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Letter to the Editor

Anaphylaxis caused by sodium caseinate contained in canned coffee

Dear Editor,

Cow's milk allergy (CMA) is frequently seen in infants and young children.¹ The major cow's milk (CM) allergens are casein and whey protein (WP), including α -lactalbumin and β -lactoglobulin. Casein exists as micellar casein in CM and its more soluble derivatives, such as sodium and calcium caseinate, are frequently used as emulsifier and stabilizer in foods. The clinical features of CMA vary from urticarial reactions to life-threatening anaphylaxis. The incidence of CMA is estimated to be 2%–6% in early childhood, decreasing to 0.1%–0.5% in adulthood, as adult-onset CMA is rare, and a majority of CMA patients in childhood acquire tolerance to CM proteins by the time they reach adulthood. We herein report a patient with adult-onset CMA who experienced an anaphylactic reaction after ingesting canned coffee containing sodium caseinate.

A 38-year-old man presented with a history of an anaphylactic reaction 10 min after drinking canned coffee, accompanied by generalized urticaria, palpitations, dyspnea and loss of consciousness. He was transferred to the emergency hospital and treated with hydration and intravenous antihistamines. One week later, he ingested a small amount of canned coffee containing sodium caseinate and immediately felt oropharyngeal pruritus. Two months after the anaphylactic reaction, he also reported experiencing the development of urticaria 30 min after ingesting drinkable yogurt, although the symptoms had disappeared spontaneously within 1 h. He was referred to our hospital for a detailed examination. His medical history included atopic dermatitis and alopecia universalis, these were treated with hydrocortisone butyrate ointment (for the face), betamethasone butyrate propionate ointment (for the trunk and limbs), and betamethasone butyrate propionate lotion (for the scalp).

He had been drinking black coffee and drinkable yogurt every day for more than one year without any symptoms except for one episode of an urticarial reaction. A laboratory examination revealed a total serum IgE titer of 2517 IU/ml. His specific IgE antibody levels for house dust mite, CM, casein, α -lactalbumin and β -lactoglobulin, as determined using an ImmunoCAP system (Phadia, Uppsala, Sweden), were 156.0 UA/ml, 1.11 UA/ml, 1.74 UA/ml, 0.14 UA/ml and 0.14 UA/ml (normal, <0.34), respectively. A skin prick test was performed using the undiluted canned coffee, which contained several ingredients, including sodium caseinate, emulsifiers, CM and sugars, 1% solution of the individual ingredients and undiluted black coffee. When the average wheal diameter induced by the allergen was >3 mm, the result was considered positive. The results were positive for undiluted canned coffee and 1% sodium caseinate

solution (wheal diameters, 4×4 and 10×10 mm, respectively; positive control, histamine hydrochloride [10 mg/ml]: wheal diameter, 4×5 mm; negative control, saline: wheal diameter, 0×0 mm) and negative for undiluted black coffee and 1% solution of emulsifiers, CM and sugars. No positive results were obtained in a skin prick test with undiluted canned coffee containing sodium caseinate in three healthy subjects. As the concentration of sodium caseinate in the canned coffee was 0.15%, a skin prick test with 0.1% solution of sodium caseinate was then performed, and the result was also positive.

An oral challenge test was performed with the patient's informed consent using 1% sodium caseinate solution. The amount of intake was gradually increased every 20 min, and he developed generalized pruritic wheals after ingesting 120 ml of 1% sodium caseinate solution (1.2 g sodium caseinate) (Fig. 1). He was treated with intravenous antihistamines, and the symptoms were relieved within 1 h. A diagnosis of anaphylaxis due to sodium caseinate was made. A detailed history-taking revealed that an urticarial reaction after consuming drinkable yogurt had once previously occurred after working all night. We therefore hypothesized that cofactors were required for the induction of an allergic reaction to CM in this patient. A total of 100 ml CM (2.8 g casein), which contains larger amounts of casein than the estimated amount required from the previous challenge test, was used for this challenge test. However, neither the intake of CM, CM plus aspirin (500 mg) nor CM plus 15-min exercise induced any symptoms, whereas the intake of CM plus aspirin and exercise induced pruritic erythema and wheals on the trunk and upper limbs, confirming his allergic responses to CM in the presence of multiple cofactors (Table 1). He subsequently avoided ingesting CM proteins and was free from symptoms.

CMA in adults is rare, and the clinical features of CMA in adults are quite different from those in infants and young children.^{2,3} The clinical characteristics of adult CMA are as follows: allergic responses predominantly to casein, symptoms of respiratory tract and skin (more frequently than in infants and young children) and difficulty acquiring tolerance to CM. In addition, cofactors, such as exercise, fatigue, stress and aspirin, which lower the threshold for the development of allergic reactions, are required for the initial induction of allergic symptoms in many adult CMA patients. Indeed, our patient had once previously experienced an urticarial reaction due to drinkable yogurt at a time when he had been exhausted, and oral challenge with CM revealed that the combination of exercise and aspirin intake were required to reproduce this urticarial reaction.

However, allergic responses were induced after challenge with sodium caseinate without the need for any other cofactors. Our patient showed relatively low titers of specific IgE antibodies against

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Fig. 1. Generalized pruritic wheals developed after oral challenge tests with 1% sodium caseinate solution.

Table 1

Results of oral challenge tests of cow's milk (CM) with exercise and/or intake of aspirin as cofactors.

Challenges with			Results
Cow's milk (100 ml)	Exercise (15 min)	Aspirin intake (500 mg)	
+	–	–	No symptoms
+	+	–	No symptoms
+	–	+	No symptoms
+	+	+	Wheals on the trunk and upper limbs

CM and casein. A previous report showed that WP and casein in CM were characterized as fast and slow proteins, respectively, based on their rate of digestion,⁴ and micellar casein in CM exhibits much larger particles and is more slowly digested and absorbed than caseinates.⁵ We therefore speculated that the allergic responses had been reproduced more easily and in response to smaller allergen quantities with sodium caseinate than CM.

Our patient had experienced recurrent eczema in the lips and perioral regions due to atopic dermatitis several years previously, and the symptoms has been refractory to treatment recently. He had no history of food allergy, and specific IgE antibody against

CM had been negative in childhood. This history supported the dual-allergen-exposure hypothesis for pathogenesis of food allergies, in which allergic sensitization results from percutaneous exposure.⁶ Bito reported a case of adult CMA possibly sensitized by CM-containing bath salts percutaneously, in which the specific IgE antibodies were positive for CM and casein and negative for α -lactalbumin and β -lactoglobulin, as in our patient.⁷ We therefore hypothesized that our patient had been sensitized to CM proteins through the barrier-disrupted skin of his mouth and then developed an anaphylactic reaction after drinking canned coffee containing sodium caseinate.

To our knowledge, few reports have described the possible development of adult-onset CMA through percutaneous sensitization with CM. Similar case reports are required to clarify whether or not sodium caseinate more easily induces allergic symptoms than CM in patient with casein allergy.

Conflict of interest

The authors have no conflict of interest to declare.

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