients or inpatients of the University Hospital of Caen, France, were recruited to the study. They were divided into four groups according to clinical criteria. Group 1 consisted of 45 patients from the Dermatology Department treated for chronic urticaria and/or angioedema. Group 2 consisted of 30 healthy adult volunteers from the local blood bank, who had no history of urticaria or angioedema. Group 3 consisted of 32 patients who exhibited a thyroid disorder consisting of either a goiter or thyroid nodules and/or hypo- or hyperthyroidism, associated with thyroid autoantibodies – either anti-TG and/or anti-TPO and/or anti-TSH receptor (TSI) antibodies. Group 4 consisted of 22 patients with one of the previously mentioned thyroid disorders, without thyroid autoantibodies. Patients from groups 3 and 4 were recruited and diagnosed in the Endocrinology Department. Urticaria was defined as a papulo-oedematous, pruriginous, mobile, fugacious eruption lasting for a maximum of 24 h, and angioedema as an oedema involving the mucosa and deeper layers of the skin. Chronicity was defined as at least 3 crises a week for at least 6 weeks.

Patients who were under the age of 18, pregnant women and patients suffering from amiodarone-induced thyroid disorders were excluded from the study. All the patients received written and oral information about the purpose and special design of the study and gave their informed consent.

Methods

All the participants were examined and treated by the same dermatologist. In addition, all the biochemical analyses were performed by the same laboratory.

Inpatients of group 1, the investigations involved a medical anamnesis, a physical examination, measurement of blood pressure and a daily routine laboratory screening (haemoglobin, haematocrit, complete blood count, erythrocyte sedimentation rate, liver and kid-

ney function tests). CH50, C3, and C4 components of the complement system were evaluated by nephelometric measurements. Immunological tests included antinuclear antibodies (ANA) (Hep-2 cell, indirect immunofluorescence), anti-double- and anti-single-stranded DNA antibodies (dsDNA, ssDNA) (ELISA, Biomedical Diagnostics), anti-extractable nuclear antigens (ENA) (ELISA), IgM rheumatoid factors (RF) (ELISA), IgE antibodies directed against mixed food allergens (milk, egg, fish, wheat, peanut, soy, brewer's yeast, garlic, celery, sesame, kiwi, hazelnut, shrimp, banana) (Trophatop®; Pharmacia CAP System RIA) [1, 2, 4]. Assessment of thyroid function consisted in measuring the serum concentrations of the thyroid-stimulating hormone (TSH) using an immunoradiometric assay (DYNOTest TSH1; BRAHMS), free thyroxine (FT₄) by radioimmunoassay (RIA-FT₄; Immunotech, Beckman Coulter), anti-TG and anti-TPO antibodies by ELISA (TPO: Interchim; TG: Valbiotech; human anti-IgG antibodies: Caltag) and TSI by RIA (TRAK-Assay; BRAHMS). Skin biopsies of the urticarial lesions were performed for histologic examination and for direct immunofluorescence detection of vascular immunoglobulin deposits.

The subjects in group 2 were questioned; their medical history excluded previous urticaria. They were compared with patients of group 1. They were matched for sex and age with subjects of group 1. Anti-TG and anti-TPO were measured.

In groups 3 and 4, the patients were physically examined by a dermatologist and questioned about previous urticaria crises. The diagnosis of thyroid disease was made by an endocrinologist who also checked the presence (group 3) or absence (group 4) of anti-TG, anti-TPO and TSI. The patients were followed up for at least 1 year after their inclusion in the study, and asked to come to the University hospital in case of a possible urticarial skin eruption.

Statistical Analysis

This survey contains 4 mutually exclusive populations and deals with two independent questions: is there a link between chronic urticaria and the presence of thyroid autoantibodies? Is chronic urticaria more frequent in patients affected by autoimmune thyroid diseases than in those affected by non-autoimmune thyroid diseases?

Due to the qualitative nature of the variables and the relatively low number of subjects, bilateral Fisher's exact statistics were used for testing the prevalence of thyroid antibodies among the patients suffering from chronic urticaria (group 1) or not (group 2), and for the prevalence of chronic urticaria among patients suffering from thyroid disorders with thyroid antibodies (group 3) or without (group 4). The level of statistical significance was taken to be $p < 0.05$. We used Epi-Info® Release 6 from the CDC for calculation.

