

Adult-onset sheep's milk allergy in a patient without cow's milk allergy

Suzuki K¹, Futamura K¹, Hasegawa E^{2,3}, Aoki Y^{2,3}, Nakamura M^{2,3}, Matsunaga K^{1,2},
Yagami A¹

¹Department of Allergology, Fujita Health University School of Medicine, Aichi, Japan

²Department of Integrative Medical Science for Allergic Disease, Fujita Health
University School of Medicine, Aichi, Japan

³General Research and Development Institute, Hoya Co., Ltd., Aichi, Japan

Corresponding author

K. Suzuki

Department of Allergology, Fujita Health University School of Medicine, 3-6-10

Otobashi, Nakagawa-ku, Nagoya, Aichi 454-8509, Japan

E-mail: kayokos@fujita-hu.ac.jp

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Palabras clave:

Alergia a leche de oveja. Sensibilización percutánea. Prick test. Alfa-S2 caseína. Immunoblotting y electroforesis bidimensional.

Most childhood-onset sheep's and goat's milk allergies co-occur with cow's milk allergy because of the high sequence homology between corresponding proteins[1]. Alvarez et al. reported adult-onset sheep's and goat's milk allergies without cow's milk allergy [2]. Sensitization in food allergy is traditionally considered to occur via the intestinal tract; therefore, sheep's milk allergy is mainly reported from countries with a higher consumption of goat's and sheep's milk products [3]. In 2013, >2,000 wheat allergy cases in Japan were induced after sensitization by a facial soap that contained hydrolyzed wheat protein[4]. Another case report described a patient with percutaneous sensitization-induced fish allergy[5]. Therefore, percutaneous sensitization is a route through which food allergies develop.

In Japan, people regularly consume cow's milk products and not sheep's or goat's milk products. Herein, we report a Japanese case of adult-onset sheep's milk allergy without cow's milk allergy that was possibly induced by occupational

percutaneous sensitization to sheep's milk cheese.

A 25-year-old woman with moderate-severity atopic dermatitis and asthma had three anaphylactic episodes that were managed with injectable antihistamines and systemic steroids. The patient had previously received topical steroid treatment for atopic dermatitis at a private clinic. Before the first occurrence of allergic symptoms at 21 years of age, the patient had worked regularly (6 days per week) at her part-time job for 1 year. The atopic dermatitis lesions on her hands were aggravated because she washed dishes without gloves at her workplace. Moreover, she occasionally handled Pecorino cheese (made from sheep's milk) without gloves during her work. Her first anaphylactic episode occurred at 21 years of age and was associated with hand numbness, laryngeal swelling, diarrhea, and vomiting after eating pasta and bread at her workplace. At 22 years of age, the symptoms recurred after eating pasta in Italy. At 23 years, the patient experienced sneezing, rhinorrhea, vomiting, and facial edema after eating salad topped with grated cheese at a restaurant in Japan. She suspected her symptoms in all previous allergic episodes were due to the cheese. The patient had no allergic symptoms on consumption of cow's milk or yogurt and cheese made from cow's milk.

Her total immunoglobulin E (IgE) level was 974.0 IU/mL, and her specific IgE

antibody (CAP-FEIA) levels were as follows: sheep's milk 1.16 UA/mL, sheep's milk whey 0.83 UA/mL, cow's milk 0.08 UA/mL, α -lactalbumin <0.1 UA/mL, β -lactoglobulin <0.1 UA/mL, casein 0.07 UA/mL, mold cheese made from cow's milk 0.24 UA/mL, and cheese made from cow's milk <0.1 UA/mL. We performed prick-prick tests to identify allergy-causing foods and used physiological saline and histamine dihydrochloride 10 mg/mL (Torii Pharmaceutical Co., Ltd, Tokyo, Japan) as negative and positive controls, respectively, and commercially available Pecorino cheese made from sheep's milk, sheep's milk yogurt, goat's milk, and Parmesan and Camembert cheese made from cow's milk. The patient manifested positive reactions to Pecorino cheese, sheep's milk, sheep's milk yogurt, goat's milk, and histamine dihydrochloride (wheal diameter: 3.5, 5, 5.5, 3, and 6 mm, respectively) during the prick-prick test, but did not react to Parmesan and Camembert cheese.

To identify causative antigens, we performed two-dimensional electrophoresis and immunoblotting using previously reported methods, with slight modifications, followed by mass spectrometry [4]. The IgE antibody reacted specifically with the α -S2 casein in sheep's milk in this case, compared to those in the adult negative control sample from an individual without sheep's milk and cow's milk allergies, atopic dermatitis, or asthma.

The causative protein for the patient's anaphylaxis was the α -S2 casein (accession no.

P04654) in sheep's milk, despite no observable IgE binding to the α -S2 casein (accession no. P02663) in cow's milk (Supplementary Fig.1).

In concordance with clinical symptoms, antigen analysis revealed that the patient's specific IgE antibody bound to the α -S2 casein in sheep's milk but not to that in cow's milk. Different portions of the amino acid sequences of these two proteins were considered antigenic in this case. A comparison of the amino acid sequences of α -S2 casein from sheep's (accession no. P04654), cow's (accession no. P02663), and goat's milk (accession no. P33049) showed 89% homology of sheep's and cow's milk protein, but 98% homology of sheep's and goat's milk protein on BLAST (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>). The antigenic epitope is suspected to be present in the sequence portion of only sheep's and goat's milk. Ah-Leung et al.[6] studied 28 patients with goat's and sheep's milk allergies; 26 of these patients did not have cow's milk allergy, similar to the result in our case. On enzyme allergosorbent tests, goat's or sheep's milk allergy involves the casein fraction but not whey proteins. Goat's or sheep's milk allergy occurs at higher ages than does cow's milk allergy, and the former is associated with higher severity of symptoms on ingestion of minor quantities. Our patient developed anaphylactic symptoms on consuming cheese sprinkles on salad, despite daily consumption of cow's milk without any symptoms. We considered that the

patient may have been percutaneously sensitized to sheep's milk at work, which eventually resulted in anaphylaxis. The patient had no history of ingestion of or contact with goat's milk products; therefore, the positive response to the goat's milk prick-prick test was attributed to a cross-reaction with the α -S2 casein in sheep's milk. We recommended that the patient should avoid both goat's and sheep's milk and products derived from these. The patient has not experienced any immediate allergic reaction to date.

The following two mechanisms are considered as causes of allergy to goat's and sheep's milk: (1) cross-reactivity to cow's milk and (2) percutaneous sensitization to α -S2 casein in goat's or sheep's milk. As seen in this case, a patient not allergic to cow's milk and sensitized to α -S2 casein may manifest severe allergic symptoms after ingesting even small quantities of goat's or sheep's milk products. Thus, even a small amount of cheese sprinkled on a salad should be considered as a possible cause of anaphylaxis.

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Conflicts of Interest

KM is employed in an endowed department that is sponsored by Hoya Co., Ltd. The rest of authors declare they have no conflicts of interest.

Ethical considerations

The study design for two-dimensional electrophoresis and immunoblotting was approved by the Fujita Health University (approval no. HM16-371).

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