

LETTER TO THE EDITOR

A case of late-onset anaphylaxis to fermented soybeans (natto)

Dear Editor,

Natto, a traditional Japanese food, is made from soybeans fermented by *Bacillus subtilis*. It has recently been reported that natto sometimes causes IgE-mediated late-onset anaphylaxis, which is characterized by an anaphylaxis reaction occurring approximately half a day after ingestion.^{1,2} It is hypothesized that poly-gamma-glutamic acid, a high-molecular-weight, biodegradable polymer produced by *Bacillus subtilis*, delays the release of the antigen into the bowel, which delays the reaction.² Therefore, direct injection of the antigen into tissue by the prick-prick test evokes quick positive reaction.^{1,2} Here we present a case of late-onset anaphylaxis to natto.

A 26-year-old male was referred to our dermatology department because of two recent episodes of anaphylaxis. The first episode occurred around 10 am. The patient suddenly presented urticarial rashes all over the body with severe dyspnea and hypotension. He had not eaten anything that day. He was transported to a hospital by ambulance, diagnosed with anaphylaxis, and treated with systemic steroid and epinephrine therapy. On the second occasion, the patient experienced anaphylaxis around 1:30 pm. He had had breakfast around 6 am and lunch around 1 pm. Because the second episode occurred just after lunch, we suspected the possibility of food allergy, but the levels of serum IgE specific to each ingredient in the lunch were normal. Consistently, anaphylaxis has not recurred even when the patient has eaten the same foods taken at the lunch. A detailed medical history revealed that he had had natto at breakfast, more than 7 hours before the second anaphylaxis occurred. It was not clear whether he had consumed natto prior to his first episode. We suspected the possibility of late-onset anaphylaxis due to natto, and performed a prick-prick test with natto. This induced pruritus and wheal within 15 min after the test, with a score of 4+ (Fig. 1). Informed consent was not obtained for provocation test with natto. A prick-prick test and provocation test with tonyu, another soybean product, was negative. The serum IgE level specific for soybeans was also negative. We therefore diagnosed the patient with late-onset anaphylaxis due to natto. We prohibited the patient from taking natto, and there has been no recurrence since then.

Anaphylaxis to natto develops within 5–12 hours after ingestion.^{1–3} This is in contrast to most other trigger foods which usually cause anaphylaxis within 30 min after ingestion.⁴ Therefore, dietary history of consumption tends to focus on food

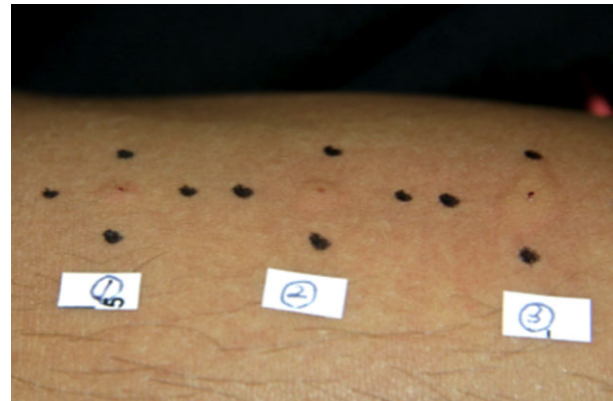


Figure 1. Prick-prick test. (a) Wheal reaction at 15 min after the test. The placard marked (1) indicates the saline test site; (2) indicates 1% histamine (as a positive control, 6 mm × 6 mm); and (3) indicates natto (15 mm × 6 mm).

intake just before the anaphylaxis episode. In this case, for example, neither the patient nor his medical staff initially paid much attention to what foods were eaten half a day prior to the first anaphylaxis episode. It remains unknown whether the patient's first anaphylaxis episode was caused by natto, but more careful recording of dietary history might have expedited his diagnosis.

Since anaphylaxis is a life-threatening disease, quick identification of the allergens involved is extremely important. Although late-onset anaphylaxis is a rare disease, it should always be considered as a differential diagnosis; to enable this, dietary history must be taken over the 12 h prior to anaphylaxis.

ACKNOWLEDGMENTS: We thank Dr. Zenro Ikezawa and Dr. Michiko Aihara for helpful advice and discussion.

CONFLICT OF INTEREST: None declared.

Tetsuya HONDA, Mikiko MICHIGAMI,
Yoshiki MIYACHI, Kenji KABASHIMA
Department of Dermatology, Kyoto University Graduate School of Medicine,
Kyoto, Japan

REFERENCES

- 1 Inomata N, Osuna H, Ikezawa Z. Late-onset anaphylaxis to *Bacillus natto*-fermented soybeans (natto). *J Allergy Clin Immunol* 2004; **113**: 998–1000.
- 2 Inomata N, Osuna H, Kawano K *et al.* Late-onset anaphylaxis after ingestion of *Bacillus Subtilis*-fermented soybeans (Natto): clinical review of 7 patients. *Allergol Int* 2007; **56**: 257–261.
- 3 Matsubayashi R, Matsubayashi T, Yokota T *et al.* Pediatric late-onset anaphylaxis caused by natto (fermented soybeans). *Pediatr Int* 2010; **52**: 657–658.
- 4 Simons FE, Arduzzo LR, Bilo MB *et al.* World Allergy Organization anaphylaxis guidelines: summary. *J Allergy Clin Immunol* 2011; **127**: 587–593. e1-22.