Results

Frequency of Thyroid Autoantibodies in Patients with Chronic Urticaria (Group 1) and in Healthy Controls (Group 2)

In patients of group 1 (table 1), urticaria crises were observed once a day, and 3 times a week in 31 and 14 patients, respectively. Angio-oedema was associated with urticaria in 15 patients and was never found alone in any patient. Urticaria crises were observed for 3 months to 15

years. Two patients did not receive any therapy. Antihistamines were active in 16 patients, and inefficient in 20 patients, among whom 8 had received oral corticosteroid therapy. All the patients had normal thyroid hormone concentrations (TSH = 0.1–5 mU/l; FT₄ = 11–22 pmol/l).

Table 1. Demographic description of the study patients

	Patients	Males	Females	Mean age years	Age range years
Group 1	45	10	35	43	18–71
Group 2	30	10	20	40	19–70
Group 3	32	2	30	43	20–68
Group 4	22	4	18	50	22–88

Table 2. Thyroid antibodies in patients with chronic urticaria (group 1)

Patient No.	Anti-TPO, IU/ml	Anti-TG, IU/ml	TSI, IU/ml
9	40	<25	<15
11	<25	200	<15
12	315	<25	<15
18	240	<25	<15
19	3,000	150	<15
22	526	<25	<15
23	<25	173	<15
32	<25	91	<15
33	70	200	<15
34	154	200	<15
43	<25	40	<15
44	315	106	<15
Normal values	<25	<25	<15

Skin biopsies were obtained from 29 patients. Histological findings were consistent with urticaria, except for one biopsy, which exhibited signs of vasculitis. The blood pressure test was positive in 4 patients.

Thyroid autoantibodies were detected in 12 of 45 patients (1 male, 11 female). Mean age was 49 years (range: 28–71 years). As shown in table 2, 4 out of these 12 patients exhibited anti-TPO antibodies alone, 4 of 12 anti-TG alone, and another 4 of 12 exhibited both. No patient exhibited TSI antibodies. Nine of 12 patients with thyroid autoantibodies had urticaria crises once a day. Crises were associated with angioedema in 5 of 12 patients, and were resistant to antihistamines in 6 of 12 patients. Urticaria activity and the characteristics of the patients were the same among patients with anti-TPO or anti-TG antibodies.

Only 1 healthy control in group 2 (table 1) had detectable anti-TPO antibodies (100 IU/ml), none had anti-TG antibodies.

The frequency of thyroid autoantibodies was significantly increased ($p < 0.01$) in patients with chronic urticaria in comparison with healthy controls (table 3).

In group 1, there is no statistically significant difference concerning the frequency of the crises ($p = 0.72$), the association of urticaria with angioedema ($p = 0.92$) and the resistance to antihistamines ($p = 0.65$) between the patients with and without thyroid autoantibodies.

Frequency of Chronic Urticaria in Patients with Thyroid Disease with (Group 3) and without (Group 4) Thyroid Autoantibodies

Four patients of group 3 (table 1) had a history of chronic urticaria, and 3 of these 4 presented with urticaria during the post-inclusion year.

Two patients of group 4 (table 1) had a history of chronic urticaria. One of them presented with urticaria during the post-inclusion year.

Table 3. Frequency of thyroid antibodies in groups 1 and 2, and frequency of chronic urticaria in groups 3 and 4

Patients	Group 1 chronic urticaria (n = 45)	Group 2 healthy controls (n = 30)	Group 3 thyroid disease with thyroid antibodies (n = 32)	Group 4 thyroid disease without thyroid antibodies (n = 22)
With thyroid antibodies	12 (26.7%)*	1 (3.3%)	32 (100%)	0 (0%)
With chronic urticaria	45 (100%)	0 (0%)	4 (12.5%)**	2 (9.1%)

* $p < 0.01$; odds ratio = 10.55; 95% CI = 1.28; 230 compared with group 2.
** $p = 0.7$; odds ratio = 1.43; 95% CI = 0.19; 12.61 compared with group 4.

Table 4. Abnormal values of complement (CH50, C3, C4), ANA and RF in patients of group 1

Patient No.	Immunological investigations ¹							RF IU
	complement			antinuclear antibodies				
	CH50 IU/ml	C3 mg/ml	C4 mg/ml	ANA	dsDNA AU	ssDNA AU	ENA	
1	48	48	N	1/1280	N	450	pos.	50
2	58	N	N	1/1280	N	N	neg.	23
3	N	N	N	1/1280	N	N	neg.	N
4	N	N	N	1/320	N	N	n.d.	N
5	56	N	N	1/160	N	N	neg.	N
6	51	N	N	N	N	N	neg.	N
7	N	N	N	1/160	N	N	n.d.	17
9	N	N	N	1/160	N	N	n.d.	N
43	N	N	N	1/320	N	350	n.d.	N
44	N	N	N	1/320	N	N	n.d.	n.d.
Normal values	70–140	750–1,400	100–340	>1/80	<100	<200		<10

N = Normal; n.d. = not done; pos. = positive (anti-SSA/Ro+SSB/La); neg. = negative; ENA = anti-extractable nuclear antigen; RF = rheumatoid factor; AU = arbitrary units; IU = international units.
¹ Except for antithyroid antibodies.

