

Report

Comparison of chronic autoimmune urticaria with chronic idiopathic urticaria

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Abstract

Background Chronic urticaria has been described in patients with *Helicobacter pylori* infection. Despite numerous studies, the correlation between *H. pylori* infection and chronic urticaria is doubtful. Our study was performed to determine the prevalence of *H. pylori* infection in autoimmune urticaria and in patients suffering from autoimmune urticaria and autoimmune thyroiditis

Methods The authors widely investigated 48 patients. The examinations were extended principally to autologous serum skin test, antithyroid antibodies, and the presence of *H. pylori* infection as well as detection of antibodies against *H. pylori*.

Results Out of the 48 patients, 26 were regarded as having autoimmune origin. The prevalence of antithyroid antibodies was different in the two groups of patients with urticaria. There were 11 patients (42.3%) in the autoimmune group compared with three patients (13.6%) in the nonautoimmune group with antithyroid peroxidase antibody ($P = 0.03$). The difference in the prevalence of *H. pylori* infection was significant between autoimmune urticaria with and without thyroid autoimmunity (90.9% vs. 46.7%; $P = 0.02$). Autoimmune thyroiditis was connected with CagA + *H. pylori* strains, as the *H. pylori*-specific IgG antibodies revealed significant differences in a prevalence of 120 kDa ($P < 0.05$).

Conclusions The authors observed a relationship between autoimmune urticaria and autoimmune thyroiditis. The results strengthen the possibility of cross-reactivity being triggered between CagA plus *H. pylori* strains and some other organ-specific autoimmune diseases such as autoimmune urticaria and autoimmune thyroiditis. This indicates a possible role of *H. pylori* in triggering autoimmune urticaria in at least a select group of patients.

Introduction

Chronic idiopathic urticaria is one of the enigmas of dermatology. In the past 10 years, two possibilities have been put forward to explain its nature: *Helicobacter pylori* and the autoimmune origin. It has been pointed out that chronic urticaria can be of autoimmune origin in approximately 30–50% of the cases.^{1–3} Skin testing with autologous serum is a reasonably sensitive and specific marker of histamine-releasing activity on basophils.⁴ It is widely used for the diagnosis of chronic autoimmune urticaria. Urticaria can assume a more severe form, but patients with autoimmune urticaria exhibit no distinctive clinical features.⁵

We compared patients with autoimmune urticaria and patients with nonautoimmune urticaria by means of clinical and laboratory investigations. Our aim was to find a relationship between thyroid autoimmunity and infection with *H. pylori* as a causal factor in autoimmune urticaria.

Patients and Methods

Forty-eight patients (30 women and 18 men, 14–75 years of age; mean: 40.8 ± 16.4 years) with chronic urticaria were investigated. They had no food allergy or intolerance, contact allergy, bacterial focus or parasitic infection, physical urticaria, urticarial vasculitis, hypocomplementemic urticaria, or polysystemic autoimmune diseases. The duration of symptoms ranged between 2 and 240 months (mean 18.4 ± 19.1).

We performed an autologous serum test: 0.1 mL of autologous serum and autologous serum diluted with 1 : 1 physiological saline were administered to the patients' forearms (flexor sides). The reaction was examined after 30 min. A wheal with a diameter of at least 1.5 mm greater than that of a control wheal induced with saline solution was accepted as positive.⁵ As concerns the thyroid function: thyroxine (free T4), thyroid-stimulating hormone (TSH), and antithyroid peroxidase antibody (TPO) levels were investigated. Free T4 and TSH were measured by microparticle enzyme

immunoassay (MEIA; Abbott Laboratories, IL, USA) and TPO by sequential immunometric assay with an IMMULITE Analyzer (DPC, UK).

All patients underwent gastroscopy and urease testing. None had dyspeptic symptoms in their history or during the observation period, and only mild gastritis was seen on endoscopy. *Helicobacter pylori*-specific IgG determination and immunoblotting for the detection of antibodies (IgG) against *H. pylori* were performed by RIDA® (R-Biopharm GmbH, Darmstadt, Germany) with the following molecular weights: 120 kDa (CagA), 87 kDa (VacA), 67 kDa (OMP 67), 62 kDa (urease B), 58 kDa (heat-shock protein), 54 kDa (flagellin), 47 kDa, 33 kDa, 29 kDa (urease H), 28 kDa (hcpA: *H. pylori* cysteine-rich protein A), 25 kDa (urease D), and 19 kDa.

Fisher's exact test was applied to compare the prevalence of thyroid autoimmunity and *H. pylori* infection in the two study groups. Analysis of variance between the values of basophil cells and IgE were estimated with the Mann-Whitney test. $P \leq 0.05$ was considered statistically significant.

Results

The 48 patients with urticaria were divided into two subgroups based on the autologous serum test. The autologous serum test was positive in 26 patients (54.2%): 16 women and 10 men (autoimmune group). The autologous serum test was negative in 22 patients (45.8%): 13 women and nine men (nonautoimmune group).

The basophil cell count was $0.030 \pm 0.012 \times 10^9/L$ in the autoimmune group, and was $0.046 \pm 0.011 \times 10^9/L$ in the nonautoimmune group: the difference was significant: $P = 0.001$. The IgE level was 175.7 ± 196.7 IU/mL in the autoimmune group, and 213.2 ± 237.9 IU/mL in the nonautoimmune group, but the difference was not significant (Table 1). We found no difference in the prevalence of *H. pylori* infection between the two groups. On the basis of the urease test, histology and *H. pylori*-specific-IgG, 17 of the 26 autoimmune cases (65.4%) and 13 of the 22 nonautoimmune cases (59.1%) were infected with *H. pylori*.

