

Clinical Communications

Peanut-induced food protein–induced enterocolitis syndrome (FPIES) in infants with early peanut introduction

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Clinical Implications

- Peanut food protein–induced enterocolitis syndrome appears to be increasing, possibly related to early introduction. Increased awareness of this trend is crucial, particularly given the already high rate of misdiagnosed food protein–induced enterocolitis syndrome.

The results of the Learning Early about Peanut Allergy (LEAP) study demonstrated that early introduction of peanut to infants at high atopic risk could reduce the development of IgE-mediated peanut allergy, resulting in recommendations supporting early introduction of peanut.^{1,2} Food protein–induced enterocolitis syndrome (FPIES) is a non–IgE-mediated gastrointestinal food hypersensitivity that typically presents in early infancy with profuse vomiting, lethargy, and diarrhea, usually 1 to 4 hours after ingestion of a food trigger.³ A population-based study estimated FPIES prevalence in the United States among children younger than 18 years at 0.51%.⁴ Peanut has not been recognized as a major trigger of FPIES, and generally represents less than 2% of cases in large series. Common triggers of FPIES are typically first foods such as milk, soy, rice, and oat.^{5–7} An unintended consequence of introducing peanut early may be peanut-triggered FPIES.

In 2018, Robbins et al⁷ described 3 cases of peanut FPIES in children after early dietary peanut introduction, raising awareness about a possible increase in the incidence of peanut FPIES in the setting of changing peanut introduction guidelines.² In contrast, a review of 160 patients with FPIES who underwent physician-supervised oral food challenge (OFC) at our academic center during a 10-year period (2001–2011), before the LEAP study and the implementation of the early introduction guidelines, reported no cases of peanut-related FPIES.⁵ In Israel, early introduction of peanut has been the practice for some time, and Katz et al⁸ described a large cohort of infants, with FPIES triggered by cow's milk, in 2011, but no data were presented regarding the incidence of peanut FPIES in the population. To investigate the current frequency and to investigate characteristics of peanut-triggered FPIES, we reviewed 14 cases presenting to our center in the last 2 years.

We performed a retrospective chart review to identify patients with FPIES to peanut in their first year of life. We identified 14 patients with a clinical history of convincing FPIES to peanut or an FPIES reaction upon peanut OFC. Those not challenged

satisfied FPIES clinical diagnostic criteria by meeting 1 major and 3 or more minor criteria, according to international consensus guidelines.⁵ Their individual characteristics and reaction history are described in Table I.

The cohort included 7 females (50.0%). The median age of peanut introduction was 6 months (range, 5–8 months), and the median age of peanut FPIES reaction was 7 months (range, 5–10 months). In this cohort, 10 of 13 patients (76.9%) had negative skin prick test (SPT) result to peanut (no SPT result was available for 1 patient) and 5 of 11 (45.5%) patients had undetectable serum IgE (sIgE) to peanut (no result available for 3 patients). One patient had a markedly elevated sIgE level to peanut of 7.30 kU/L, whereas all others had levels 0.53 kU/L or lower. Four patients (28.6%) had FPIES to other foods, including oat, rice, cow's milk, pea, lentil, corn, and almond. Six patients (42.9%) had a history of eczema, and 6 patients (42.9%) had a diagnosis of IgE-mediated food allergy (see Table I).

Except for 1 patient without SPT result and 3 patients without sIgE levels to peanut, it is notable that 3 patients (23.1%) had a positive SPT result to peanut (range, 3–6 mm) and 6 (54.5%) had a detectable sIgE level to peanut (range, 0.24–7.30 kU/L), for an overall sensitization rate of 43% (Table I). None of those sensitized patients had a history of typical IgE-mediated symptoms. Comorbid sensitization to FPIES solid food triggers has been recognized in up to 25% of children with FPIES, described as atypical FPIES, and is associated with a higher likelihood of symptom persistence.⁵

It is noteworthy that the median age of peanut introduction was lower than the median age of the initial reaction. This is because 9 patients (64.3%) did not react on their first exposure to peanut. This phenomenon was previously reported by Mehr et al,⁹ who noted that in their cohort of 311 cases of FPIES, 33 (11%) reacted after 2 tolerant exposures and 75 (24%) reacted after 3 or more tolerant exposures.

OFC is the criterion standard to confirm the diagnosis of FPIES if the diagnostic criteria are not met.³ In 9 of our cases (64%), clinical criteria for the diagnosis of FPIES were satisfied⁵ and OFC was not performed. When the diagnosis was in question, patients were offered an OFC, with 5 patients (35.7%) undergoing an OFC that confirmed FPIES to peanut. As described in the international consensus guidelines for the diagnosis and management of FPIES,³ a typical clinical history is sufficient to diagnose FPIES, and the recommendation is to wait at least 12 to 18 months from the last reaction before assessing resolution by OFC.

