

Chronic Headaches and Sleepiness Caused by Facial Soap (Containing Hydrolyzed Wheat Proteins)-Induced Wheat Allergy

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Abstract

A 38-year-old woman was suffering from irregular headaches and sleepiness. She had used soap containing Glupearl 19S (hydrolyzed wheat proteins) every day for approximately one year and had experienced an episode of rash eruption on her face seven months ago. Wheat-specific IgE antibodies were detected in her serum. A Western blot analysis revealed a high titer of IgE antibodies against Glupearl 19S and wheat proteins. The patient was sensitive to these compounds in a skin prick test. After avoiding eating wheat, her headaches and sleepiness disappeared. A hidden food allergy is a possible cause of these symptoms.

Key words: Glupearl 19S, food allergy, additive, mild symptoms, prostaglandin D2

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Introduction

In October 2010, the Ministry of Health, Labour and Welfare in Japan announced that the best-selling “green tea soap” contains allergens capable of sensitizing the user to a wheat allergy and may cause a food allergy to wheat, sometimes in the form of anaphylaxis. Following this announcement, the responsible cosmetics company conducted a voluntary recall of the soap in May 2011. By that time, however, at least 471 users of the soap had suffered from wheat allergies after consuming foods containing wheat products. The company changed the formulation of the soap to make it free of the hydrolyzed wheat protein additive (Glupearl 19S) in December 2010. By that time, however, more than 40 million bars of the soap had been sold, suggesting that some consumers may have suffered from a wheat allergy without being diagnosed. The mechanism underlying the development of the facial soap allergy is as follows: the hydrolyzed products of the wheat proteins in the facial soap sensitized the user through the skin or rhinoconjunctival mucous membranes, after which IgE antibodies against the pro-

teins caused an allergic reaction upon the natural uptake of wheat proteins in foods through the alimentary tract (1). Indeed, a severe clinical form of food allergies, wheat-dependent exercise-induced anaphylaxis (WDEIA), attracted nationwide attention. WDEIA is the most common form of food-dependent exercise-induced anaphylaxis (FDEIA). In patients who experience strenuous exercise, such as running, after eating a causative food (e.g., wheat; case of WDEIA), usually within two hours, FDEIA can emerge as a serious systemic reaction, including generalized urticaria, angioedema, erythema, dyspnea, abdominal pain and/or loss of consciousness (2). FDEIA is the most severe form of allergic food reactions. Considering the countless number of facial soap users, of whom a portion were sensitized to wheat additives, it is likely that there are many patients with milder symptoms of wheat allergies who did not develop FDEIA.

Our report describes the case of a woman who was later found to have a wheat-dependent food allergy. She exhibited atypical symptoms for an allergy; however, we considered that the symptoms were caused by an allergic reaction.

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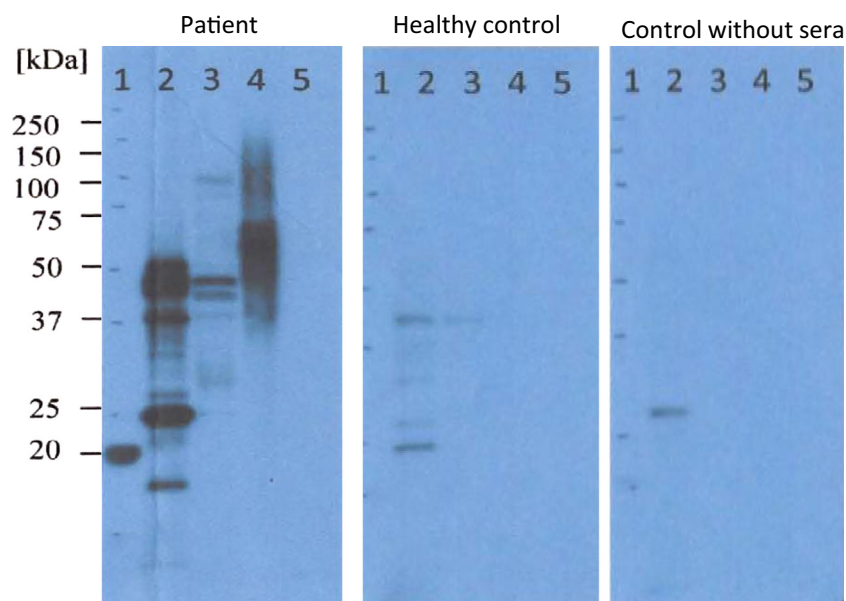


Figure. A Western blotting analysis of wheat protein fractions and hydrolyzed wheat proteins in the sera of the patient, a healthy control subject and a control subject without sera. Lane 1, marker; Lane 2, soluble wheat proteins; Lane 3, insoluble wheat proteins; Lane 4, Glupearl 19S; Lane 5, omega-5 gliadin. The IgE in the patient's serum reacted to soluble and insoluble wheat proteins and Glupearl 19S, but not to omega-5 gliadin.