Table 1 Characteristics of patients with chronic autoimmune urticaria and chronic nonautoimmune urticaria

Characteristics	Autoimmune (n = 26)	Nonautoimmune (n = 22)	P
Age	46.5 ± 18.6	36.1 ± 18.9	0.03*
Basophil cell count (G/L)	0.030 ± 0.012	0.046 ± 0.011	0.001*
Total IgE (IU/mL)	175.7 ± 196.7	213.2 ± 237.9	NS
Infected with <i>H. pylori</i> (n/%)	17 (65.4%)	13 (59.1%)	NS
TPO Ab (n/%)	11 (42.3%)	3 (13.6%)	0.03†

*Mann-Whitney test.

†Fisher's exact test.

Table 2 Survey of thyroid autoimmunity in patients with chronic autoimmune urticaria (n = 26)

Characteristics	With TPO (n = 11)	Without TPO (n = 15)
Infected with <i>H. pylori</i>	10 (90.9%)	7 (46.7%)
Without <i>H. pylori</i>	1 (9.1%)	8 (53.3%)

Fisher's exact test: $P = 0.024$.

The prevalence of antithyroid antibodies was different in the two groups of urticaria. In the autoimmune group we found 11 patients (42.3%) with TPO compared with three patients in the nonautoimmune group (13.6%). The differences in prevalence of TPO between the two groups were significant ($P = 0.03$).

In a further analysis of the autoimmune patients with TPO, we found differences in the frequency of *H. pylori* infection as compared with the autoimmune patients without TPO (Table 2). We found 10 patients with TPO infected with *H. pylori* (90.9%) in the autoimmune group, with only one patient in this group being noninfected. Of the 15 autoimmune patients without TPO, seven (46.7%) were infected with *H. pylori*. The difference in the prevalence of *H. pylori* infection was significant between those with autoimmune urticaria with and without thyroid autoimmunity ($P = 0.02$).

We investigated *H. pylori*-specific IgG in all 17 infected patients in the autoimmune group (with and without TPO). We found antibody to 120 kDa in 14 patients (82.4%), to 87 kDa in 16 (94.1%), to 67 kDa in 16 (94.1%), to 62 kDa in six (35.3%), to 58 kDa in 17 (100%), to 54 kDa in 14 (82.4%), to 47 kDa in eight (47.1%), to 44 kDa in 10 (58.8%), to 33 kDa in nine (52.9%), to 29 kDa in 12 (70.6%), to 28 kDa in 16 (94.1%), to 25 kDa in 13 (76.5%), and to 19 kDa in 16 (94.1%). The *H. pylori*-specific IgG antibodies revealed a similar prevalence in subjects with TPO (10 patients) and in those without TPO (seven patients), except for 120 kDa CagA: (patients with vs. without TPO: 120 kDa: 10 vs. 4; 87 kDa 9 vs. 7; 67 kDa: 10 vs. 6; 62 kDa: 4 vs. 2; 58 kDa: 10 vs. 7; 54 kDa: 8 vs. 6; 47 kDa: 5 vs. 3; 44 kDa: 5 vs. 4; 33 kDa: 5 vs. 4; 29 kDa: 7 vs. 5; 28 kDa: 9 vs. 7; 25 kDa: 8 vs. 5; and 19 kDa: 9 vs. 7) The difference between the patients with and without thyroid autoimmunity was significant only in the case of 120 kDa ($P < 0.05$).

Discussion

Clinical diagnosis of autoimmune urticaria is currently based on autologous serum skin testing. We distinguished two groups of chronic urticaria patients on the basis of autologous skin testing. We found no laboratoric differences between the autoimmune and nonautoimmune groups except for the

basophil count, as according to previous data.⁵ We observed a relationship between autoimmune urticaria and autoimmune thyroiditis. Positive autologous serum skin testing was previously described in patients with autoimmune urticaria associated with thyroid autoimmunity.⁶ Thyroidal autoimmunity is well known to be associated with chronic urticaria. Numerous studies have found a prevalence of 14–20% of thyroid autoimmunity in chronic urticaria patients.^{7–9}

In the present study we found a characteristic difference in the prevalence of *H. pylori* in autoimmune urticaria with coexistent autoimmune thyroiditis compared with no thyroid autoimmunity. In this context, there is growing evidence that the phenomenon of parasite-host mimicry may initiate or maintain autoimmunity.¹⁰ Numerous cross-reacting (auto)antibodies may contribute to the pathogenesis of the stomach and duodenal alterations caused by *H. pylori*.¹¹ Various findings have previously been published suggesting an association between *H. pylori* infection and some extradigestive diseases such as Sjögren syndrome, scleroderma, Schönlein-Henoch purpura, and thyroiditis.^{12–15} Hizal *et al.* describe a positive correlation between *H. pylori* infection and autologous serum skin testing.¹⁶

We found a connection between autoimmune thyroiditis and CagA plus *H. pylori* strains. Monoclonal antibodies to a *H. pylori* strain with CagA positivity reacted with follicular cells of the thyroid gland, and the *H. pylori* organism possessing the CagA pathogenicity island carries a gene encoding for an endogenous peroxidase. There is a molecular similarity between human thyroid peroxidase and *H. pylori* peroxidase; this causes immunologic cross-reactivity and might be a possible factor in the development of autoimmune thyroid disease.¹⁵

Our findings suggest the possibility of cross-reactivity being triggered between CagA plus *H. pylori* strains and some other organ-specific autoimmune diseases, such as autoimmune thyroiditis and autoimmune urticaria. This indicates a possible role of *H. pylori* in triggering autoimmune urticaria in at least a select group of patients.

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