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CASE REPORT

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Acute typical food protein-induced enterocolitis syndrome triggered by egg white: Two case reports

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Abstract
Food protein-induced enterocolitis syndrome (FPIES) is a non-immunoglobulin E (IgE)-mediated food allergy characterized by gastrointestinal symptoms such as vomiting and diarrhea. Since 2018, hen's egg yolk has been the most common trigger for FPIES in Japan, whereas typical egg white (TEW) FPIES remains rare. Herein, we present two cases of acute TEW FPIES in young children. A 17-month-old girl experienced recurrent vomiting and lethargy following egg white ingestion, despite previously tolerating half an egg yolk and 5 g of egg white. Initial tests showed no sensitization markers (egg white-specific IgE < 0.1 kUA/L; ovomucoid [OVM]-specific IgE < 0.1 kUA/L; skin prick test [SPT] negative). Three oral food challenges (OFCs) at 6-month intervals at our hospital all triggered vomiting and lethargy. Procalcitonin and thymus- and activation-regulated chemokine levels remained elevated for 24 hours, and even after 31 months, the patient had not achieved egg white tolerance. A 14-month-old girl presented with vomiting and lethargy after egg white ingestion while on a strict egg yolk- and egg white-free diet. Blood tests again showed no sensitization markers (egg white-specific IgE < 0.1 kUA/L; OVM-specific IgE < 0.1 kUA/L; SPT negative). Two OFCs at 6-month intervals confirmed FPIES, and even after 2 years, the patient had not achieved egg white tolerance. These cases highlight that egg white can trigger FPIES. Thorough medical history taking and diagnostic evaluation, including OFCs, are essential to distinguish FPIES from immediate-type food allergies.

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Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a non-immunoglobulin E (IgE)-mediated food allergy categorized into acute and chronic types. Both forms primarily present with gastrointestinal symptoms such as vomiting and diarrhea[1,2]; however, acute FPIES can lead to shock in some patients. The prevalence of FPIES has been reported to range from 0.015% to 0.7%.[2-5] Since the publication of the consensus guidelines in 2017, which outlined diagnostic and management strategies, the number of reported cases has increased worldwide, including in Japan.[6-8] Trigger foods associated with FPIES show substantial regional variations.[2,9] Cow's milk has been a common trigger food globally since the early recognition of FPIES[8] and remains the most frequently reported in Europe, followed by fish.[10] In the United States, oats are the most common trigger food.[11] Hen's eggs are widely recognized as a global trigger food,[12] with Japan reporting them as the most common cause.[13,14] Among hen's egg components, egg yolk is particularly prevalent as a trigger food in Japan,[13] with a dramatic increase in cases reported since 2018.[14-17]

However, cases of FPIES caused by egg white are extremely rare compared with those triggered by egg yolk. Although egg white FPIES has been reported,[18] these cases often involve sensitization to egg white or ovomucoid (OVM), leading to their classification as atypical FPIES.[1,2] During infancy, egg white commonly triggers immediate-type food allergies; hence, when sensitization to egg white or OVM is observed, careful differentiation between atypical FPIES and immediate-type food allergy is necessary.[1,2] Consequently, even if a patient fulfills the diagnostic criteria for FPIES, it is essential to consider that previously reported instances of egg white FPIES may not represent true FPIES.

Here, we report two cases of patients suspected of having typical egg white (TEW) FPIES based on their medical history.

Case Report

Case 1

An 18-month-old girl presented with vomiting episodes following egg white ingestion. At 11 months of age, she consumed 10 g of egg white and experienced three episodes of vomiting 3 hours later. At 12 months of age, an oral food challenge (OFC) with 1/30th of a whole egg was conducted at her previous medical institution, resulting in four episodes of vomiting and pallor 210 minutes post-ingestion requiring intravenous hydration. The patient was referred to our institution with suspected egg white FPIES. Before onset of the symptom, she had been able to tolerate half an egg yolk and 5 g of egg white. At her initial evaluation at our institution, blood test results revealed total immunoglobulin E (IgE) of 11 IU/mL, egg white-specific IgE < 0.1 kUA/L, egg yolk-specific IgE < 0.1 kUA/L, and OVM-specific IgE < 0.1 kUA/L. The skin prick test (SPT) revealed no sensitization, with egg white at 0 mm × 0 mm/2 mm × 2 mm, negative control at 0 mm × 0 mm/2 mm × 2 mm, and positive control at 8 mm × 6 mm/20 mm × 12 mm. The patient completely avoided egg white but could tolerate one whole egg yolk. She had no other food allergies or allergic diseases.

