

The Requirement of Oral Food Challenge in Determining Allergic Proctocolitis in Infants

Aysenur **Kaya** MD¹, Ersoy **Civelek** MD¹, Can Naci **Kocabaş** MD²

1 Ankara Children's Hematology Oncology Training and Research Hospital,
Department of Pediatric Allergy and Immunology, Ankara, Turkey

2 Mugla Sıtkı Kocman University, Department of Pediatric Allergy and Immunology,
Mugla, Turkey

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Correspondence: **Professor Dr. Can Naci Kocabaş, MD**

Address : Mugla Sıtkı Kocman University, Department of Pediatric Allergy and
Immunology, Mugla, Turkey

Phone : +90 506 7188089

Fax : +90 312 3472330

E-mail : **cankocabas@gmail.com**

Aysenur **Kaya** M.D. : aysenurkaya99@yahoo.com

Ersoy **Civelek** : ersoycivelek@gmail.com Associate Professor

Can Naci **Kocabas** : cankocabas@gmail.com Professor

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Letter to the Editor:

We greatly thank Haufmann KM et al for their interest in our article (1) and would like to provide some clarifications regarding their questions.

Food protein induced proctocolitis (FPIP), also known as allergic proctocolitis (AP), is characterized by the presence of mucoid, frothy, and bloody stools in an otherwise healthy infant (2). As rightly pointed out by Haufmann et al and emphasized in our article rectal bleeding may have other causes and benign bleedings (idiopathic neonatal transient colitis (INTC)) that are not a result of food allergies may spontaneously recover in infants, therefore an accurate differential diagnosis becomes essential (1,3).

AP diagnosis was made on the basis of the following methodology in our study: Mothers of infants whose symptoms resolved typically 72 to 96 hours (with significant blood in stool, resolution took 1 week) after the elimination were recommended to retake causative foods as part of their normal daily diet after 3 weeks. If infants who had rectal bleeding, diarrhea and mucus or blood in stool after reexposure to the offending food (via breast milk), they were diagnosed as having AP. Those patients (n:18) having had no symptoms after OFC were excluded from our study (otherwise probable INTC cases). Under these considerations, OFC was applied to all (60/60) of our patients and AP was confirmed in all our patients. Additionally, recurrence of symptoms were observed in the patients incidentally exposed to allergenic food during the follow-up period. Since all the patients were referred to our clinic with an AP pre-diagnosis and our study was essentially designed to provide clinicians more information on the natural course, prognosis and offending foods of AP, our INTC or AP cases should not be taken as suggestion of a general ratio.

The exact prevalence of AP is unknown; the estimated prevalence ranges from 0.16% to 64% of infants with isolated rectal bleeding (3,4,5,6). INTC and AP rectosigmoidoscopy both show nodular lymphoid hyperplasia with a pale mucosal surface and diffuse eosinophil infiltration in the lamina propria (7,8). Mori et al indicated that microarray analysis enhanced expression of CCL11 (eotaxin-1) was more dominant in neonatal transient eosinophilic colitis, whereas the expression of CXCL13 was more dominant in food protein-induced proctocolitis (7, 9). CXCL13 and its receptor CXCR5 control the organization of B cells within follicles of lymphoid tissues (10). The pathophysiology of non Ig-E gastrointestinal food allergies remains unknown. There is an urgent need for further studies to characterize mucosal inflammation. In agreement with Haufmann et al, rather than resorting to clinical suspicion and pathological diagnosis, which may lead to confusion, OFC should be conducted as was the case with our study.

References

1. Kaya A, Toyran M, Civelek E, et al. Characteristics and Prognosis of Allergic Proctocolitis in Infants. *J Pediatr Gastroenterol Nutr* 2015;61:69-73.
2. Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol*. 2010 Feb;125(2 Suppl 2):S116-25.
3. Arvola T, Ruuska T, Keranen J, et al. Rectal bleeding in infancy: clinical, allergological, and microbiological examination. *Pediatrics* 2006;117:e760-8.
4. Nowak-Węgrzyn A, Katz Y, Mehr SS, Koletzko S. Non-IgE-mediated gastrointestinal food allergy. *J Allergy Clin Immunol* 2015;135:1114-24.
5. Elizur A, Cohen M, Goldberg MR, et al. Cow's milk associated rectal bleeding: a population based prospective study. *Pediatr Allergy Immunol*. 2012;23:766-70.
6. Xanthakos SA, Schwimmer JB, Melin-Aldana H, et al. Prevalence and outcome of allergic colitis in healthy infants with rectal bleeding: a prospective cohort study. *J Pediatr Gastroenterol Nutr* 2005;41:16-22.
7. Ohtsuka Y. Food intolerance and mucosal inflammation. *Pediatr Int* 2015;57:22-9.
8. Jang HJ, Kim AS, Hwang JB. The etiology of small and fresh rectal bleeding in not-sick neonates: should we initially suspect food protein-induced proctocolitis? *Eur J Pediatr* 2012;171:1845-9.
9. Mori M, Ohtsuka Y, Ishida A, et al. Outcome of infants presenting rectal bleeding: a retrospective study in a single institution. *Pediatr Int* 2014;56:884-90.
10. Ansel KM¹, Ngo VN, Hyman PL, et al. A chemokine-driven positive feedback loop organizes lymphoid follicles. *Nature*. 2000;406:309-14.