

A case of food protein–induced enterocolitis syndrome to mushrooms challenging currently used diagnostic criteria

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Clinical Implications

- We present a case report of food protein–induced enterocolitis syndrome (FPIES) to mushrooms that highlights the caveats of diagnosing acute FPIES in clinical practice, particularly in older children and when solid foods are involved.

TO THE EDITOR:

Food protein–induced enterocolitis syndrome (FPIES) is a potentially severe non–IgE-mediated food hypersensitivity. This syndrome is still underrecognized despite its relatively high prevalence.¹ Two clinical forms have been described, ie, the chronic form with persistent vomiting and diarrhea when the food is continuously ingested and the acute form that occurs typically after a period of avoidance with profuse emesis, diarrhea, lethargy, and/or hypotension 2–4 hours after food ingestion.² Although FPIES is typically encountered in infants, it has been described in older children and adults.^{3,4} The diagnosis should be suspected in patients with a typical clinical history, and an oral food challenge (OFC) might be needed to confirm the diagnosis.^{5–7} FPIES was initially described to cow’s milk and soy in formula-fed infants. However, more recently solid foods have also been incriminated, mainly grains, but also egg, meats, peanut, seafood, fruits, and vegetables.⁸ We report the first case of FPIES to mushrooms, including a description of this syndrome, and a discussion on the relevance of the currently used diagnostic criteria.

A non-atopic healthy 9-year-old girl presented for evaluation of 2 episodes of profuse vomiting more than 2 hours after ingestion of a meal containing unknown species of mushrooms that occurred when she was 7 years old. Typical IgE-mediated symptoms, such as urticaria, sneezing, or wheezing, were absent. In both episodes, the symptoms, including lethargy, disappeared within 4 hours without any treatment. Mushrooms were not a part of the usual diet of the patient. Other potentially causative foods were reintroduced subsequently in the diet without any reactions. Although mushroom poisoning was suspected at that time, the pediatrician recommended eliminating mushrooms from her diet.

The patient presented to our allergy clinic 2 years after the initial reaction for evaluation. Although FPIES to mushrooms was suspected based on the clinical symptoms, we performed a prick-to-prick test to “common white” mushrooms (*Agaricus bisporus*) to exclude an associated IgE-mediated sensitization. The skin test was negative. To confirm the diagnosis of FPIES, an OFC was performed. Three hours after ingestion of an

age-appropriate portion (22.5 g) of cooked “common white” mushrooms (*A. bisporus*), our patient experienced 2 episodes of vomiting with mild lethargy. The complete blood count showed an increase in the neutrophil count from an initial value of 3180 cells/mm³ to 7240 cells/mm³ 4 hours after ingestion. An intravenous bolus of normal saline solution and a standard dose of methylprednisolone were administered with resolution of the symptoms within an hour.

Based on the clinical history and a positive OFC, FPIES to mushrooms was diagnosed and strict avoidance of all mushrooms was recommended due to lack of data about cross-reactivity between mushrooms in FPIES.

Diagnosis of FPIES to solid foods can be challenging and is often delayed because of a low index of suspicion, particularly in older children and to foods rarely eliciting allergic reactions.⁸ Indeed, although milk and soy FPIES typically present in infancy, FPIES to solid foods has been increasingly reported in older children and adults.^{3,4,8} Misdiagnosis can lead to incorrect management, with a potential detrimental impact on health and increased medical costs. Thus, it is important to consider FPIES in children of any age presenting with recurrent isolated gastrointestinal symptoms after ingestion of a specific food. Mushrooms, typically involved in food poisoning, have never been previously described as a cause of FPIES. In the literature, there are no fully validated diagnostic criteria for FPIES. Initially, Powell proposed diagnostic criteria mainly for the chronic form of FPIES to milk and soy, including an age restriction (less than 2 months of age for onset of symptoms and less than 9 months at the time of diagnosis).⁹ In 1986, the same author modified those criteria, particularly removing the age limit, but still focusing on the chronic form of FPIES to milk and soy.⁵ Recently, those criteria were adapted to incorporate the acute form of FPIES, as presented by our patient, but still including an age restriction (Table 1).^{6,7} Based on our case report and the recent literature with increasing cases of acute FPIES to solid foods that occur in older children and even in adults, reevaluation of the clinical diagnostic criteria is needed to reduce FPIES underdiagnosis.

