

LETTER TO THE EDITOR

Prevalence and predictors of hypothyroidism in patients with chronic spontaneous urticaria

Dear Editor,

Chronic spontaneous urticaria (CSU) has been associated with autoimmune hypothyroidism.¹ Elevated levels of thyroid peroxidase IgG-autoantibodies (TPO-Ab) and thyroglobulin IgG-autoantibodies (TG-Ab) are found in a large proportion of patients with CSU² and international guidelines recommend including TPO-Ab in the basic diagnostic workup.³ The clinical impact of concomitant hypothyroidism and antithyroid autoantibodies (AABs) in patients with CSU is, however, unknown. We therefore explored clinical characteristics and predictors of hypothyroidism in patients with CSU.

In total 607 consecutive, newly referred, adult patients with CSU from a dermatological university department were interviewed about the presence of previously diagnosed thyroid disease, chronic inducible urticaria (CIndU), angioedema and patient reported outcomes (PROs) were collected. The following biochemical markers were obtained: basophil histamine release assay (BHRA), total IgE, thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), TPO-Ab and TG-Ab.

Known thyroid disease was present in 61 patients (10.1%), of whom 41 had hypothyroidism (6.8%), 10 had hyperthyroidism (1.6%) and 10 had other thyroid diseases (1.6%). Furthermore, 16 patients (2.5%) without known thyroid disease had altered TSH levels (4 elevated, 12 lowered) but normal T3 and T4, which may suggest undiagnosed subclinical thyroid disease.

Patients with CSU and known hypothyroidism were more likely to be women (87.8% vs. 69.2%, $p=0.012$), older in age (45 vs. 35 years, $p<0.001$), have later onset of CSU (40 vs. 30 years, $p<0.001$), and less likely concomitant CIndU (12.2 vs. 26.4%, $p=0.042$), compared with CSU patients without thyroid disease. No significant differences were found for angioedema and urticaria duration.

Biochemically, CSU patients with known hypothyroidism were more likely to have positive BHRA (25.6 vs. 11.6%, $p=0.021$), elevated TSH (12.2 vs. 0.7%, $p<0.001$), elevated TPO-Ab (65.2 vs. 10.1%, $p<0.001$) and elevated TG-Ab (54.5 vs. 11.2%, $p<0.001$) (Table 1). Median levels of T4 were higher (115 vs. 94 nmol/L, $p<0.001$) and total IgE levels were lower (34 vs. 73 kIU/L, $p=0.002$).

No significant correlations were found between TPO-Ab and PROs. In CSU patients with hypothyroidism, TPO-Ab correlated negatively with T4 ($r=-0.57$, $p=0.01$). For CSU patients without thyroid disease TPO-Ab correlated positively with the degree of

basophil activation in BHRA ($r=0.13$, $p=0.024$). For both groups, TPO-Ab correlated positively with TSH (patients with hypothyroidism: $r=0.53$, $p=0.10$, patients without thyroid disease: $r=0.24$, $p<0.001$) and TG-Ab (patients with hypothyroidism: $r=0.50$, $p=0.18$, patients without thyroid disease: $r=0.38$, $p<0.001$).

Our study showed that hypothyroidism is present in approximately 7% of CSU patients and associated with clinical and biochemical features consistent with autoimmune CSU (type IIb).⁴ Concomitant treatment with thyroid hormone substitution may diminish differences in PROs and biochemical parameters. However, previous studies on the efficacy of thyroid drugs on CSU symptoms have yielded inconsistent results.² Our findings may assist physicians in treating patients with CSU and hypothyroidism as type IIb CSU is usually more refractory to treatment compared with type I CSU. Furthermore, it is clinically relevant to assess and monitor symptoms and biochemical parameters of thyroid disease in patients who fit these characteristics but without known hypothyroidism.

