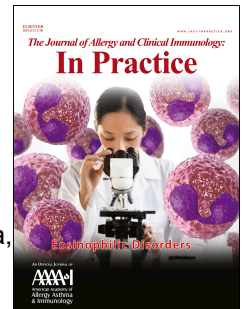


Journal Pre-proof

Chronic Food Protein-Induced Enterocolitis Syndrome Due To Solid Food

Sonsoles Infante, MD PhD, Vicente J. Albéndiz-Gutiérrez, MD, Alberto Alvarez-Perea, MD PhD, Paula Cabrera-Freitag, MD PhD, Cristina Morales-Cabeza, MD, Victoria Fuentes-Aparicio, MD, Lydia Zapatero, MD PhD



PII: S2213-2198(20)30094-5

DOI: <https://doi.org/10.1016/j.jaip.2020.01.036>

Reference: JAIP 2666

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 27 September 2019

Revised Date: 13 January 2020

Accepted Date: 14 January 2020

Please cite this article as: Infante S, Albéndiz-Gutiérrez VJ, Alvarez-Perea A, Cabrera-Freitag P, Morales-Cabeza C, Fuentes-Aparicio V, Zapatero L, Chronic Food Protein-Induced Enterocolitis Syndrome Due To Solid Food, *The Journal of Allergy and Clinical Immunology: In Practice* (2020), doi: <https://doi.org/10.1016/j.jaip.2020.01.036>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

CHRONIC FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME DUE TO SOLID FOOD

Sonsoles Infante MD PhD^{1,2}, Vicente J. Albéndiz-Gutiérrez MD¹, Alberto Alvarez-Perea MD PhD^{1,2}, Paula Cabrera-Freitag MD PhD^{1,2}, Cristina Morales-Cabeza MD², Victoria Fuentes-Aparicio MD^{1,2}, Lydia Zapatero MD PhD¹.

Affiliations:

1. Paediatric Allergy Unit. Hospital General Universitario Gregorio Marañón, Madrid, Spain.
2. Gregorio Marañón Health Research Institute (IiSGM), Madrid, Spain.

Corresponding author: Sonsoles Infante MD PhD.

Paediatric Allergy Unit. Hospital General Universitario Gregorio Marañón. O'Donnell 48, 28009 Madrid. Spain.

E-mail: sonsoles.infante@salud.madrid.org

Telephone number: +34 629069509

Compliance with ethical standards

Conflict of interest: Sonsoles Infante, Vicente J. Albéndiz-Gutiérrez, Alberto Alvarez-Perea, Paula Cabrera-Freitag, Cristina Morales-Cabeza, Victoria Fuentes-Aparicio and Lydia Zapatero declare that they have no conflict of interest.

Human and Animal rights: This article does not contain any studies with human or animal subjects performed by any of the authors.

Word count: 891.

Clinical Implications box: Chronic FPIES has usually been reported in infants younger than 4 months of age fed with cow's milk or soy-based infant formula. We present two novel cases of chronic FPIES due to solid food.

34

35

36 To the Editor:

37 As stated in the last International Consensus, acute Food Protein-Induced Enterocolitis
38 Syndrome (FPIES) is a non-IgE-mediated food allergy that typically presents in
39 infancy, with repetitive protracted vomiting that begins 1 to 4 hours after food ingestion.
40 Vomiting is often accompanied by lethargy and pallor and can be followed by diarrhea
41 several hours later [1]. Symptoms typically resolve within 24 hours and children are
42 asymptomatic between episodes with normal growth. The clinical presentation of
43 chronic FPIES is less well-characterized. It has usually been reported in infants younger
44 than 4 months of age, fed with cow's milk (CM)- and soy-based infant formula [2].
45 Symptoms occur over several days or weeks and do not have a clear relationship with
46 the offending food. Children have intermittent vomiting, diarrhea and failure to thrive or
47 poor weight gain. The severe form can develop dehydration and hypovolemic shock.
48 Symptoms resolve within days up to a fortnight after removing the offending food from
49 the infant's diet [3]. Diagnosis may be unclear if it is based only on clinical history.
50 This is why the most important criterion for chronic FPIES diagnosis is the appearance
51 of acute FPIES symptoms when the food is reintroduced into the patient's diet. [1]. We
52 report two cases of children with chronic FPIES due to fish.

53 Case report 1 was a 16-months-old girl, with personal history of CM allergy. At the age
54 of 12 months, hake was introduced into her diet. The child developed continuous daily
55 mucous diarrhea. Parents denied vomiting, failure to thrive, or other symptoms. After 2
56 months of once a week hake intake, her parents decided to remove fish from her diet.
57 The diarrhea resolved within a few days. After 2 months of a fish-free diet, her parents
58 reintroduced hake into her diet. Four hours after the ingestion, she presented protracted
59 vomiting (more than 10 times) accompanied by pallor and extreme lethargy. She
60 required emergency department assistance and intensive intravenous fluid therapy for
61 rehydration. Symptoms resolved after several hours. Fish was removed again from her
62 diet and she had remained asymptomatic since then. Skin prick testing (SPT) with
63 commercial extracts (LETI®), of different fish species, including hake, were negative.

