

The patient was a 31-year-old woman who had had seasonal rhinoconjunctivitis and asthma for the last 10 years. Ten minutes after eating a BN, she developed pharyngeal itching, lip swelling, dysphonia, dyspnea, wheezing, and generalized macular exanthema. She was treated with epinephrine, intravenous corticosteroids, and antihistamines v.o. The symptoms resolved within 4–5 h. She had previously developed oral allergy syndrome after eating almond (A), walnut (W), sunflower seed (S), and hazelnut (H). She had suffered from abdominal pain after eating chestnut (CH). She tolerated peanut (P) and pistachio (PI). Prick tests (PT) with common inhalants were positive for pollen from *Olea*, Poaceae, *Artemisia*, and *Plantago*.

Prick-by-prick (PBP) with BN and PT with a 1:10 w/v BN extract were positive. PT and PBP with A, P, CH, SS, and PI were positive. PBP with H, W, and cashew nut were positive. A wheal 5 mm greater than saline control was considered positive. Twenty-five atopic and nonatopic control subjects were negative. Specific IgE (UniCAP, Pharmacia®) was determined with the following results: A, P, CH, and PI, class 2; H and S, class 3; IgE for BN, class 2 (2.37 kU/l). SDS–PAGE (12.5%) was carried out by the method of Laemmli.

For analysis of the BN proteins within the low-molecular-weight range, a tricine-SDS–PAGE system was prepared. In both tests, the samples were under reducing conditions (RC) – with β -mercaptoethanol – and no reducing conditions (NRC) – without this agent, which causes rupture of the interchain disulfide links. SDS–PAGE under NRC revealed six bands of 48.7 (21%), 40 (15.3%), 37.7 (2.6%), and 10.2 kDa (43.8%). Under RC, SDS–PAGE showed 10 bands from 33.7 to 10.3 kDa. In the tricine SDS–PAGE, under NRC, appeared nine bands of 30.1 (22.7%), 28.2 (15.9%), 25.9 (4.8%), 25.2 (2.3%), 20 (2.7%), 17.8 (3%), 8.8 (8.3%), 7.7 (34%), and 5.6 kDa (5.7%). The tricine SDS–PAGE under RC showed nine bands from 25 to 5 kDa. The SDS–PAGE immunoblotting assay under

NRC revealed IgE binding to five bands of 52.2, 41.4, 39, 33.4, and 23.7 kDa. IgE binding under RC was restricted to two bands of 33.4 and 21.4 kDa. The tricine SDS–PAGE immunoblotting, under NRC, revealed IgE binding to bands of 19.3, 18.4, and a wide band of 7.22 kDa, probably the 2S albumin. A loss of binding was observed under RC. This fact revealed the importance of the tertiary structure of proteins in the IgE recognition of epitopes.

The increased consumption of tropical nuts, especially in the UK and the USA, in recent years has increased IgE-mediated hypersensitivity. The first cases of anaphylaxis were reported by Hide (2) in 1983. In 1991, Arshad et al. (3) reported 12 allergic reactions, seven of which were anaphylaxis. In 1996, Ewan (4) investigated the clinical features of acute allergic reactions to peanuts and other nuts in 62 patients; 42% of them were multisensitized to nuts. BN was the second sensitizing nut after peanut. Also in 1996, Nordlee et al. (6) [as in a previous study (5)] demonstrated that 2S albumin is the major allergen of BN (Ber e I). Moreover, they showed that transgenic soybean, enriched with 2S albumin of BN, can bind IgE from subjects allergic to BN. In 1997, Bartolome et al. (7) reported the first case of anaphylaxis in Spain caused by oral contact with a BN.

BN consumption in Spain is still very low compared with the USA and the UK. Here we report the second known case of anaphylaxis in Spain.

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Urticaria and adult celiac disease

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Key words: celiac disease; urticaria.

● CELIAC sprue is a chronic malabsorption disease that occurs in predisposed individuals secondary to ingestion of gluten. We report a case of chronic urticaria associated with celiac disease with a marked improvement of symptoms after adoption of a gluten-free diet.

