

Chronic urticaria and *Helicobacter pylori*

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Background: Although the clinical manifestations of chronic urticaria (CU) are similar in most patients, a variety of factors should be taken into consideration. In general, the cause of CU cannot be determined in most patients, and it is considered idiopathic. In the past several years, relationships between some patients with CU and hepatitis C or autoimmune thyroid diseases have been established. Similarly, other factors may also be considered as possible causes to explain certain patients with CU. Previously, some patients with CU have had their disease attributed to *Helicobacter pylori* (HP), but the relationship was only clinical.

Objective: None of the patients previously described included an immunological study. Thus, we studied a patient with CU, who showed marked clinical improvement after eradication of HP, to demonstrate an IgE relationship with this skin disease.

Methods: First, blood analytical parameters, roentgenograms, fecal examination for parasites, and skin tests were performed to try to establish an etiology. In addition, endoscopy with gastric biopsy confirmed HP colonization, and eradication treatment was prescribed. To investigate an immunological relationship, other tests performed included the following: HP-specific IgG, histamine release induced by HP, HP-specific IgE, and sodium dodecyl sulfate-polyacrylamide gel electrophoresis with immunoblotting.

Results: The blood analytical parameters, roentgenograms, fecal examination for parasites, and skin tests were all negative. In contrast, the tests for HP-specific IgG, histamine release induced by HP, and HP-specific IgE were all positive. In addition, the sulfate-polyacrylamide gel electrophoresis with immunoblotting showed specific IgE binding to an extract of HP.

Conclusions: Our results may indicate an immunological IgE relationship between HP colonization and CU in this particular patient.

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CASE REPORT

A 51-year-old woman, who had a history of cutaneous rash with wheals and daily pruritus 6 months before, without dyspnea or dysphagia, and occasional facial angioedema, consulted our department. She did not relate her symptoms to any particular food, drug, cosmetics, metals, chemical products, clothes, animals, or any other factors. She did not have a personal or family

history of atopy. At our department, a physical examination did not reveal any lesions at that moment. We did observe dermographism with erythema and slight edema.

METHODS

The following blood analytical parameters were performed: blood cell count; biochemistry; C₃ and C1 inhibitor levels; T3, T4, and thyroid-stimulating factor levels; antithyroid antibodies; hepatitis; and hydatid cyst serology. Roentgenograms were taken of her chest and abdomen; feces were examined for parasites.

The following skin tests were performed using a battery of commercially available common inhalants,

foods (milk, egg, fish, cereals mix, nuts mix), *Anisakis simplex*, and latex (ALK-Abelló, Madrid-Spain). We measured the largest wheal diameter and considered a reaction to be positive if the wheal size induced by the allergen was >3 mm over negative control (saline, 0.9%); histamine (10 mg/mL) was used as positive control.

We also used a histamine release test with an ultrasonicated *Helicobacter pylori* (HP) extract. Dilutions of the extract were incubated with the patient's serum specimen according to the method of Siraganian and Hook¹ with an Autoanalyzer II (Technicon Corporation, Tarrytown, NY).

Other immunologic tests of the patient's serum specimen included testing for total IgE, *A. simplex*-specific IgE, and HP-specific IgG; these tests were performed using commercially available immunoassays (Pharmacia and Upjohn Diagnostics GmbH and Company, Freiburg, Germany).

The test for HP-specific IgE in the patient's serum specimen was performed in our immunology department using a commercial IgG kit (Pharmacia, Piscataway, NJ) with minor modifications (α -IgE peroxidase was used as a detection modality instead of IgG).

The sulfate-polyacrylamide gel electrophoresis and immunoblotting were performed in our immunology department. Gel electrophoresis of an ultrasonicated HP extract was carried out in 12% polyacrylamide gel in reducing conditions according to the method of Laemmli.² After electrophoresis the membranes were incubated overnight with the patient's serum diluted 1/5 in phosphate-buffered saline-Tween 20. Later, they were incubated for 60 minutes at room temperature with monoclonal antihuman IgE, alkaline phosphatase-conjugated.

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Gastroenterology Tests

After obtaining informed consent from the patient, the [^{13}C]urea breath test and endoscopy with gastric biopsy were performed by the gastroenterology department.

Symptom Scores

We measured the patient's urticaria symptoms (pruritus, hot flushing, dyspnea, and dysphagia) using scores from 0 to 3 (0, asymptomatic; 1, few symptoms; 2, moderate; and 3, severe).

RESULTS

The following tests were normal: blood analytical parameters, examination of feces for parasites, chest and abdominal roentgenograms, skin prick tests with common allergens, total IgE (42 IU/mL; normal range: 0 to 170 IU/mL), specific IgE against *A. simplex* (<0.35 kU/L), and specific IgE against latex (<0.35 kU/L). In contrast, the specific IgG against HP was positive (>100 U/mL), the histamine release test against HP was positive (15%), and the specific IgE against HP showed 0.467 optical density (OD). Five patients with chronic urticaria (CU) due to *A. simplex* sensitization were used as controls. All of them showed a negative histamine release test against HP (2% to 5%), and the specific IgE against HP test was performed in two of them, both with negative results (<0.200 OD).