The frequency of chronic urticaria was not significantly different ($p = 0.7$) between patients with autoimmune thyroid disease and patients with thyroid disease without thyroid autoantibodies (table 3).

Other Biological, in Particular Immunological Investigations

Further immunological investigations of patients in group 1 showed abnormal values of CH50, C3, C4 and/or antinuclear antibodies (ANA) and/or RF in 10 of 45 patients (table 4). Among these 10 patients, 9 had positive ANA, 4 ad a moderate decrease of CH50, 3 had positive RF, and 3 (No. 9, 43, 44) also had thyroid autoantibodies. This immunological assessment and the clinical findings led to the diagnosis of Gougerot-Sjögren syndrome in patient 1. No patient had specific IgE against food allergens.

Blood cell counts and erythrocyte sedimentation rate were abnormal in 1 of 45 patients, i.e. the patient with Gougerot-Sjögren syndrome.

Comment

The association between chronic urticaria and thyroid has been a subject of controversy. Some reports link chronic urticaria with hyperthyroidism [15] or hypothy-

roidism [16]. In France, thyroid hormones are often routinely assayed in patients with chronic urticaria [17]. More recently, some studies have suggested that there may be a link between chronic urticaria and thyroid autoimmunity [6–11]. However, this link was assumed in studies searching TMA, which are less sensitive and less specific than anti-TPO antibodies [6, 8, 9]; moreover these studies did not measure TSI antibodies [6, 8–10], nor did they use a control group [6, 10, 11]. As a consequence, the results of these studies are difficult to interpret. For these reasons, we performed this case-control study and measured all the thyroid autoantibodies (anti-TG, anti-TPO and TSI antibodies). In order to evaluate the role of autoimmune disorders in chronic urticaria and to exclude connective tissue diseases among our patients with chronic urticaria and thyroid antibodies, we measured other autoantibodies, such as ANA, DNA, ENA, RF, and determined the level of CH50, C3, and C4.

We detected thyroid autoantibodies in 26.7% of patients with chronic urticaria. This result is consistent with previous studies (table 5) in which thyroid autoantibodies were present in 12–33% of the patients with chronic urticaria [6, 8–11]. The frequency of thyroid antibodies in the control group was 3.3%, which compares with the frequency of TG and TPO or TMA antibodies (0–5.6%) in previous studies [8, 9]. Our study shows that, in patients with chronic urticaria, the frequency of thyroid autoanti-

Table 5. Frequency of thyroid antibodies in patients with chronic urticaria, according to the literature

	Patients		Thyroid antibodies, %		Thyroid antibodies studied	
	chronic urticaria	healthy controls	chronic urticaria	healthy controls	chronic urticaria	healthy controls
Leznoff et al., [8]	140	427	12.1	5.6	TMA	TMA
Leznoff and Sussman [6]	624		14		TMA+TG	
Turkas et al., [9]	94	80	11.7	3.7	TG	TG
Turkas et al., [9]	94	80	9.57	3.7	TMA	TMA
Gaig et al., [10]	170		14.7		TG+TPO	
Zauli et al., [11]	70		33		TG+TPO+TSI	
Zauli et al., [11]	52		23		TG+TPO+TSI	
Ryhal et al., [25]	25	75	20	0	TG+TPO	
Present study	45	30	26.7	3.3	TG+TPO+TSI	TG+TPO

bodies (26.7%) is significantly higher ($p < 0.01$) than the 3.3% frequency in the control group, demonstrating a statistical association between chronic urticaria and anti-TPO and/or anti-TG antibodies.