Case Report

A 38-year-old healthy woman suddenly developed itchy edema on her face one day in December 2010. Since then, she sometimes experienced itching in her eyes and on her face, regardless of the season. Her family doctor prescribed antipruritic eye drops and antihistamine medicines, which reduced her symptoms, after which she stopped using the medicines.

At around the same time, she sometimes experienced headaches and sleepiness/drowsiness without any other symptoms. Occasionally, her eyes were itchy for an unknown reason when she experienced headaches and sleepiness. Her symptoms prompted her to visit our outpatient clinic in August 2011. Her headaches were mild and not pulsatile, although they emerged almost every day at irregular times of the day. She described the symptom as being a type of sleepiness/drowsiness that continued for two to three hours. The headaches were unlikely tension-type headaches. Possible organic causes of headaches were excluded on cranial computed tomography; however, we were unable to identify the cause of the headaches in the first series of medical examinations. The patient sometimes used loxoprofen, a nonsteroidal anti-inflammatory drug (NSAID), for her headaches; however, the medication neither alleviated nor enhanced her symptoms. Since the cause of the allergic reaction and headaches was unknown at that time, we conducted a multiple antigen simultaneous test (MAST). Her serum contained a high titer (16.80 LC (<1.39)) of IgE antibodies specific for wheat allergens, as determined on an en-

zyme immunoassay that detected no IgE antibodies against 32 other allergens, such as cedar pollen, house dust, milk, eggs, soybeans, fungus, etc. The results surprised the patient because she had been eating bread every day for breakfast and lunch. At that time, however, we did not anticipate the clinical significance of the RAST results with respect to the patient's primary symptoms: headaches and sleepiness.

After seeing the issues related to the tea soap-associated wheat allergy on TV and in the newspaper in November 2011, the patient recalled that she had used the tea soap every day for approximately one year from 2009 to 2010. She wondered about the possible association between the use of the soap and the results of the RAST and consulted us again. We subsequently conducted specific examinations for the allergy induced by the soap. A skin prick test showed a positive reaction to a solution of the tea soap (100×, 1,000×), wheat extract (Torii Pharmaceutical Co. Ltd., Tokyo, Japan), a solution of the hydrolyzed products of the insoluble fraction of the wheat proteins (HWP) (provided by Shimane University) and a 0.01% solution of Glupearl 19S (a HWP contained in the tea soap) provided by the National Hospital Organization Sagamihara Hospital. A Western blot analysis also revealed the presence of IgE antibodies specific for Glupearl 19S in the patient's serum, whereas no antibodies to omega-5 gliadin were detected (Figure). The results fulfilled the diagnostic criteria for the immediate-type wheat allergy induced by Glupearl 19S proposed by the Japan Society of Allergology (1, 3). Realizing that she had a food allergy to wheat, the patient recalled that her first allergic episode occurred while she had worked hard to remove snow from her car parking lot after eating

bread for lunch. The episode did not appear to be as severe as anaphylaxis, although it was probably caused by the same mechanism as WDEIA, which is triggered by exercise after wheat intake. To treat the itching on her eyes and face, the patient avoided eating any products containing wheat, and the symptoms disappeared. Unexpectedly, her headaches and sleepiness also disappeared. After recovering, the patient reported that she experienced headaches and sleepiness one or two hours after eating bread or pasta.

Discussion

The present patient did not exhibit any of the typical severe symptoms of a food allergy to wheat products. However, we suspected that her headaches and sleepiness were associated with a wheat allergy caused by sensitization to the hydrolyzed products in the facial soap. This is the first case of headaches and sleepiness as symptoms of an allergic reaction among facial soap users.

