

Two patients with acute pancreatitis after undergoing oral food challenges

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Clinical Implications

- We report 2 children who developed acute pancreatitis after oral food challenges to raise awareness about this rare complication. Evaluation for acute pancreatitis should be considered for severe abdominal pain during the food challenge to elucidate the potential mechanism.

TO THE EDITOR:

Acute pancreatitis (AP) associated with food allergy (FA) is rare and difficult to distinguish from a usual food-allergic reaction. We report 2 cases of AP due to hen's egg and buckwheat allergies.

Patient 1 was a 3-year-old boy. He had a history of eczema at 3 months and an egg white (EW)-specific immunoglobulin E (sIgE) level of 22.9 Ua/mL (ImmunoCAP) at age 8 months. At age 1 year, he accidentally ingested mayonnaise and developed transient facial urticaria 30 minutes later. At age 2 years, his EW-, egg yolk (EY)-, and ovomucoid-sIgE levels were 10.6, 2.34, and 12.9 Ua/mL, respectively. Because EW-sIgE levels decreased, a heated egg oral food challenge (OFC) was performed at age 3 years.

The OFC food was a hamburger steak with raw EY as a binder, cooked by a dietician. During the OFC, the patient ingested 52 mg of egg protein, measured by the FASTKIT ELISA (Nippon Meat Packers, Inc, Tsukuba, Japan). After 45 minutes, he complained of mild epigastric pain. The OFC was stopped, and he was observed without medication. After 130 minutes, he developed severe abdominal pain, lower leg urticaria, recurrent vomiting, and drowsiness. He was treated with an intramuscular adrenaline injection (0.1 mg/kg), intravenous infusion of hydroxyzine pamoate (1 mg/kg), and hydrocortisone sodium succinate (7 mg/kg). His skin and neurological symptoms resolved soon, but hospitalization was required because of persistent abdominal pain. On day 2, blood examination showed an elevated pancreatic amylase (p-AMY) level (641 IU/L). The p-AMY level increased to 1374 IU/L, and the lipase level was 776 IU/L, according to residual serum that was collected after the patient had severe abdominal pain on day 1. Abdominal computed tomography (CT) showed swollen pancreas on day 3; AP was diagnosed. He was treated with gabexate mesilate (1 mg/kg/h), nafamostat mesilate (0.1 mg/kg/h), ulinastatin (200 U/kg/h), sulbactam sodium/cefoperazone sodium (70 mg/kg/d), and prednisolone sodium succinate (2 mg/kg/d). His pain resolved on day 4. The serum amylase levels normalized on day 5. The pancreas remained swollen on day 6 (Figure 1); after hospital discharge, it was normalized on CT.

Strict elimination of egg from the diet was continued. However, at age 6 years, he accidentally ingested cheesecake; 20 minutes afterward, he developed epigastric pain and generalized urticaria. When he arrived at our hospital, urticaria resolved. Nevertheless, hospitalization was required because his pain persisted for 3 hours without medication. Elevated p-AMY (1806 IU/L) and lipase (3931 IU/L) levels were seen. His EW-, EY-, and ovomucoid-sIgE levels were 11.8, 3.43, and 13.0 Ua/mL, respectively. Abdominal CT (Figure 1) showed pancreatic enlargement and intrahepatic bile duct dilation. Thus, recurrent pancreatitis was diagnosed. He was treated with loratadine (5 mg), betamethasone (2 mg), gabexate mesilate (1 mg/kg/h), sulbactam sodium/cefoperazone sodium (60 mg/kg/d), methylprednisolone sodium succinate (3 mg/kg/d), and famotidine (1 mg/kg/d). His pain resolved after 12 hours. The pancreatic enzyme level normalized on day 3.

Patient 2 was a 9-year-old boy. At age 4 years, he developed laryngeal pain and urticaria after ingesting buckwheat. His buckwheat-sIgE level was 12.3 Ua/mL; thus, food elimination was started. At age 8 years, as his sIgE level decreased to 2.32 Ua/mL, a buckwheat OFC was performed. During the OFC, he ingested 5.4 g of buckwheat protein. After 7 minutes, he developed mild laryngeal pain. After 90 minutes, he developed a persistent cough. The respiratory symptom resolved with a bronchodilator inhalation (procaterol, 30 µg). After 160 minutes, he was treated with an intramuscular adrenaline injection (0.1 mg/kg) and an intravenous infusion of hydroxyzine pamoate (2 mg/kg) because of generalized urticaria, vomiting, and hypotension. These symptoms resolved soon, but epigastric pain developed after 260 minutes. His abdominal pain weakened after another intramuscular adrenaline injection, but it recurred after 6 hours. As his pain was long-lasting, he was hospitalized. Increased levels of p-AMY (667 IU/L) and lipase (465 IU/L) were seen. Abdominal CT (Figure 1) showed pancreatic enlargement. Therefore, AP was diagnosed. He was treated with nafamostat mesilate (0.1 mg/kg/h), famotidine (2 mg/kg/d), piperacillin (100 mg/kg/d), and betamethasone (0.13 mg/kg/d). His pain resolved and the pancreatic enzyme levels normalized on day 3.

