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Letter to the Editor

Acquisition of tolerance to egg allergy in a child with repeated egg-induced acute pancreatitis

Dear Editor,

Egg allergy is one of the most common food allergies.¹ In Japan, egg accounts for 38.3% of all immediate food allergy-causing antigens.² Most people with food allergies acquire tolerance in infancy. For egg allergy, 30% of patients acquire tolerance before the age of 3 years and 73% acquire tolerance before the age of 6 years.³

Food allergies can cause various symptoms,² and pancreatitis may occur in some rare cases.^{4–6} However, the prognosis, such as tolerance acquisition, is unknown. There have been no reports on the prognosis for patients who developed pancreatitis due to a food allergy.

We report the case of a patient who was confirmed to have acquired tolerance after repeated food allergy-induced acute pancreatitis.

Case report

The patient was a 3-year-old boy with no digestive organ disease. Owing to atopic dermatitis during infancy and an egg white-specific immunoglobulin E (sIgE) level of 22.9 kU_A/L at the age of 8 months, he was directed to avoid consuming eggs, and subsequently visited our hospital for food allergies (eggs and milk). At the age of 3 years, he acquired tolerance for milk. At the same age, he ingested egg yolks contaminated with 0.5 g egg white (0.05 g egg white protein) in an oral food challenge (OFC), and developed abdominal pain (mild at 45 min, progressing to severe at 130 min after ingestion), recurrent vomiting, and leg hives. He was administered intramuscular adrenaline and intravenous hydrocortisone and hydroxyzine pamoate. Subsequently, the hives improved immediately, but the abdominal pain continued. The next day, blood tests showed an elevated pancreatic amylase level (1374 IU/L), and abdominal computed tomography (CT) revealed pancreatic swelling. Therefore, he was diagnosed with pancreatitis.⁴ At the age of 6, he accidentally ingested processed egg (cheesecake), which resulted in severe abdominal pain and generalized urticaria. Following blood tests and abdominal CT, he was diagnosed with recurrent pancreatitis and instructed to completely avoid consuming eggs. We have previously reported the details of the development of pancreatitis in this patient.⁴ However, when he was 10 years old, he and his family expressed a strong desire for an OFC to confirm tolerance. Since approximately

4 years had passed since the previous immediate symptoms, OFC was planned, considering his safety, to confirm tolerance.

This study was designed in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Sagami Hospital National Hospital Ethics Committee (approval number 160107). Because of the risk of pancreatitis, informed consent/assent was obtained from the patient and his parents.

Although single OFC is recommended in the PRACTALL guidelines,⁷ we performed stepwise OFC. If symptoms were to appear, multiple stepwise OFCs would induce less severe symptoms than a single OFC, by employing low exposure amounts in the beginning.^{8,9} According to published methods, we established the following OFC regimens for the present patient from the age of 10 to 11 years⁸ (Fig. 1): a quarter of a hard-boiled egg yolk (egg protein 1.8 mg), and 194 mg, 776 mg, 3100 mg, and 6200 mg of egg protein, measured using a FASTKIT® version III enzyme-linked immunosorbent assay (ELISA) kit (Cosmo Bio, Tokyo, Japan). We performed each OFC in two separate steps, 1 h apart. The first dose comprised a quarter of the predetermined total OFC dose, and the second dose comprised the remaining three quarters. All OFCs were performed over 3 days in the hospital, in the presence of doctors, nurses, and parents. For each OFC, we contacted a tertiary emergency medical facility and obtained approval for transfer in case of pancreatitis onset.

For the OFCs with 194 and 776 mg egg protein, egg powder was prepared from heated whole egg components in the research institution of Kewpie (Tokyo, Japan). A microbiological examination was performed to confirm its safety. Using FASTKIT® version III ELISA, we determined that the powder contained 194 mg egg protein, with an antigen level equivalent to 1/32 of a heated 60-g whole egg. We used 1 and 4 packages of powder for the 194 mg and 776 mg OFC, respectively. For the OFCs with 3100 and 6200 mg egg protein, we used pumpkin cake cooked at our hospital (Supplementary Table 1).

