

LETTER TO THE EDITOR

Fermented soybean-induced late-onset anaphylaxis in a 7-year-old junior surfer

Dear Editor,

Fermented soybeans (*natto*) have been significantly involved in late-onset anaphylaxis in Japan.¹ One case of cuttlefish-induced late-onset anaphylaxis was also reported.² The major *natto* allergen is poly(γ -glutamic acid) (PGA), which is also produced by cnidarians, such as jellyfish. In the previous study, more than 80% of the adult patients had a history of participation in marine sports, especially surfing.¹ However, there have only been three known pediatric cases of *natto* anaphylaxis and in these cases, there was no history of marine sports/activities.^{3–5} Here, we report the first pediatric case of *natto*-induced, late-onset anaphylaxis with 3 years of regular surfing.

A 7-year-old boy was referred to our clinic with a history of four previous anaphylactic reactions. During one episode, he developed generalized urticaria, facial and lip swelling, wheezing and dyspnea at 4 PM. Earlier that day at 7 AM, his breakfast had included *natto*. The other two anaphylactic reactions occurred at 3 AM while the patient was asleep. His previous meal was approximately 9 h prior to the onset of anaphylaxis. Therefore, we suspected that he was suffering from late-onset anaphylaxis due to the food ingested 9 h earlier. Additionally, he also had allergies to crab and was a junior surfer who had been regularly surfing for 3 years.

Specific immunoglobulin E measurements using the ImmunoCAP system (Thermo Fisher Scientific, Waltham, MA, USA) were positive for shrimp (0.74 UA/mL) but negative for soybean and crab. Skin prick tests were positive for *natto* mucilage (Okame, Ibaragi, Japan; wheal diameter, 9.1 mm $\times$ 7.1 mm) and PGA (Wako Pure Chemical, Osaka, Japan; 1 mg/mL in saline, 13.7 mm $\times$ 6.8 mm). In addition, jellyfish (Kanetoku, Hyogo, Japan) induced a positive reaction (8.0 mm $\times$ 5.0 mm). The soybean extract (Torii Pharmaceutical, Tokyo, Japan), however, did not produce a positive reaction. Furthermore, in basophil activation tests, the PGA extract enhanced basophil CD203c expression (Fig. 1). He was diagnosed with *natto*-induced, late-onset anaphylaxis. After diagnosis, he avoided eating jellyfish. However, he has been continuing marine sports wearing a wet suit to prevent more exposure to jellyfish via the skin. He has also avoided consuming *natto* and PGA-containing products, such as preservatives and thickeners for food and cosmetics (e.g. emulsions, lotions). He did not develop any further anaphylactic reactions in the 2 years following diagnosis.

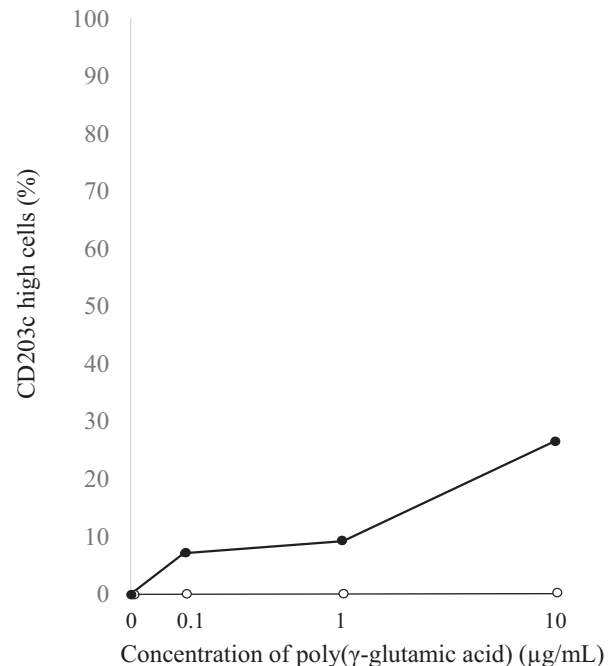


Figure 1. Results of basophil activation tests (BAT) with poly(γ -glutamic acid) (PGA). Closed circles indicate BAT results obtained with peripheral blood mononuclear cells (PBMC) from the patient. Whole-blood BAT showed 26.6% CD203c-positive cells at a PGA extract concentration of 10 μ g/mL, indicating that PGA enhanced basophil CD203c expression. Open circles indicate the mean values of BAT results obtained with PMBC from three control subjects without *natto* allergy. The results of BAT using a positive control (anti-immunoglobulin E) showed 54.3% and 66.3–95.2% CD203c-positive cells in the patient and controls, respectively.

The other three reported pediatric cases of *natto* allergy all experienced anaphylactic shock.^{3–5} The duration between *natto* ingestion and anaphylaxis onset ranged 2.5–8, 12–13 and 3 h.^{3–5} Only one of these cases is documented to have undergone a skin prick test with PGA, which was positive.⁴ However, this patient had no history of participation in marine activities. We suspected that in our case, like adult cases, sensitization to PGA might have been due to repeated cnidarian stings, which were likely received during surfing. The

concomitant sensitization to jellyfish in our case supported this hypothesis.

In conclusion, our case study indicated that surfing may be a risk factor for PGA sensitization not only in adult cases but only in a subset of pediatric cases in *natto* allergy.

CONFLICT OF INTEREST: None declared.

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REFERENCES

- 1 Inomata N, Miyakawa M, Aihara M. Surfing as a risk factor for sensitization to poly(γ -glutamic acid) in fermented soybeans, natto, allergy. *Allergol Int* 2018; **67**: 341–346.
- 2 Shibasaki M, Ehara T, Takita H. Late anaphylactic reaction to cuttlefish. *Ann Allergy* 1989; **63**: 421–422.
- 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 Mori S, Tsumagari S, Kurihara K. A case of a 7-year-old girl with late-onset anaphylaxis to fermented soybeans. *Pediatr Allergy Immunol* 2017; **28**: 501–502.
- 5 Horimukai K, Nakatani K, Yoshida K *et al*. Late-onset anaphylaxis after ingestion of *Bacillus subtilis*-fermented soybeans (natto) which could increase its allergenicity gradually with time: a case report of 7-year old boy. *Jpn J Pediatr* 2011; **64**: 1659–1662 (Japanese).