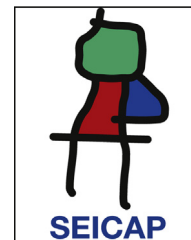




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ORIGINAL ARTICLE

Hashimoto's disease is a frequent comorbidity and an exacerbating factor of chronic spontaneous urticaria



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Abstract

Background: The precise pathogenesis of chronic spontaneous urticaria (CSU) remains unknown. However, an important association between CSU and autoimmune disorders such as Hashimoto's disease (HD) has been reported.

We investigated the frequency of HD as a comorbidity of CSU and the prevalence rate of autoreactivity among CSU patients with HD.

Patients and methods: The presence of thyroid autoantibodies and the levels of thyroid hormones were examined in 40 CSU patients who showed urticaria symptoms for >4 weeks. Patients who were diagnosed with HD, including subclinical ones, and were in need of treatment received thyroid therapy, and the changes in their urticarial symptoms were observed. An autologous serum skin test (ASST) was also performed to examine the relation of CSU with autoreactivity. **Results:** Eleven of the 40 CSU patients were diagnosed with HD, and 4 of the 5 patients who received and completed thyroid therapy showed considerable remission of urticarial symptoms during and after treatment. In addition, the rate of positive ASST results tended to be higher in CSU patients with HD (5 of 7) than in those without HD (2 of 6).

Conclusions: The comorbidity rate of HD in CSU patients was high, and such patients tended to have a positive ASST. Thyroid therapy in CSU patients with HD can lead to a considerable remission of urticarial symptoms, which may suggest that HD is possibly involved in the aetiology of CSU, or is at least a potential exacerbating factor for CSU.

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Introduction

Chronic spontaneous urticaria¹ (CSU) is a common disorder; however, its precise pathogenesis remains unknown. Some reports have suggested that approximately 30–50% of CSU shows autoreactivity.^{2–6} More interestingly, various autoimmune disorders have been associated with CSU,⁷ such as Hashimoto's disease (HD), one of the most frequent forms of autoimmune thyroiditis. According to previous reports,^{8–21} 12–37% (median, 26%) of chronic urticaria patients have thyroid autoantibodies (see Table 1). In some cases, the existence of thyroid disease can be identified simply by the presence of aberrant thyroid hormone levels. However, it is necessary to examine thyroid autoantibody and thyroid hormone levels to fully detect HD because many patients with HD have normal hormone levels without legible clinical symptoms except for the presence of thyroid autoantibodies and slight goitre (swelling of the thyroid gland). HD develops gradually over several years and the patient's levels of thyroid hormones gradually decrease from the baseline levels in each individual. Thus, many HD patients have no symptoms and normal hormone level in their early disease stage and do not have diagnosis of HD among general population, but such subclinical HD patients are recommended watchful waiting.

In this study, the comorbidity rate of HD (or thyroid autoimmunity) in CSU patients and the possible influence of thyroid therapy on urticarial symptoms in Department of Dermatology, Fukuoka National Hospital, National Hospital Organization were examined. The frequency of autoreactivity among CSU patients with HD was also investigated.

Patients and methods

The levels of free thyroxine (T4), thyroid-stimulating hormone (TSH), anti-thyroglobulin (Tg) antibody, and anti-thyroid peroxidase (TPO) antibody were examined in serum samples from 40 CSU patients (6 men and 34 women; age range, 17–67 years; median, 55 years), including the cases 1 and 2 described below, who had visited the Department of Dermatology, Fukuoka National Hospital, National Hospital

Table 1 Reported positive rates of thyroid autoantibodies among CSU patients.

Authors	TAA positive (%)	Publication year
Leznoff et al.	17/140 (12%)	1983
Leznoff et al.	90/624 (14%)	1989
Collet et al.	8/45 (18%)	1997
Turktas et al.	17/94 (18%)	1997
Gaig et al.	25/170 (15%)	2000
Zauli et al.	35/122 (29%)	2001
Asero et al.	66/257 (26%)	2003
Verneuil et al.	12/45 (27%)	2004
Toubi et al.	17/129 (12%)	2004
Palma-Carlos et al.	16/56 (29%)	2005
Faridhosseni et al.	22/60 (37%)	2006
Cebeci et al.	41/140 (29%)	2006
Gargemis et al.	31/95 (33%)	2009

TAA, thyroid autoantibodies.

Table 2 Severity of CSU symptoms.

Levels of severity	Symptom
6	Shock or similar to shock
5	Cannot manage a social life
4	Manage to live with large difficulties
3	Tolerable but uncomfortable
2	Mild symptoms
1	Symptoms is not recognized

Organization during a period from June, 2010 to March, 2012 and agreed to the tests.

When either abnormal hormone levels or antithyroid antibodies were detected, subjects were sent to endocrinologists for the diagnosis of HD. HD was diagnosed if subjects were antithyroid antibody positive and had goitre of any degree according to the diagnosis criteria of HD.²² HD patients with normal thyroid hormone levels do not necessarily become a target of the treatment. However, thyroid therapy (oral thyroid hormone replacement therapy for three months) was offered for such HD patients as well as those with abnormal hormone levels according to their consent since we previously experienced a CSU patient with highly suspected HD (as being negative for conventional thyroid autoantibodies but with significantly abnormal hormone levels) who showed remarkable improvement of his intractable CSU symptoms after thyroid therapy (data not shown). Meanwhile, HD patients did not receive thyroid therapy when the endocrinologists judged that thyroid therapy was not required. Triiodothyronine was used as treatment for HD since it acts on the thyroid gland directly and shows therapeutic effects in a shorter time than thyroxine.²³ The changes in their urticarial symptoms were carefully observed during and after the thyroid therapy. We assessed the severity of CSU symptoms using Japanese Guidelines for Diagnosis and Treatment of Urticaria^{24,25} (Table 2). An autologous serum skin test (ASST) was also performed according to standard methodology⁷ on 13 of the 40 CSU patients who provided consent for checking if their intractable urticaria was of the autoreactive type. Diagnosis criteria of ASST in the current study were based on those of the National Hospital Organization Sagamihara National Hospital, as shown in Table 3. ASST was basically conducted under treatment with antihistamines; however, medication of antihistamines was temporarily suspended for more than three days prior to retest for those with negative results according to the subject consent.

Table 3 Diagnosis criteria of autologous serum skin test from "The practical side of allergy test and immunotherapy" compiled under the supervision of Dr. Kazuo Akiyama at National Hospital Organization Sagamihara National Hospital.

	Wheal (mm)	Flare (mm)
Negative (–)	0–5	0–9
Pseudo-positive (±)	6–8	10–19
Positive (+)	9–15	20–39
Strong positive (2+)	Over 16	Over 40

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