However, TSI were not detected in our study, while Zauli et al. [11] found them in 2 of 70 patients with ‘chronic urticaria of known cause’ and in 1 of 52 patient with ‘idiopathic chronic urticaria’. These results suggest that TSI are not commonly found in chronic urticaria. TSI are found primarily in patients with Graves’ disease, whereas anti-TG or anti-TPO antibodies are usually found in patients with Graves’ disease or Hashimoto’s thyroiditis [18]. Among our patients, we diagnosed 4 cases of Hashimoto’s thyroiditis and 3 cases of thyroid nodules. Five patients had thyroid autoantibodies without thyroid disease and no Graves’ disease was noted. Our results confirmed a previous study [6], showing that chronic urticaria was more frequently associated with Hashimoto’s thyroiditis than with Graves’ disease.

In accordance with previous reports [6–11], all the patients with thyroid autoantibodies, had normal thyroid hormone concentrations.

In agreement with previously reported studies, a female prevalence was noted for urticaria with thyroid autoantibodies; therefore, it would seem to be interesting to test for antithyroid autoimmunity particularly in women [6, 7, 11]. In our patients with chronic urticaria with thyroid antibodies, chronic urticaria was not more severe than in those without thyroid antibodies based on the frequency of crises, the association with mucosal angioedema and histamine resistance.

To strengthen our hypothesis of a link between chronic urticaria and thyroid autoimmunity, we also compared

the frequency of chronic urticaria in patients with thyroid diseases with (group 3) and without (group 4) antibodies. We found 12.5% and 9.1% of patients with chronic urticaria, respectively, but no significant difference in the frequency of chronic urticaria between the two groups. Our results differ from those of Lanigan et al. [12], who found 14 of 50 patients (28%) with chronic urticaria in the group of autoimmune thyroid diseases versus 2 of 50 patients (4%) with non-autoimmune thyroid diseases. However, these results could be overestimated, because in their study, the diagnosis of chronic urticaria was based on the anamnesis and no eruption was certified by a dermatologist. We did not find a significant increase in the frequency of chronic urticaria in the group with autoimmune thyroid disease compared with the group with non-autoimmune thyroid disease, but this may be due to the low statistical power of these groups. However, chronic urticaria seems to be more frequent in patients with thyroid pathologies, both with and without antibodies, than in the general population, where it is estimated at 4 – 6% [2].

Standard biochemical tests excluded other aetiologies of chronic urticaria among our patients with chronic urticaria and thyroid antibodies, and confirmed the findings of Kozel et al. [19], who demonstrated that laboratory investigations were necessary for the aetiologic assessment of chronic urticaria only depending on the clinical context. Among the patients without thyroid autoantibodies in group 1, immunological tests have only revealed a Gougerot-Sjögren syndrome. This represents 2.2% of the patients with chronic urticaria in our study, a figure similar to that reported in the literature [20]. 8.8% of our patients had a moderate decrease in CH50 activity. None of them had a family history of chronic urticaria. Previous

studies [21, 22] found 10–13.8% of patients with a decrease in complement but especially, in the study by Passeron et al. [23], complement components in a group of chronic urticaria patients were not different from those in a group of healthy individuals. We found that 20% of patients had significant ANA levels. In the studies by Turkas et al. [9] and Sibbald et al. [24], ANA were present in 5.3 and 15% of the cases. However, Ryhal et al. [25] did not find more ANA in patients with chronic urticaria than in a control group. Therefore, extensive immunological tests are unnecessary and should only be carried out if routine laboratory tests are abnormal and in a clinical context.

The mechanism linking thyroid autoimmunity with chronic urticaria remains obscure.

Our work shows that anti-TG and anti-TPO antibodies are found statistically significantly more frequently in

patients with chronic urticaria than in the general population. These results suggest the need systematically for including anti-TG and anti-TPO antibodies in the assessment of chronic urticaria and/or angioedema, particularly in women, but the measurement of TSI seems to be less relevant, since no abnormalities were found. Based on a literature review, Zauli et al. [26] suggested to screen for serum thyroid antibodies and thyrotropin levels, especially in women, and in patients with thyroid autoimmune disease of any type. Based on our results and the literature, we think that it is indicated to search for thyroid antibodies in chronic urticaria. Moreover, it would probably be interesting to try a thyroid hormone therapy, if the usual treatment with antihistaminics is ineffective in patients with chronic urticaria with thyroid antibodies, as suggested in some studies [10, 13, 14].

