

LETTER TO THE EDITOR

Immediate-onset anaphylaxis of *Bacillus subtilis*-fermented soybeans (*natto*)

Dear Editor,

I read the Letter to the Editor entitled "Involvement of poly (γ -glutamic acid) as an allergen in late-onset anaphylaxis due to fermented soybeans (*natto*)" by Inomata *et al.*¹ with interest. *Natto* is a traditional Japanese preserved food made by fermenting soy beans with *Bacillus subtilis natto*, a type of hay bacillus. In recent years, there have been increasing opportunities to consume *natto* throughout the world, due to the boom in health foods and Japanese foods. Unlike ordinary food allergies, *natto* anaphylaxis is distinguished by symptoms that appear with a delay of 5–12 h after ingesting *natto*.^{1–4} To our knowledge, we report the first case of immediate-onset anaphylaxis in which symptoms appeared 30 min after ingesting *natto*.

The patient was a 72-year-old woman who had ingested *natto*. Thirty minutes later, she developed urticaria with intense itching over the entire body, epigastralgia and nausea. Upon arrival at the hospital, hypotension and decreased oxygen saturation were observed, and a diagnosis of shock was made. She was treated with an i.m. injection of adrenaline and an i.v. injection of hydrocortisone sodium succinate, which relieved the symptoms. Her medical history included gastric ulcer and anaphylactic shock after p.o. administration of scopolamine butylbromide. She had suffered from a stomachache due to a gastric ulcer for a year. A blood test showed that antigen-specific immunoglobulin E was negative for soybeans. Prick test results were found to be positive for *natto*, viscous material and poly- γ -glutamic acid (PGA; 0.1 and 1 mg/mL) (Fig. 1), and negative for *B. subtilis natto* and soybeans. These findings led to a diagnosis of anaphylactic shock due to PGA in *natto*. Subsequent avoidance of ingestion of *natto* and other foods containing PGA has not resulted in recurrence of symptoms.

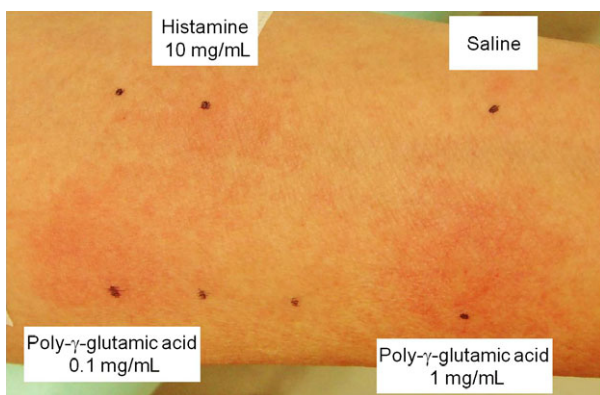


Figure 1. Prick test reactions to poly- γ -glutamic acid (0.1 and 1 mg/mL), histamine and saline.

Poly- γ -glutamic acid is a viscous material produced during the *natto* fermentation process, and a macromolecular polymer with a molecular weight of 100–1000 kDa. PGA consists of D- and L-glutamic acid units connected by amide linkages between α -amino and γ -carboxylic acid groups.⁵ The patient's medical history included anaphylactic shock after administration of scopolamine butylbromide. This drug has the structure of the butyl group, which is similar to that of glutamic acid, implying that cross-reactions between PGA and scopolamine butylbromide may occur. The hypothesized mechanism of late-onset anaphylaxis to fermented soybeans is delayed absorption or release into the bowel. In this case, the symptoms appeared 30 min after ingesting *natto*. It has been reported that epithelial damage of the digestive organs is associated with abnormal intestinal permeability.⁶ Therefore, in our case, the inflammation of the digestive organs might have affected absorption of PGA although the precise mechanisms are not clear. Therefore, it is necessary to consider the possibility of not only delayed-onset, but also immediate-onset *natto* allergy.

CONFLICT OF INTEREST: The authors have no conflict of interest.

Chika IKEMOTO,^{1,*} Risa TAMAGAWA-MINEOKA,^{1,*} Koji MASUDA,¹ Saori IIDA,¹ Naoko INOMATA,² Norito KATO¹

¹Department of Dermatology, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Kyoto, and ²Department of Dermatology, Yokohama City University Hospital, Kanagawa, Japan

REFERENCES

- 1 Inomata N, Nomura Y, Ikezawa Z. Involvement of poly (γ -glutamic acid) as an allergen in late-onset anaphylaxis due to fermented soybeans (*natto*). *J Dermatol* 2012; **39**: 409–412.
- 2 Inomata N, Osuna H, Ikezawa Z. Late-onset anaphylaxis to *Bacillus subtilis*-fermented soybeans. *J Allergy Clin Immunol* 2004; **113**: 998–1000.
- 3 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.
- 4 Inomata N, Chin K, Nagashima M, Ikezawa Z. Late-onset anaphylaxis due to poly (γ -glutamic acid) in the soup of commercial cold Chinese noodles in a patient with allergy to fermented soybeans (*natto*). *Allergol Int* 2011; **60**: 393–396.
- 5 Shih IL, Van YT. The production of poly- γ -glutamic acid from micro-organisms and its various applications. *Bioresour Technol* 2001; **79**: 207–225.
- 6 Arrieta MC, Bistritz L, Meddings JB. Alterations in intestinal permeability. *Gut* 2006; **55**: 1512–1520.

Correspondence: Risa Tamagawa-Mineoka, Ph.D., M.D., Department of Dermatology, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan. Email: risat@koto.kpu-m.ac.jp

*These authors contributed equally to this work.