At the age of 10–11 years, all OFC results were negative, and subsequent intake at home did not induce symptoms. We then instructed him to ingest egg freely. Finally, at the age of 14, he was able to consume raw egg without symptoms; therefore, we concluded that he had developed tolerance.

Throughout the OFC process, serum amylase was within the normal range. At the age of 10, his egg white-sIgE level was 6.65 kU_A/L and ovomucoid-sIgE level was 7.37 kU_A/L; at the age of 11 years, egg white-sIgE level was 3.84 kU_A/L and ovomucoid-sIgE level was 3.18 kU_A/L (Fig. 2).

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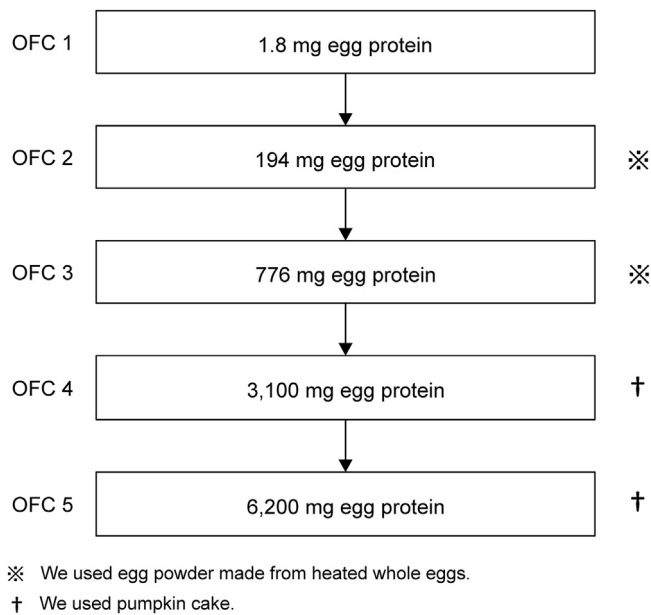


Fig. 1. OFC schedule. The OFC was implemented stepwise, beginning with a small amount. We performed each OFC in two separate steps, performed 1 h apart. The first dose comprised a quarter of the predetermined total OFC dose, and the second dose comprised the remaining three quarters. OFC, oral food challenge.

Discussion

We herein report the first case of tolerance acquisition in a patient who developed repeated food allergy-induced acute pancreatitis. A few cases of food allergy-induced acute pancreatitis have been reported, but its prognosis is unknown.^{4–6} There are no reports of OFC with causal foods in children with a history of pancreatitis. Although the mechanism of pancreatitis has not yet been clarified, Gastaminza *et al.* have suggested the possibility of bile flowing into the pancreatic duct because of swelling of the Vater papillary region due to allergic inflammation.⁵ Additionally, Inamura *et al.* reported inflammation of the Vater papilla in a patient with banana allergy-induced acute pancreatitis.⁶ In our case, upper gastrointestinal endoscopy was not performed; however, there were no congenital abnormalities. Additionally, the patient was not administered any drug known to induce pancreatitis.⁴

Regarding the natural history of egg allergy, most patients are expected to develop tolerance in infancy.³ However, in cases with severe symptoms, many patients are hesitant to undergo OFC. Moreover, it is known that the frequency of developing abdominal symptoms with egg allergies is significantly higher than that with other food antigens.¹⁰ We recommend that, for patients who developed food allergy during infancy, stepwise OFC should be performed for confirmation of tolerance. In conclusion, patients who develop food allergy-induced acute pancreatitis can acquire tolerance; hence, OFC may be performed under careful management.

