

CASE REPORT

Celiac Disease and Chronic Urticaria Resolution: A Case Report

M. CANDELLI, MD, E. C. NISTA, MD, M. GABRIELLI, MD, L. SANTARELLI, MD, G. PIGNATARO, MD,
G. CAMMAROTA, MD, GIOVANNI GASBARRINI, MD, and ANTONIO GASBARRINI, MD

KEY WORDS: celiac disease; chronic urticaria.

Idiopathic chronic urticaria (ICU) is a chronic, relapsing cutaneous disease of uncertain origin characterized by recurring attacks of hives, sometimes associated with angioedema without evidence of a causal agent. Celiac disease is a disorder due to individual intolerance to gliadin and related proteins. The classical clinical pattern of celiac disease includes symptoms of malabsorption such as diarrhea, bloating, abdominal pain, and anemia. Moreover, it is associated with several immunological diseases (autoimmune thyroiditis, type 1 diabetes mellitus). We report a case of ICU remission during a long-term gluten-free diet which relapsed after discontinuation of dietetic therapy.

CASE REPORT

A 28-year-old female patient came to our attention at the Day Hospital of Internal Medicine and Gastroenterology of the Catholic University of Rome for the occurrence of abdominal pain and diarrhea associated with urticaria. She had a history of idiopathic chronic urticaria (ICU) and a diagnosis of celiac disease when she was 19 years old. In fact, 9 years previously she had made a gastroenterologic visit for chronic anemia, severe bloating, and recurrent urticaria. Since she was 5 years old she had experienced frequent relapses of urticaria (3 relapses/years) with pruritic generalized hives (red, circular, or confluent weals) treated with corticosteroids and H₁-receptor antagonists. The diagnosis of ICU made based on clinical and laboratory parameters. The patient was negative on skin prick tests to the most common food (cereals, fish, shrimp, nuts, milk, eggs, tomatoes, apples, soybeans) and inhalant (bacteriofagoides, graminaceae, parietaria, trees, molds, pollens, animal epithelium, yeasts) allergens. Total IgG, IgA, and IgE were normal. Blood exams revealed a microcytic anemia with iron deficiency (Hb, 9.9 g/dL;

MCV, 74; iron, 7 µg/dL; ferritin, 3.6 pg/mL). Platelet and white cell counts, erythrocyte sedimentation rate, C-reactive protein, transaminase, creatinine, glycemia, free T₃, free T₄, thyroid-stimulating hormone, and complement (C₃ and C₄) were within the normal range. Fecal tests for ova and parasites and for hemocult blood were negative. IgG and IgA antiendomysium antibodies and antigliadin antibodies were positive. The patient underwent an upper digestive endoscopy with duodenal biopsies. Histology showed severe villous atrophy, plasma cell infiltrate, and crypt hyperplasia. Diagnosis of celiac disease was made and a gluten-free diet was prescribed. In the next 3 months she experienced only a mild attack of urticaria resolved with H₁-blockers (loratidine). Then the symptoms of ICU completely disappeared for 9 years.

This patient came to our attention when a reactive depression induced her to discontinue the gluten-free diet for about 3 months. We collected blood and plasma samples from the patient and strongly suggested that she resume the gluten-free diet. Therapy with anti-H₁-receptor antagonists and corticosteroids was prescribed, with resolution of cutaneous symptoms. Antiendomysium antibody and recombinant human antitransglutaminase were positive. Antibodies against thyroglobulin and microsomal antigens were negative.

The patient was reevaluated 3 months after the gluten free-diet was resumed and every 3 months for 1 year. Urticaria symptoms and gastrointestinal symptoms completely disappeared throughout the follow-up period.

DISCUSSION

ICU is a frequent cutaneous disease of uncertain origin. The pathogenesis of ICU was once considered to be related to an idiosyncratic or allergic reaction to drugs, food, or other environmental antigens, but these theories were never supported by evidence-based medicine (1). More recently the infectious hypothesis was proposed. Although several studies confirm the association between ICU and chronic infections (in particular, gastric *H. pylori* infection), larger randomized and placebo-controlled trials should be performed to test this supposition seriously (2–4). The autoimmune hypothesis remains

Manuscript received January 13, 2004; accepted February 23, 2004.

From the Internal Medicine Department, Catholic University, Rome, Italy.