In both cases, the previous serum amylase levels were normal before the OFC. Magnetic resonance cholangiopancreatography showed no abnormality that may have caused pancreatitis. Drug-induced pancreatitis seemed to be unlikely because there was no previous report of pancreatitis due to adrenaline, hydroxyzine, hydrocortisone, and procaterol. Therefore, AP associated with FA was diagnosed. Both patients never experienced recurrent pancreatitis after they avoided their allergens.

AP associated with FA is rare. We found only 9 previous cases published in PubMed¹⁻⁸ and 8 reported by the Japan Medical Abstracts Society⁹⁻¹⁵ (Table I). Among these patients, the characteristics of their abdominal symptoms were recurrent, persistent, or severe. Regarding such symptoms during an OFC, AP may be one of the causative differential diagnoses.

The incidence rate of AP associated with FA is unknown. We predicted the frequencies of AP after OFC as 0.04% (2 of 5220) among positive OFCs and as 0.08% (2 of 2598) among those

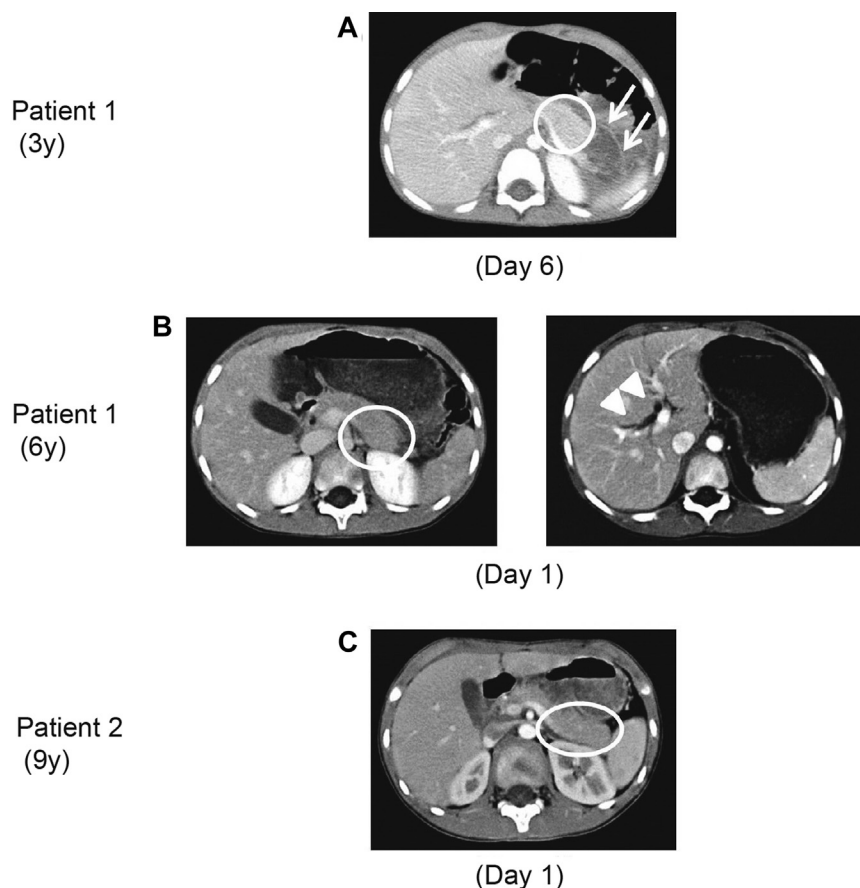


FIGURE 1. Imaging findings. **A**, Abdominal CTscan showing the swollen pancreas (circle) and pseudocyst in the pancreatic tail (arrow) in patient 1. **B**, Abdominal CT scan showing the swollen pancreas (circle) and dilated intrahepatic bile duct (arrowhead) in patient 1. **C**, Abdominal CT scan showing the swollen pancreas (circle) in patient 2.

