

Two cases of an infant with Down syndrome with solid food protein-induced enterocolitis syndrome

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Food protein-induced enterocolitis syndrome (FPIES) is a form of non-immunoglobulin E (IgE)-mediated gastrointestinal food allergy (non-IgE-GIFA). Most patients with acute type FPIES present with recurrent vomiting within 1–4 h, and/or diarrhea within 24 h, of ingesting the triggering food.¹ Food protein-induced enterocolitis syndrome is divided into two types depending on whether the causative food is solid or not. The most common liquid food triggering FPIES is cow's milk, and common solid food triggers include grains, fish, meat, vegetables, etc.¹ Solid FPIES in patients with Down syndrome (DS) has never been reported. Here we report two Japanese children with DS in whom solid FPIES was initially suspected based on their medical history and later diagnosed by an oral food challenge test (OFC). Informed consent to publish the details of the cases was obtained from the legal guardians of the patients.

Patient 1, a 10-month-old male, was born by normal vaginal delivery with a birthweight of 2,782 g at 40 weeks' gestation. DS was diagnosed based on chromosome test results. He had no cardiac or gastrointestinal complications. He had a history of infantile eczema. He started ingesting baby food at age 6 months and experienced repeated vomiting 2–3 h after ingesting about half a teaspoon (2–3 g) of egg yolk on two occasions. He experienced a similar episode two more times prior to the current consultation. He had never ingested egg white. The results of a skin prick test (SPT) with egg yolk and egg white (Torii and Co., Ltd, Tokyo, Japan), a prick to prick test using boiled egg yolk and egg white, and a blood test egg yolk and egg white-specific IgE antibody on ImmunoCAP (Thermo Fisher Scientific/Phadia, Uppsala, Sweden) were negative. Table 1 summarizes the history of patient 1 and patient 2.

Table 1. Summary of patient profiles

	Case 1	Case 2
Sex	Male	Male
Age at first episode (months)	6	10

	Case 1	Case 2
Suspected food	Egg yolk	Cod fish
Symptoms	Vomiting	Vomiting
Past history	–	GER, hypothyroidism
Allergic comorbidity		
Eczema	+	+
IgE-mediated food allergy	–	Egg white
Family history of allergy	HF (parents)	AD (father), HF (parents)
Age at OFC (months)	14	31
Food	Egg yolk	Cod fish
Dose (g)	2	10
Symptoms	Vomiting	Vomiting, lethargy, pallor
Laboratory data		

Egg yolk, egg white and codfish-specific IgE antibody were assessed used ImmunoCAP (Thermo Fisher Scientific / Phadia, Uppsala, Sweden). Skin prick tests were done using reagents (Torii and Co., Ltd, Tokyo, Japan). AD, atopic dermatitis; GER, gastroesophageal reflux; HF, hay fever; OFC, oral food challenge.

At age 14 months he underwent an OFC with 2.0 g of boiled egg yolk and vomited several times within 2 h after ingesting the food. However, he had no symptoms after ingesting 7.5 g of boiled egg white. Based on these results, FPIES due to egg yolk was diagnosed. The patient's parents were instructed to avoid feeding him egg yolk only. The patient thereafter experienced no further episodes of vomiting due to an unknown cause.

Patient 2, a 20-month-old male, was born by cesarean section with a birthweight of 2,914 g at 38 weeks' gestation. Down syndrome was diagnosed based on chromosome test results. He had no cardiac complications but received the diagnosis of gastroesophageal reflux (GER) disease based on clinical symptoms, such as repetitive retching, choking, and vomiting during or after feeding. He had a history of infantile eczema. He required tube feeding, but began ingesting baby food at age 7 months after remission of the vomiting. However, he experienced more than three episodes of repetitive vomiting again at age 10 months within about 2–4 h after meals, in all instances after ingesting approximately 10 to 15 g of codfish. He was referred to our department for a suspected allergic reaction. The results of sensitization tests, including a prick-by-prick test with raw and boiled codfish and a serum

codfish-specific IgE antibody test, were negative.

Oral food challenge was performed at age 2 years using 10 g of boiled codfish. He vomited repeatedly and had lethargy and pallor 2 h afterwards. Based on these results, FPIES due to codfish was diagnosed. Since avoiding codfish, he experienced no further allergic reactions. The patient was able to eat other kinds of fish, such as tuna, salmon, swordfish, porgy, and whitebait without any allergic reaction.

According to the nationwide survey in Japan, about 0.5% of infants have FPIES.² Several risk factors for FPIES have been reported, including a slight male preference, atopy, and birth by cesarean section.¹ However, the correlation between chromosomal abnormalities and the incidence of non-IgE-GIFA has not been proven, and only one previous report describing two cases of non-IgE-GIFA in patients with DS caused by cow's milk (CM), one of which was diagnosed as FPIES, has been published.³ In comparison with the healthy immune system, the immune system in DS is marked by deficiencies and dysregulations, which may lead to lower (deficiency) or higher (dysregulation) allergic sensitization. Lower IL-10 may be involved in the pathophysiology of FPIES¹ and DS patients reportedly have impaired IL-10 production.⁴ These facts may be associated with FPIES development in DS.

Gastrointestinal abnormalities, including GER, are common in patients with DS, who also often experience masticatory dysfunction and aspiration during feeding, which delay the introduction of solid food and contribute to exacerbating their feeding disorder.⁵ In these patients it may thus be difficult to identify vomiting as a symptom of an allergic reaction. Moreover, FPIES is considered difficult to diagnose because the presenting symptoms are non-specific and do not resemble typical allergic symptoms (there is no skin or respiratory involvement) and time interval between ingestion and symptom onset may be long (1–4 h).¹ It should also be borne in mind that the diagnosis of solid food FPIES tends to be made later than for CM-FPIES, probably because the causative foods are perceived to be hypo-allergenic and there is currently no definitive diagnostic test.¹ The present report underscores the fact that in children with DS, vomiting due to an unknown cause should prompt detailed history-taking to ascertain whether any ingested food items were common to the vomiting episodes.

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Disclosure

The authors declare no conflict of interest.

Author contributions

N.K. provided medical care and wrote the manuscript. H.F. and H.Y. also provided medical

care. H.F., H.Y., K.Y., and M.N. critically reviewed the manuscript. All the authors read and approved the final version.

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