Figure 1 shows the sulfate-polyacrylamide gel electrophoresis and immunoblotting results. Our patient's serum recognized two protein bands with specific IgE antibodies (lane 1). The band from 60 to 70 kD is wide and diffuse, and the other band is at 29 to 27 kD. A control serum from a person with no HP colonization did not show any bands (lane 2).

The [^{13}C]urea breath test was positive and HP was demonstrated in a gastric biopsy. A standard antibiotic and omeprazol treatment were prescribed to eradicate HP. The length of the eradication treatment was 8 days. [^{13}C]Urea breath tests administered 3 months later and 1 year later were negative. Nine months after starting treat-

ment to eradicate HP, the patient's IgG against HP was 68 U/mL and specific IgE was 0.328 OD.

The patient's symptom scores were monitored for 8 weeks before and 1 year after the eradication treatment. Two weeks before starting treatment and just after endoscopy with gastric biopsy confirmed HP colonization, the patient's CU symptom scores were as follows: pruritus, 3; heat, 2; flushing, 2; dyspnea, 0; and dysphagia, 0. Cetirizine (10 mg/24 hours) was prescribed as necessary to control symptoms. Two weeks later, before beginning the eradication treatment, her scores were as follows: pruritus, 2; heat, 2; flushing, 2; dyspnea, 0; and dysphagia, 0; and her cetirizine intake was 10 mg/48 hours. Three, 6, 9, and 12 months after the eradication treatment, all scores

were 0, she was asymptomatic, and she did not need antihistamines.

DISCUSSION

Although most patients with CU are diagnosed as idiopathic,³ allergic and nonallergic factors should be taken into consideration.^{4,5} Clinical manifestations appear and disappear over months or years for no apparent reason, and only those attributed to physical factors (cold, heat, pressure, etc), infections, contact dermatitis, allergy, or any other known reason allow us to establish a diagnostic etiology.

To establish an etiology, our patient was initially studied by the common diagnostic tests. All tests were negative, and only specific IgG against HP was positive.

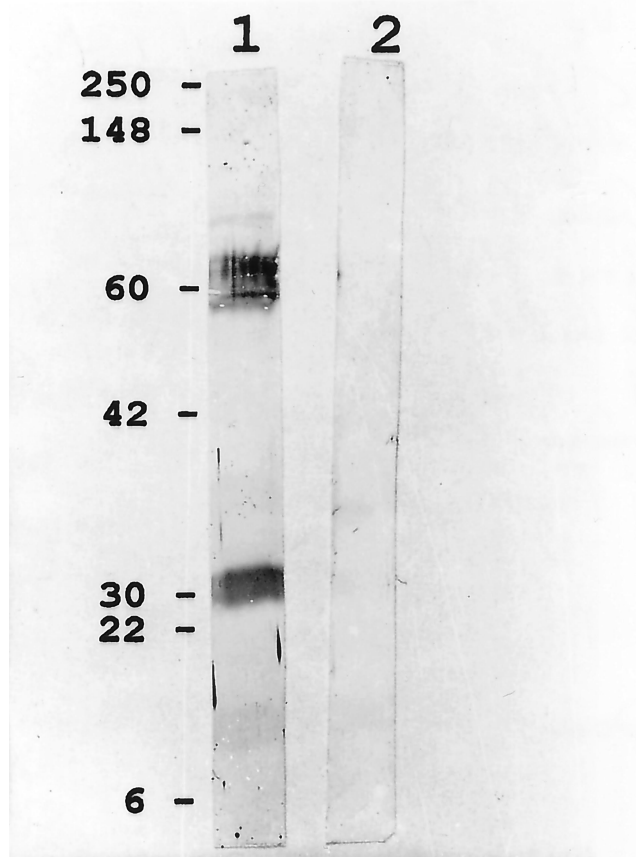


Figure 1. Two protein bands were recognized with specific IgE antibodies from our patient's serum (lane 1). The control patients' serum did not recognize any bands (lane 2).

To confirm the existence of an HP colonization, the patient had a [¹³C]urea breath test and endoscopy with gastric biopsy.

The [¹³C]urea breath test and endoscopy confirmed the HP colonization; negative [¹³C]urea breath tests performed 3 and 12 months after the treatment confirmed HP eradication.

Our patient showed a dramatic clinical improvement as measured by symptom scores of urticaria before and after the treatment.

Other authors^{6,7} have previously reported clinical improvement in patients with CU after HP eradication. Because CU symptoms can disappear spontaneously without specific treatment, we performed diagnostic tests to determine the presence of IgE antibodies against HP. We used a modification of the IgG kit against HP because a commercial ELISA for specific IgE antibodies against this bacterium was not available.

Overall, the positive histamine release test and the elevated levels of specific IgE against HP lead us to suspect that an IgE-mediated immune response existed against this bacterium in our patient.

Our patient's serum recognized two protein bands from an HP extract with specific IgE antibodies (Fig 1). A 60- to 70-kD wide diffuse band includes the molecular mass for urease, the major protein described in HP. Another 29- to 27-kD band probably included a urease subunit.⁸

The findings of specific IgE antibodies to HP, clinical improvement, and decreases in IgG and IgE levels 9 months after the eradication treatment may indicate an immunological IgE relationship between CU and HP colonization in our patient.

More patients and longer study intervals will be necessary to confirm an IgE relationship between HP and CU.

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