At 19 months of age, an OFC with 1/32th of an egg white was conducted following the Japanese Guidelines for Food Allergy,[19] using the open single-dose method under the supervision of an allergy specialist. At 146 minutes after starting the OFC, the patient experienced seven episodes of vomiting and lethargy, requiring intravenous hydration, leading to a diagnosis of TEW FPIES. At 25 months of age, a second OFC with 1/32th of the egg white was performed. Blood test results showed no changes in sensitization status, with total IgE at 11 IU/mL, egg white-specific IgE < 0.1 kUA/L, egg yolk-specific IgE < 0.1 kUA/L, and OVM-specific IgE < 0.1 kUA/L. At 181 minutes post-OFC, the patient experienced four episodes of vomiting and lethargy, and the OFC was deemed positive. At 30 months of age, a third OFC with 1/32th of the egg white was performed. Again, there were no changes in the sensitization status, with total IgE at 8 IU/mL, egg white-specific IgE < 0.1 kUA/L, egg yolk-specific IgE < 0.1 kUA/L, OVM-specific IgE < 0.1 kUA/L, procalcitonin (PCT) at 0.05 ng/mL, and thymus and activation-regulated chemokine (TARC) at 581 pg/mL (Table 1). At 190 minutes post-OFC, the patient experienced six episodes of vomiting and lethargy, resulting in a positive OFC and necessitating hospitalization. Post-symptom PCT and TARC levels were elevated, measuring 0.79 ng/mL and 2,184 pg/mL at the 5th hour and 1.42 ng/mL and 3314 pg/mL at the 24th hour, respectively. At 31 months of age, the patient had not achieved tolerance to egg white.

Case 2

A 14-month-old girl presented with a history suggestive of egg white FPIES. At 8 months of age, she consumed 10 g of whole egg and experienced three episodes of vomiting and lethargy 150 minutes later. At the same age, after consuming 1 g of egg white, she experienced six episodes of vomiting and lethargy 180 minutes post-ingestion. The patient was referred to our institution with suspected egg white FPIES. Before the onset of symptoms, she had been able to tolerate up to 5 g of whole egg. At her initial evaluation, blood test results revealed a total IgE of 4 IU/mL, egg white-specific IgE < 0.1 kUA/L, egg yolk-specific IgE < 0.1 kUA/L, and OVM-specific IgE < 0.1 kUA/L. The SPT revealed no sensitization, with egg white at 1 mm × 1 mm/3 mm × 2 mm, negative control at 0 mm × 0 mm/1 mm × 1 mm, and positive control at 9 mm × 8 mm/12 mm × 11 mm. She was on a strict exclusion diet for both egg white and egg yolk. During her visit, she had no other food allergies or allergic diseases.

At 15 months of age, an OFC with 1/32th of an egg white was conducted. At 134 minutes post-OFC, the patient experienced three episodes of vomiting and lethargy, leading to the diagnosis of TEW FPIES.

At 21 months of age, a repeat OFC with 1/32th of the egg white was performed. Blood test results showed no changes in the sensitization status, with total IgE at 6 IU/mL, egg white-specific IgE < 0.1 kUA/L, egg yolk-specific IgE < 0.1 kUA/L, OVM-specific IgE < 0.1 kUA/L, PCT < 0.02 ng/mL, and TARC at 443 pg/mL (Table 1).

Table 1 Patient characteristics.

Patient	1	2
Age	18 months	14 months
Sex	Female	Female
Allergic complications	None	None
Total IgE (IU/mL)	8	6
Egg white-specific IgE[a] (kUA/L)	< 0.1	< 0.1
Egg yolk-specific IgE (kUA/L)	< 0.1	< 0.1
Ovomucoid-specific IgE (kUA/L)	< 0.1	< 0.1
TARC[b] (pg/mL)	581	443
PCT[c] (ng/mL)	0.05	< 0.02
SPT[d]	No sensitization	No sensitization

[a]IgE: immunoglobulin E; [b]TARC: thymus and activation-regulated chemokine; [c]PCT: procalcitonin; [d]SPT: skin prick tests.