AUTHOR CONTRIBUTION

NHP contributed to data curation, formal analysis, administration, and writing original paper. DGZ contributed to data curation, formal analysis, investigation, methodology, and review. JAS contributed to data curation, investigation, methodology, and review. CV contributed to methodology, review, and supervision. KB contributed to methodology, review, and supervision. MNG contributed to methodology, review, and supervision. SFT contributed to conceptualization, funding, methodology, investigation, project administration, resources, supervision, and review/editing. All authors have read and approved the final manuscript.

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None.

CONFLICT OF INTEREST STATEMENT

Katrine Baumann is a part-time employee of RefLab ApS. The other authors have nothing to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TABLE 1 Clinical and biochemical characteristics of CSU patients with diagnosed hypothyroidism compared with CSU patients without known thyroid disease.

	Chronic spontaneous urticaria patients		
	With hypothyroidism (n = 41)	Without thyroid disease (n = 546)	P-value ^m
Clinical characteristics			
Sex, n (%)			
Female	36 (87.8)	377 (69.2)	0.012
Male	5 (12.2)	168 (30.8)	
Age (years), median (min-max)	45 (27–81)	35 (18–91)	<0.001
Age onset (years), median (min-max)	40 (17–78)	30 (0–89)	<0.001
Disease duration (years), median (min-max)	1 (0–44)	1 (0–69)	0.961
CIndU, n (%)	5 (12.2)	144 (26.4)	0.042
Angioedema, n (%)	23 (56.1)	240 (44.0)	0.134
PROs, median (min-max)			
^a UAS7	21 (0–42)	24 (0–42)	0.311
^b UCT	6 (0–15)	5 (0–16)	0.938
^c DLQI	7 (0–25)	8 (0–30)	0.542
^d VAS	7.3 (0–10)	7 (0–10)	0.461
Biochemistry			
^e TSH (10 ^{−3} IU/L), median (min-max)	1.4 (0.0–19.8)	1.4 (0.0–9.0)	0.298
Elevated TSH, n (%)	5 (12.2)	4 (0.7)	<0.001
Lowered TSH, n (%)	13 (31.7)	12 (2.3)	<0.001
^f T3 (nmol/L), median (min-max)	1.9 (1.3–4.5)	1.8 (0.8–2.8)	0.440
^g T4 (nmol/L), median (min-max)	115 (85.0–157.0)	94 (12.2–158.0)	<0.001
^h Elevated TPO-Ab (kIU/L), n (%)	15 (65.2)	31 (10.1)	<0.001
ⁱ Elevated TG-Ab (kIU/L), n (%)	12 (54.5)	34 (11.2)	<0.001
^j Positive BHRA, n (%)	10 (25.6)	61 (11.6)	0.021
^k Total IgE (10 ^{−3} IU/L), median (min-max)	34 (1.0–598.0)	73 (1.0–12800.0)	0.002
^l Lowered IgE (10 ^{−3} IU/L), n (%)	22 (56.4)	164 (31.2)	0.001

^aUrticaria Activity Score over the past 7 days.

^bUrticaria Control Test.

^cDermatology Life Quality Index.

^dVisual Analogue Scale.

^eData were available for 565 patients (with hypothyroidism n = 41, without thyroid disease n = 524).

^fData were available for 41 patients (with hypothyroidism n = 9, without thyroid disease n = 32).

^gData were available for 293 patients (with hypothyroidism n = 19, without thyroid disease n = 274).

^hData were available for 331 patients (with hypothyroidism n = 23, without thyroid disease n = 308).

ⁱData were available for 325 patients (with hypothyroidism n = 22, without thyroid disease n = 303).

^jData were available for 510 patients (with hypothyroidism n = 36, without thyroid disease n = 474).

^kData were available for 545 patients (with hypothyroidism n = 39, without thyroid disease n = 506).

^lData were available for 564 patients (with hypothyroidism n = 39, without thyroid disease n = 525). Lowered IgE levels are defined by IgE levels <40 · 10⁻³ IU/L.⁵

^mThe Mann–Whitney U statistical test was used to compare medians of nonparametric data from two unpaired groups.

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