TABLE I. Previous cases of acute pancreatitis associated with an FA

Food	Case	Examination and findings	Reference
Fish	37 y, M	Hyperamylasemia	Boquien et al ⁸
Egg, potato, beef, fish	17 y, M	AMY, 2150 IU/L; US and CT, increased volume of the pancreas (+)	Matteo and Sarles ¹
Milk, beef	40 y, F	AMY, 2038 IU/L	
Milk	23 y, M	Milk-sIgE, 2.17 Ua/mL; AMY, 2061 IU/L; lipase, 921 IU/L; US, swollen pancreas (+)	de Diego et al ²
Egg	40 y, M	EW-sIgE, 1.21 Ua/mL; lipase, 239 IU/L; elastase I, 823 ng/dL	Toyoshima ⁹
Cod Roe	7 y, F	Immunoblot (+); AMY, 2410 IU/L; lipase, 2080 IU/L; US, swollen pancreas (+)	Iwata et al ³
Kiwi	48 y, M	SPT (+); AMY, 835 IU/L; lipase, 290 IU/L	Gastaminza et al ⁴
Buckwheat	9 y, F	Buckwheat-sIgE, class 5; AMY, 1831 IU/L; trypsin, 700 ng/mL; US and CT, swollen pancreas (+)	Nikaidou et al ¹⁰
Banana	47 y, F	Banana-sIgE, 2.18 Ua/mL; AMY, 945-2609 IU/L; lipase, 1893 IU/L	Inamura et al ⁵
Egg, wheat	2 y, M	EW-sIgE, >100.0 Ua/mL; wheat-sIgE, 90.8 Ua/mL; AMY, 2109 IU/L; lipase, 7173 IU/L; CT, swollen pancreas (+)	Noda et al ¹¹
Shrimp	19 y, M	Scratch test (+); p-AMY, 515 IU/L; CT, high-density peripancreatic fat tissue (+)	Ogata et al ¹²
Egg	1 y, M	EW-sIgE, 3.82 Ua/mL; AMY, 1303 IU/L; lipase, 2768 IU/L	Ibuki et al ¹³
Wheat	1 y, M	Wheat-sIgE, 64.7 Ua/mL; AMY, 541 IU/L; lipase, 3671 IU/L	
Peanuts	8 y, F	Peanut-sIgE, 10.2 Ua/mL; p-AMY, 694 IU/L; lipase, 1830 IU/L	Nakata et al ¹⁴
Codfish	8 y, M	Codfish-sIgE, 1.30 Ua/mL; AMY, 2559 IU/L; lipase, 219 IU/L; US, swollen pancreas (+)	Pellegrino et al ⁶
Milk	28 y, M	Milk-sIgE, 2.47 Ua/mL; lipase, 202 IU/L; trypsin, >900 ng/mL; PLA2, 756 ng/dL; CT, intestinal wall edema (+)	Suzuki et al ⁷
Peanuts	3 y, M	Peanut-sIgE, 37.1 Ua/mL; p-AMY, 2081 IU/L; CT, swollen pancreas (+)	Shimizu et al ¹⁵

AMY, Amylase; F, female; M, male; PLA2, pancreatic phospholipase A2; SPT, skin prick test; US, ultrasound.

with abdominal symptoms, which were calculated from 20,031 total OFCs at our hospital during the past 10 years.

The mechanism of pancreatitis associated with FA is unclear. Fourteen of 17 cases had IgE sensitization. Gastaminza et al⁴ speculated that AP may be caused by papilla Vater closing with mucous edema and bile flowing into the pancreas. Inamura et al⁵ reported papilla Vater edema on upper gastrointestinal endoscopy after patients ingested a banana. In patient 1, we detected intrahepatic bile duct dilation on CT, which may indicate papilla Vater closing; this has not been reported in past cases.

More than half of previous cases have been reported from Japan. Eosinophilic gastroenteritis (EgE) may be a possible mechanism. EgE occurred more frequently in Asians than in whites.¹⁶ Suzuki et al⁷ reported gastrointestinal eosinophilic infiltration on biopsy after patients ingested milk. In Asian countries, the fact that more OFCs are performed may explain why more cases of AP were reported from Japan.¹⁷

More cases are needed to elucidate the mechanism of AP associated with FA in the future.

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Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

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