At 135 minutes post-OFC, the patient experienced 10 episodes of vomiting and lethargy, necessitating hospitalization. Post-symptom PCT and TARC levels were elevated, measuring 1.47 ng/mL and 2,428 pg/mL at the 5th hour and 2.41 ng/mL and 3195 pg/mL at the 24th hour, respectively. At 2 years of age, the patient had not achieved tolerance to egg white.

The procedures were approved by the Ethics Committee of Showa University School of Medicine (No. 2024-286-A). Written informed consent was obtained from the families and guardians.

Discussion

In these cases, the diagnosis of TEW FPIES was based on the sensitization status, clinical presentation of allergic symptoms, and elevation of PCT[20] and TARC levels.[21] Egg white is the most common trigger food for immediate-type food allergies in Japan.[19] FPIES has been frequently reported with egg yolk, leading to a substantially low awareness of egg white FPIES. Because of the high frequency of egg yolk being implicated in FPIES, it is often suspected to be the trigger food when allergic reactions such as vomiting occur after egg consumption. However, as demonstrated by these cases, TEW FPIES do exist. To avoid unnecessary dietary restrictions, an accurate diagnosis through detailed medical history, blood tests, and OFC is crucial. These steps are crucial for distinguishing between immediate-type allergies and FPIES as well as accurately identifying the specific trigger food.

In Japan, the increase in egg yolk FPIES cases has been attributed to the early introduction of egg yolk into the diet.[14] Similarly, reports from other countries have documented an increase in FPIES cases associated with the early introduction of peanuts.[22,23] Studies have highlighted the role of early introduction of egg white in preventing the subsequent development of food allergies[24] and atopic dermatitis.[25] Consequently, introducing egg white early has become common practice. Given these trends, it is likely that similar to egg yolk and peanuts, early introduction of egg white may lead to the development of egg white FPIES. Further investigations are warranted to better understand the relationship between early dietary exposure and the onset of FPIES.

Despite the limited number of egg white FPIES cases, uncertainties regarding the acquisition of tolerance remain. Therefore, periodic confirmation through OFC is considered the gold standard.[26] The tolerance acquisition rate for egg yolk has been reported to be 64% at 2 years of age,[27] with recommended OFC intervals of 6–18 months.[2,28-30] Accordingly, it is necessary to continue confirming the tolerance using the appropriate OFC in both cases. In this present report, neither of these patients had achieved tolerance. Given the elevated PCT levels at the 5th hour and the 24th hour post-symptom onset, acquiring tolerance may be challenging in these cases.[31] However, continued follow-up is required to monitor disease progression.

Egg white is a common allergen in infants with IgE-mediated food allergy; it can also trigger typical FPIES presentations. OFC remains the diagnostic gold standard. Additionally, dynamic changes in biomarkers, such as TARC and PCT, following symptom onset may provide diagnostic and prognostic support. Because management strategies, including dietary recommendations, differ markedly between FPIES and IgE-mediated food allergy, accurately distinguishing these conditions is essential for optimal clinical care.

Conclusion

To the best of our knowledge, this is the first report of acute TEW FPIES. Since egg whites can also trigger FPIES, it is crucial to conduct thorough medical history taking and examinations to carefully differentiate between FPIES and immediate-type food allergies and ensure an accurate diagnosis. This case report highlights the importance of careful assessment and precise identification of underlying food triggers in cases of suspected food allergies.

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Author Contributions

All authors contributed to the study conception and design. The first draft of the manuscript was written by Kosei Yamashita and Yuki Okada. Data collection and analysis were performed by Ikuya Sasaki, Sawa Seki, Toshiyuki Takagi, Megumi Okawa, Aiko Honda, and Chihiro Kunigami. Mayu Maeda, Taro Kamiya, and Takanori Imai encouraged to investigate and supervised the findings of this work. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no potential conflict of interest with respect to research, authorship, and/or publication of this article.

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