64 Case report 2 was a 12-month-old boy, with personal history of raw egg allergy with
65 confirmed tolerance to cooked egg. At the age of 9 months, sea bass was introduced into
66 his diet. He developed intermittent episodes of diarrhea accompanied with incessant
67 crying related to crampy abdominal pain. After several ingestions, the parents

associated the symptoms with fish ingestion, and removed the fish from his diet. His symptoms completely resolved. He was referred to our Allergy Department for evaluation. SPT with commercial extracts (LETI®) of different fish species, not including sea bass, were negative. Because the history was vague, we recommended an oral food challenge (OFC). An OFC to hake was performed, because the parents refused to test sea bass, and the child tolerated the fish without symptoms. He ate hake 3 more times at home, but each time developed watery and malodorous diarrhea accompanied with abdominal pain 1 hour after ingestion. In the last episode, diarrhea was associated with protracted vomiting and he needed emergency care assistance and intravenous fluids for recovery. Symptoms resolved within 24 hours. Fish was removed from his diet and, since then, he has remained asymptomatic.

In 1967, Gryboski reported a series of 21 patients in whom the ingestion of CM led to exclusively gastrointestinal symptoms. The main symptom was diarrhea and only four children presented with vomiting [4]. Some years later, Powell established the clinical features and standardization of challenge of what she called milk- and soy-induced enterocolitis of infancy. All the children included in her study (n=9) had protracted vomiting and diarrhea that disappeared once the offending food was removed from the child's diet [5]. These authors would set the foundations of what we known as FPIES.

The international consensus guidelines for the diagnosis and management of FPIES proposed new revised criteria for patients presenting with possible acute or chronic FPIES. They provided general criteria for patients with chronic FPIES but, given the lack of published reports of chronic FPIES, specific major and minor criteria could not be established [1]. Due to the non-specific symptoms of chronic FPIES and the absence of a clear relationship with the food intake, diagnosis can be challenging [6]. Chronic FPIES is the result of regular exposure to triggering foods, for example, CM- or soy-based infant formula [7]. In chronic FPIES, children remain asymptomatic once the offending food is removed from their diet and reintroduction of the trigger food induces acute FPIES symptoms [3,8]. Taking as a reference the diagnostic criteria of these guidelines, both cases would meet criteria of chronic FPIES. They presented exclusively with gastrointestinal symptoms, which resolved after removing fish from their diet, and both of them developed symptoms of acute FPIES when the fish was reintroduced. Strictly following the current diagnostic criteria, these would be the two first reported cases of chronic FPIES to fish. Surely, there are more cases of chronic FPIES due to solid foods but, perhaps, not correctly diagnosed or reported. Diagnosis of chronic

FPIES is a real challenge and can only be reached if it is preceded by a high degree of suspicion and awareness. Further research is needed in order to establish appropriate criteria or discover biomarkers to avoid misdiagnosis.

References

1. Nowak-Węgrzyn A, Chehade M, Groetch ME, Spergel JM, Wood RA, Allen K, et al. International consensus guidelines for the diagnosis and management of food protein-induced enterocolitis syndrome: Executive Summary-Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2017;139:1111-26.
2. Sicherer SH. Food protein-induced enterocolitis syndrome: case presentations and management lessons. *J Allergy Clin Immunol* 2005;115:149-56.
3. Weinberger T, Feuille E, Thompson C, Nowak-Węgrzyn A. Chronic food protein-induced enterocolitis syndrome: Characterization of clinical phenotype and literature review. *Ann Allergy Asthma Immunol* 2016;117:227-33.
4. Gryboski J. Gastrointestinal milk allergy in infancy. *Pediatrics* 1967;40:354-62.
5. Powell GK. Milk and soy induced enterocolitis of infancy: clinical features and standardization of challenge. *J Pediatr* 1978;93:553-60.
6. Hwang JB, Lee SH, Kang YN, Kim SP, Suh SI, Kam S. Indexes of suspicion of typical cow's milk protein-induced enterocolitis. *J Korean Med Sci*. 2007;22:993-7.
7. Agyemang A & Nowak-Węgrzyn A. Food Protein-Induced Enterocolitis Syndrome: a Comprehensive Review. *Clin Rev Allerg Immunol*. 2019. <https://doi.org/10.1007/s12016-018-8722-z> [Epub ahead of print]
8. Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D et al. Food allergy: a practice parameter update-2014. *J Allergy Clin Immunol*. 2014;134:1016-25.e43.