A 24-year-old woman came to us in May 1997 with hay fever

which had begun 2 weeks before. The patient was tested by skin prick test (SPT) with the main inhalant allergens

(house-dust mites, Gramineae, *Parietaria*, molds, trees, and animal danders) and the following food allergens: milk, soybean, apple, fish, tomato, wheat, and white egg (Bayropharm DHS, Milan, Italy), and the results were evaluated by comparing the diameter of each wheal to that induced by 10 mg/ml of histamine. SPT

A gluten-free diet eliminated symptoms in patients with concomitant celiac disease and chronic urticaria.

was positive to grass pollen, confirmed by the presence of specific IgE (*Poa pratensis*: 26.9 IU/ml; Radim, Pomezia, Italy). The total serum IgE level was 134 IU/ml. She was treated with an H₁-antihistamine (cetirizine), with complete remission of the symptoms. Three months later, this patient had generalized urticaria characterized by multiple areas of well-demarcated edematous, intensely pruritic plaques of the diameter of many centimeters, with surrounding erythema. A careful medical history revealed no indications of food, food-additive, or drug allergy. No other symptoms (weight loss, diarrhea, or malabsorption) were associated with the urticaria. She was treated with astemizole for 1 month without benefit.

In December 1997, the patient was admitted to hospital with worsening generalized urticaria. The complete diagnostic procedure comprised physical examination, chest radiography, complete blood count and differential sedimentation rate, antinuclear antibody test, C₃ and C₄ determination, stool analysis for ova and parasites, T₃, T₄, TSH, and antibodies to peroxidase or thyroglobulin evaluation, and skin biopsy. All were normal. We also investigated serum antigliadin, antireticulin, and antiendomysium antibodies. Antigliadin antibodies were positive for both IgG and IgA (Table 1 – A); antireticulin and antiendomysium serum IgA was also positive. No specific IgE antibodies to wheat flour or gluten were found. Small-bowel biopsy revealed atrophy of the microvilli and inflammation with a diffuse mononuclear infiltrate. Direct immunofluorescence performed on lesional skin failed to detect IgA deposition at papillary levels. A diagnosis of celiac disease was made; therefore, a gluten-free diet was prescribed. The urticaria improved after 1 month and totally disappeared after 3 months. No significant difference in total serum IgE level measurement during the course of the disease was observed (August 1997 during the first episode of urticarial lesions: 145

IU/ml; December 1997, when the urticaria worsened: 152 IU/ml; and, finally, March 1998, when the urticarial lesions had cleared up: 136 IU/ml). Avoiding gluten in her diet led to a decline of antigliadin titers, first the IgA isotype followed by the IgG isotype, within 3 months. Furthermore, a decrease of antiendomysium IgA titers and the disappearance of antireticulin IgA in the serum were observed, as shown in Table 1 (B and C). After 1 year of a gluten-free diet, she was still free from urticaria.

Gluten-sensitive enteropathy is a disease of the small intestine characterized by villous atrophy, crypt hyperplasia, and malabsorption. It is caused by hypersensitivity to cereal grain storage proteins of wheat, oats, barley, and rye (1). The alcohol-soluble prolamin fraction of gluten (gliadin in wheat, secalin in rye, avenin in oats, and hordein in barley) was identified as the offending substance. However, patients with celiac disease generally tolerate at least a small amounts of oats (2). An increase of atopic or immunologic disorders (such as asthma, eczema, and hay fever) in adults with celiac disease has been reported (3, 4). On the other hand, the association between chronic urticaria and inflammatory diseases is well known.

Hautekeete et al. first described a case of chronic urticaria associated with celiac disease (5). Here we report another case of chronic urticaria associated with celiac disease, in which a gluten-free diet resulted in both a decline of antigliadin antibodies and the disappearance of urticarial skin lesions. IgA antibodies, in comparison with mucosal tissue components (reticulin and endomysium), also

decline after a gluten-free diet. As widely reported, an increased mucosal permeability may facilitate the passage of antigens. Theoretically, it is possible that immune-complex-dependent sequelae might cause urticarial lesions also when concomitant celiac disease occurs. Consequently, the restoration of mucosal integrity after a gluten-free diet may explain the improvement of urticaria in our patient, but this requires further investigation.

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Table 1.

	A December 1997	B January 1998	C March 1998
IgG – antigliadin	117 IU/ml	340 IU/ml	35 IU/ml
IgA – antigliadin	236 IU/ml	170 IU/ml	84 IU/ml
IgA – antiendomysium	Positive (1:80)	Positive (1:40)	Positive (1:10)
IgA – antireticulin	Positive (1:80)	Negative	Negative
	↑	↑	
	Gluten-free diet	Improvement of symptoms	