In summary, our retrospective analysis identified 14 cases of peanut FPIES in our academic center in the last 2 years, all in the first year of life, and is the largest case series of peanut-related FPIES reported to date. This is in stark contrast to a previous review of 160 patients with FPIES evaluated in our practice from 2001 to 2011, with no reported cases of peanut FPIES.⁵ In addition, no cases of peanut FPIES with onset after age 12 months have presented at our institution. We cannot perform a statistical analysis based on a case series, but these observations are suggestive of an increase in peanut that could be associated with early introduction. The identification of such a large number of cases from 1 center in only 2 years, along with

TABLE I. FPIES with early peanut introduction

Patient	Sex	Age of first ingestion	Peanut SPT (wheal, mm)	Peanut sIgE (kU/L)	Age of FPIES reaction	FPIES reaction	Tolerated peanut before	Other known FPIES	Eczema	IgE-mediated allergy
1	Female	6 mo	0	NA	6 mo	On day 2 of peanut introduction, repetitive vomiting 90 min after ingestion, lasting 90 min	Yes	No	No	No
2	Female	6 mo	0	<0.10	7 mo	After 1 mo of regular peanut in the diet, patient became lethargic 1 h after peanut ingestion and later in the day vomited 4-5 times; had OFC, with vomiting 2 h after ingestion	Yes	No	Yes	Egg
3	Male	5 mo	6	0.53	5 mo	On day 2 and 3 of peanut introduction, had repetitive vomiting 3-4 h after ingestion	Yes	No	Yes	Peanut, milk, egg, sesame
4	Male	5 mo	0	NA	5 mo	On day 3 of peanut introduction, had repetitive vomiting 2-3 h later; tried peanut again 2 h later, vomiting for 9 h	Yes	Pea, lentil, corn	No	No
5	Female	8 mo	0	0.24	8 mo	On day 1 of peanut introduction, repetitive vomiting after 2 h and lethargy lasting 3 h	No	No	Yes	No
6	Male	5 mo	0	7.30	10 mo	After tolerating peanut butter since 5 mo, ate peanut butter and 3 h later had repetitive vomiting and lethargy; had OFC, with vomiting 90 min after ingestion of last dose	Yes	No	No	No
7	Female	8 mo	NA	0.28	10 mo	On day 3 of peanut introduction, 2 mo after first 2 ingestions, repetitive vomiting and lethargic 2 h after ingestion; tried again 6 d later with the same symptoms	Yes	No	Yes	Almond, hazelnut
8	Female	6 mo	0	<0.10	7 mo	On day 2, had facial hives on second peanut ingestion, saw allergist, SPT wheal size small, so OFC was scheduled; on OFC, vomited repeatedly 2 h after finishing ingestion; repeat OFC at 14 mo, with vomiting 2.5 h after finishing ingestion	Yes	No	No	Walnut, pecan
9	Male	6 mo	0	0.45	5 mo	On first ingestion vomited 5 h later; OFC at 8 mo, with vomiting 3-4 h later	No	Almond	Yes	No
10	Female	5 mo	0	<0.10	5 mo	On fifth day of peanut introduction, vomited after a few hours; new ingestion after a few days, multiple episodes of vomiting 3-4 h later	Yes	No	No	No
11	Female	6 mo	0	<0.10	6 mo	On first ingestion, vomited repeatedly 2 h later	No	No	No	No
12	Male	6 mo	3	<0.10	8 mo	Tolerated initially, after 2 mo had repeat vomiting 2-3 h after ingestion	Yes	Milk, almond	No	Milk
13	Male	6 mo	0	NA	6 mo	On first ingestion, vomited repeatedly 2 h later; tried again 1 mo later, again with repeated vomiting and lethargy 2 h after ingestion	No	No	No	No
14	Male	7 mo	5	0.27	7 mo	Had first ingestion on OFC for peanut, 2 h after ingestion vomited repeatedly and became pale	No	Oat, rice	Yes	Milk, egg

NA, Not applicable/available.

other recent smaller case reports, raises the possibility that peanut-related FPIES is increasing. Possible association with early introduction remains speculative in the absence of a comparison group without early introduction, requiring a prospective or case-control study. Pediatricians and allergists should consider this frequently misdiagnosed entity in the differential diagnosis of adverse reactions to peanut in infancy. Continued identification of additional cases, as well as mechanistic studies, will be vital to understanding a possible association between early dietary introduction of peanut and an increased incidence of peanut-related FPIES.

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