Address for reprint requests: Antonio Gasbarrini, MD, Internal Medicine Department, Catholic University, Gemelli Hospital, Largo Gemelli 8, 00168 Rome, Italy; angiologia@rm.unicatt.it.

the more likely one at present. In fact, ICU has been associated with autoimmune disorders (in particular, autoimmune thyroiditis) (5). Moreover, at least 40–50% of ICU is related to autoantibodies against the α subunit of the high-affinity IgE receptor Fc epsilon R1 or, less commonly, against the α subunit of IgE (6). These antibodies are able to induce the release of histamine by mast cells and the consequent formation of anaphylatoxin. However, a causal mechanism remains unknown in about 50% of ICU.

Celiac disease is a genetic disorder caused by gluten intolerance. Symptoms of celiac disease can range from the classic features, such as diarrhea, weight loss, and malnutrition, to latent symptoms, such as isolated nutrient deficiencies. It has been associated with extraintestinal symptoms and several autoimmune disorders (autoimmune thyroiditis, type 1 diabetes mellitus, alopecia) (7). An association with chronic urticaria was described in previously published case reports (8–12). The prevalence of celiac disease in chronic urticaria is unknown at present. Moreover, it has never been investigated in the two subgroups of ICU (with and without α -subunit IgE or IgE receptor autoantibodies).

It has been suggested that an increased permeability of intestinal mucosa may facilitate the absorption of antigens, which may in turn induce an acute attack of ICU by the formation of circulating immunocomplexes. This hypothesis was not supported by a case of ICU in a young celiac patient that did not improve on a gluten-free diet although complete restoration of the small bowel mucosa occurred (9,12).

The spontaneous rechallenge to gliadin peptides in our patient clearly demonstrates that, at least in this case, adherence to the gluten-free diet was a determinant for the

ICU remission. Mechanisms behind this association are not yet clarified. Autoimmunity evoked by gliadin or by other unknown antigens may be the link between ICU and celiac disease.

REFERENCES

1. Kaplan AP: Chronic urticaria and angioedema. *N Engl J Med* 346:175–179, 2002
2. Wustlich S, Brehler R, Luger TA, Pohle T, Domschke W, Foerster E: *Helicobacter pylori* as a possible bacterial focus of chronic urticaria. *Dermatology* 198:130–132, 1999
3. Di Campli C, Gasbarrini A, Nucera E, Franceschi F, Ojetti V, Sanz Torre E, Schivino D, Pola P, Patriarca G, Gasbarrini G: Beneficial effects of *Helicobacter pylori* eradication on idiopathic chronic urticaria. *Dig Dis Sci* 43:1226–1229, 1998
4. Gaig P, Garcia-Ortega P, Enrique E, Papo M, Quer JC, Richard C: Efficacy of the eradication of *Helicobacter pylori* infection in patients with chronic urticaria. A placebo-controlled double blind study. *Allergol Immunopathol* 30:255–258, 2002
5. Rottem M: Chronic urticaria and autoimmune thyroid disease: Is there a link? *Autoimmun Rev* 2:69–72, 2003
6. Greaves MW: Chronic idiopathic urticaria. *Curr Opin Allergy Clin Immunol* 3:363–368, 2003
7. Green PH, Jabri B: Coeliac disease. *Lancet* 362:383–391, 2003
8. Scala E, Giani M, Pirrotta L, Guerra EC, De Pita O, Puddu P: Urticaria and adult celiac disease. *Allergy* 54:1008–1009, 1999
9. Levine A, Dalal I, Bujanover Y: Celiac disease associated with familial chronic urticaria and thyroid autoimmunity in a child. *Pediatrics* 104:e25, 1999
10. Farkas H, Visy B, Fekete B, Karadi I, Kovacs JB, Kovacs IB, Kalmar L, Tordai A, Varga L: Association of celiac disease and hereditary angioneurotic edema. *Am J Gastroenterol* 97:2682–2686, 2002
11. Gallo C, Vighi G, Schroeder J, Strozzi M, Scibilia J, Colafrancesco M, Rota E, Ortolani C, Brusamolino R, Barberis M: Chronic urticaria atopic dermatitis and celiac disease. *Am J Gastroenterol* 87:1684, 1992
12. Hautekeer ML, DeClerck LS, Stevens WJ: Chronic urticaria associated with coeliac disease. *Lancet* 1:157, 1987