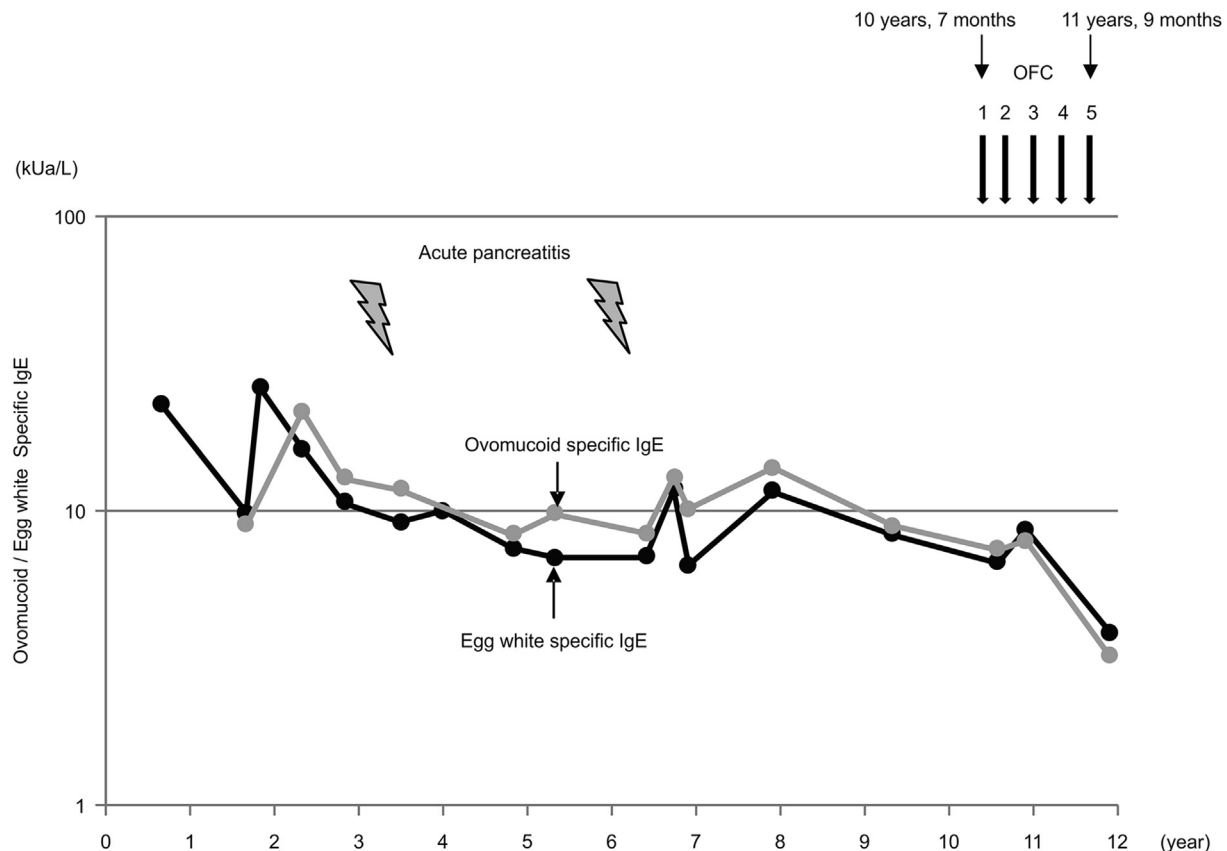


Fig. 2. Clinical outcome and laboratory data changes. OFC, oral food challenge.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.alit.2018.04.004>.

Conflict of interest

The authors have no conflict of interest to declare.

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Food	Ingredients	Directions
OFC 1	Egg yolk	An egg was heated in boiling water for 12 minutes.
Egg yolk		The egg yolk was subsequently removed and
: 1/4 egg yolk		divided into 8 pieces.
OFC 2, 3	Egg powder	Egg powder was made from heated whole egg
Egg powder		component at the Kewpie Corporation laboratory.
: 1/128 whole egg		Microbiological testing was performed to confirm
: 1/32 whole egg		its safety. Using FASTKIT® version III ELISA, we
		determined that the powder with an antigen level
		equivalent to 1/32 of a heated 60-g whole egg..
OFC 4, 5	Pumpkin 40.0 g	All ingredients were combined in a bowl and mixed
Pumpkin cake	1/2 whole egg 25.0	thoroughly using a hand mixer. The total amount of
: 1/2 whole egg	g	the mixture for one portion was measured, placed in
: 1 whole egg	Sugar 5.0 g	a silicon cup, and heated in a microwave at 1000 W
	Total 70.0 g	for 90 seconds. As the mixture tended to stick to the
		sides of the bowl, it was prepared by more than 2
		persons.

Supplementary Table 1. Recipes for oral food challenge

OFC, oral food challenge; ELISA, enzyme-linked immunosorbent assay.