References

- Leznoff A: Chronic urticaria. *Can Fam Physician* 1998;44:2170–2176.
- Sharma JK, Miller R: Chronic urticaria: Review of the literature. *J Cutan Med Surg* 1999; 3:221–228.
- O'Donnell BF, Lawlor F, Simpson J, Morgan M, Greaves M: The impact of chronic urticaria on the quality of life. *Br J Dermatol* 1997;136: 197–201.
- Grattan CE, Sabroe RA, Greaves MW: Chronic urticaria. *J Am Acad Dermatol* 2002; 46:645–657.
- Ormerod AD: Urticaria and angioedema. *Br Med J* 1984;289:903–906.
- Leznoff A, Sussman GL: Syndrome of idiopathic chronic urticaria and angioedema with thyroid autoimmunity: A study of 90 patients. *J Allergy Clin Immunol* 1989;84:66–71.
- Collet E, Petit JM, Lacroix M, Bensa AF, Morvan C, Lambert D: Urticaire chronique et pathologie thyroïdienne auto-immune. *Ann Dermatol Vénéréol* 1995;122:413–416.
- Leznoff A, Josse RG, Denburg J, Dolovich J: Association of chronic urticaria and angioedema with thyroid autoimmunity. *Arch Dermatol* 1983;119:636–640.
- Turktas I, Gokcora N, Demirsoy S, Cakir N, Onal E: The association of chronic urticaria and angioedema with auto-immune thyroiditis. *Int J Dermatol* 1997;36:187–190.
- Gaig P, Garcia-Ortega P, Enrique E, Richart C: Successful treatment of chronic idiopathic urticaria associated with thyroid autoimmunity. *J Invest Allergol Clin Immunol* 2000;10:342–345.
- Zauli D, Deleonardi G, Foderaro S, Grassi A, Bortolotti R, Ballardini G, et al: Thyroid autoimmunity in chronic urticaria. *Allergy Asthma Proc* 2001;22:93–95.
- Lanigan S.W, Short P, Moul P: The association of chronic urticaria and thyroid autoimmunity. *Clin Exp Dermatol* 1987;12:335–338.
- Rumbyrt JS, Katz JL, Schocket AL: Resolution of chronic urticaria in patients with thyroid autoimmunity. *J Allergy Clin Immunol* 1995; 96:901–905.
- Delèvaux I, André M, Tridon A, Aumaître O: Urticaire chronique et thyroïdite de Hashimoto: à propos de six cas. *Rev Méd Interne* 2001; 22:232–237.
- Mullin GE, Eastern JS: Cutaneous signs of thyroid disease. *Am Fam Physician* 1986;34:93–98.
- Lanigan SW, Adams JS, Gilkes JJH, Robinson TWE: Association between urticaria and hypothyroidism. *Lancet* 1984;i:1476.
- Crickx B: Quel bilan faire devant une urticaire chronique de l'adulte? *Ann Dermatol Vénéréol* 1993;120:652–656.
- Guillausseau C, Eyquem A, Vincens M, Laurent MF, Leger AF, Savoie JC: Intérêt de la détection des anticorps antithyroïdiens en pathologie thyroïdienne. *Pathol Biol* 1985;33: 653–658.
- Kozel MMA, Mekkes JR, Bossuyt PMM, Bos JD: The effectiveness of a history-based diagnostic approach in chronic urticaria and angioedema. *Arch Dermatol* 1998;134:1575–1580.
- Nürnberg W, Henz BM: Urticarial vasculitis syndrome; in Henz MB, Zuberbier, Grabbe, Monroe E (eds): *Urticaria*. Berlin, Springer, 1998, pp 115–124.
- Mathison DA, Arroyave CM, Bhat KN, Hurewitz DS, Marnell DJ: Hypocomplementemia in chronic idiopathic urticaria. *Ann Intern Med* 1977;86:534–538.
- Small P, Barrett D, Biskin N, Champlin E: Chronic urticaria and angioedema. *Clin Allergy* 1982;12:131–136.
- Passeron T, Bahadoran P, Pugliese P, Lacour JP, Ortonne JP: Lack of hypocomplementemia in chronic urticaria. *Arch Dermatol* 2000;136: 558–559.
- Sibbald RG, Cheema AS, Lozinski A, Tarlo S: Chronic urticaria. Evaluation of the role of physical, immunologic and other contributory factors. *Int J Dermatol* 1991;30:381–386.
- Ryhal B, DeMera RS, Shoenfeld Y, Peter JB, Gershwin ME: Are autoantibodies present in patients with subacute and chronic urticaria? *J Investig Allergol Clin Immunol* 2001;11:16–20.
- Zauli D, Grassi A, Ballardini G, Contestabile S, Zucchini S, Bianchi FB: Thyroid autoimmunity in chronic urticaria. Implications for therapy. *Am J Clin Dermatol* 2002;3:525–528.