A positive OFC is included in the currently used FPIES diagnostic criteria (Table 1).^{5–7,9} In clinical practice, the OFC is usually performed in patients with unclear clinical features or to assess tolerance acquisition. Particularly in infants with typical symptoms of FPIES that occur on 2 or more occasions, without alternative explanation for the symptoms, and who are asymptomatic when the offending food is eliminated from the diet, an OFC may not be necessary for confirmation of FPIES diagnosis.² The interpretation of OFC in patients with FPIES is currently based on 5 criteria proposed by Powell in 1986,⁵ summarized in Table II. At least 3 criteria are needed to consider the OFC positive. Our patient met 2 criteria (ie, repetitive vomiting and neutrophils increase of 4060 cells/mm³) and thus would be considered equivocal, according to Powell’s criteria. The validity of these criteria is being questioned.^{10,11} Although emesis is present in the vast majority of patients, diarrhea is only reported in 20% to 40% of patients at large and even less frequently during diagnostic OFC.^{4,11} In the recent literature, the utility of stool analysis has already been

TABLE I. Clinical diagnostic criteria for FPIES

Powell 1978 ⁹	Powell 1986 ⁵	Leonard 2012 ⁶	Sopo 2013 ⁷
1. Onset of symptoms at less than 2 months of age; infant less than 9 months at time study	1. Disappearance of the symptoms of vomiting and diarrhea, and of diagnostic findings in the stool (blood and leukocytes), after all antigens are removed from diet	1. Less than 9 months of age at initial diagnosis	1. Less than 2 years of age at first presentation (frequent feature but not mandatory)
2. While receiving the offending formula the infant has watery stools with mucus, blood and leukocytes, and a peripheral polymorphonuclear leukocytosis	2. No other cause for the colitis is demonstrable	2. Repeated exposure to causative food elicits gastrointestinal symptoms without alternative cause	2. Exposure to the incriminated food elicits repetitive and projectile vomiting, pallor, lethargy within 2-4 hours. Diarrhea may be present, much less frequently and later. The symptoms last a few hours, usually resolve within 6 hours
3. Diarrhea ceases and normal growth resumes when the offending food antigen is eliminated	3. Symptoms do not recur and weight gain is normal for one month on a low-antigen formula as the only dietary source	3. Absence of symptoms that may suggest an IgE-mediated reaction	3. Absence of symptoms that may suggest an IgE-mediated reaction
4. The response to challenge meets the criteria described in Table II	4. Challenge with milk or soy formula or other offending food antigens reproduces symptoms of vomiting within 1-3 hours and or diarrhea within 4-10 hours	4. Removal of causative food results in resolution of symptoms	4. Avoidance of the offending protein from the diet results in resolution of symptoms
		5. Re-exposure or oral food challenge elicits typical symptoms within 4 hours	5. Re-exposure or oral food challenge elicits typical symptoms within 2-4 hours. Two typical episodes are needed to establish the definitive diagnosis without the need to perform an oral food challenge

TABLE II. Criteria for positive oral food challenge

Powell 1978 ^{9*}	Powell 1986 (Criteria Currently Used) ^{5,†}
1. Diarrhea within 24 hours of challenge	1. Emesis and/or diarrhea not present during the baseline period
2. Stools contain blood and leukocytes	2. Change in total blood polymorphonuclear leukocyte count greater than 3500 cells/mm ³
3. A change from prechallenge values in the total polymorphonuclear leukocyte count greater than 4000cells/mm ³ /mm ³ occurs at 6 to 8 hours post challenge	3. Blood in stool [‡]
	4. Fecal leukocytes [‡]
	5. Fecal eosinophils [‡]

*The challenge is considered positive when the infant meets all those 3 criteria and has been previously exposed to the formula of challenge.

†The challenge is considered positive if 3 of 5 criteria are met and equivocal when 2 of 5 criteria are met.

‡A revision of currently used FPIES diagnostic criteria for a positive OFC should be discussed, particularly valuing clinical (especially vomiting) and blood testing (neutrophil increase) over stool analysis.

questioned due to the apparent lack of involvement of the lower digestive tract in these patients. Of note, the stool tests are not routinely used in OFC for FPIES in many reference allergy centers. However, further large studies are required to confirm the need to revise the currently used FPIES diagnostic criteria for a positive OFC, particularly by emphasizing clinical aspects (especially vomiting) and blood testing (neutrophil increase) over stool analysis.²

In conclusion, this case report, in addition to reporting an unusual case of FPIES to mushrooms, also highlights the caveats of diagnosing acute FPIES in clinical practice, particularly in older children and when solid foods are involved. The current clinical diagnostic criteria need to be revised based on the recent evidence to avoid underdiagnosis of FPIES.

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