The antigens and characteristics of soap-induced wheat allergies differ from those associated with conventional food wheat allergies, including WDEIA (1, 4). The mechanism underlying the development of the soap-induced allergy is as follows: the HWP (Glupearl 19S) contained in the facial soap sensitizes the user through the skin and/or rhinoconjunctival mucous membranes, after which he/she develops allergic symptoms to natural wheat proteins absorbed through the gastrointestinal tract (1, 5). Glupearl 19S is a product made via the acidic hydrolysis of the insoluble fraction of wheat in order to increase the solubility of gluten (1, 6). A portion of patients sensitized to the HWP exhibit a contact allergy several months after sensitization and subsequently develop WDEIA, a generalized allergic reaction induced by wheat ingestion (1). Patients with this soap-induced wheat allergy rarely show sensitivity to omega-5 gliadin (1, 4), a component protein of wheat to which up to 80% of conventional WDEIA patients are sensitive (7). The serum of the present patient contained IgE antibodies specific for Glupearl 19S but no IgE antibodies for omega-5 gliadin. The antigens and characteristics of the soap-induced wheat allergy are different from those of conventional food wheat allergies.

The headaches and sleepiness observed in the present case may have been caused by an allergic reaction to food. Symptoms of food allergies include not only urticaria, erythrocytic skin, edema and anaphylaxis, but also fatigue and headaches, which are often overlooked because it is difficult to identify the cause of the symptoms (8). Wheat and hydrolyzed products of wheat are used not only in bread and pasta, but also in food additives in many kinds of processed foods, which are consumed by patients unconsciously. The cause of the present patient's symptoms were difficult to recognize because she unconsciously kept eating many kinds of wheat products.

Although the symptoms observed in the present case did not fulfill the criteria for migraines, previous research on

migraines strongly suggests the important role of mast cells in the brain in the development of headaches. As early as the 1930s, however, clinical researchers have recognized a possible association between allergies and migraines and concluded that wheat intake is one of the most frequent triggers of migraines (9, 10). Subsequently, the levels of histamine in the plasma and total IgE in some migraine patients were shown to be high (11, 12). Mast cells are located perivascularly in proximity to neurons, especially in the dura, and are sometimes activated by allergic reactions, inflammatory conditions or neurologic triggers (13). The headaches observed in the present case were not typical for migraine headaches; however, the high titer of IgE antibodies in the serum strongly suggest that the IgE-mediated release of chemical mediators/cytokines from mast cells may cause headaches.

It is well established that mast cells sensitized to IgE antibodies release not only histamine and leukotrienes, but also prostaglandin D₂ (PGD₂) upon cross-binding of IgE antibodies by antigens (14) and that PGD₂ is an endogenous sleep inducer (15). Physiologically, PGD₂ is synthesized in the dura, the membrane system surrounding the brain, and is naturally secreted into the cerebrospinal fluid where it acts as the most important endogenous sleep inducer (13). It has been reported, however, that patients with mastocytosis exhibit marked overproduction of histamine and PGD₂ in addition to headaches and sleepiness (16). We wonder whether the headaches and sleepiness observed in the present case were possibly caused by this PGD₂-mediated mechanism. It is also known that cross-binding of IgE on mast cells with antigens induces the synthesis of inflammatory cytokines, such as IL6 and TNF α (17). We wonder whether the IgE-mediated release of chemical mediators, such as PGD₂ and histamine, and the subsequent formation of inflammatory cytokines by brain mast cells may be the cause of the patient's sleepiness and headaches.

The NSAID the patient sometimes used for her headaches had no effect. We speculated that the NSAID did not block the allergic reactions, but rather adversely affected the patient's allergic reactions. Aspirin itself, with or even without exercise, induces wheat-dependent anaphylaxis (18, 19). Blocking the COX-1 pathway with NSAIDs precipitates histamine release from mast cells and basophils (20). As other presumed roles of NSAIDs in wheat allergy patients, aspirin and loxoprofen are suspected to facilitate the absorption of wheat through the gastrointestinal tract and/or promote the generation of IgE against wheat allergens (20). Although the present patient did not always use loxoprofen for her headaches, loxoprofen may have affected her allergic symptoms, including headaches and sleepiness.

We expect that the present case will call the attention of physicians and neurologists to the possibility that headaches and/or drowsiness without typical allergic symptoms may be caused by an IgE-mediated mechanism.

The authors state that they have no Conflict of Interest (COI).

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