BRIEF COMMUNICATION

ALLERGIC PROCTOCOLITIS REFRACTORY TO MATERNAL OLIGOANTIGENIC DIET IN EXCLUSIVELY BREAST-FED INFANTS: A CLINICAL OBSERVATION.

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ABSTRACT

**Background:** Allergic proctocolitis (APC) is caused by food proteins, often but not exclusively of cow milk, transferred through lactation. The objective is to assess if patch tests can detect subgroups of patients requiring an aminoacid-based formula (AAF) due to multiple food allergy.

**Cases presentation:** We have prospectively enrolled 14 exclusively breast-fed infants with APC refractory to maternal allergen avoidance. All patients underwent a colonoscopy, prick and patch test for foods and breast milk. A rectosigmoidoscopy was performed after 1 month of therapy with an AAF. Prick tests were negative. Patch tests were positive in all infants, with a multiple positivity in 7/14. The offending foods were breast milk (14/14), cow milk (7/14), soy (4/14), egg (3/14), rice (2/14), wheat (1/14). Rectosigmoidoscopy after 1 month was normal.

**Conclusion:** These data suggest that patch test is a useful tool to identify subgroups of infants with multiple food allergy involving a delayed immunogenic mechanism and avoiding unnecessary maternal dietary restrictions before administering an AAF.
Background

Allergic proctocolitis (APC) is present in exclusively breast-fed infants aged from 1 to 6 months with a variable degree of rectal bleeding [1]. It is due, in the majority of cases, to cow’s milk proteins transferred via breast milk [2]. Diagnosis is based on clinical features and recovery after dietetic therapy [3]. Rectal bleeding generally resolves within 48-72 hours of cow’s milk protein maternal avoidance; it is reported that in about 5% of cases an extensively hydrolized casein-based formula must be used, with few infants requiring an amino acid-based formula (AAF) [1]. Endoscopic biopsies show superficial erosions, eosinophilic infiltration and frequent lymphoid nodular hyperplasia (LNH) [4,5]. Prick tests are typically negative, indeed a non-IgE mediated pathogenetic mechanism is thought to be involved; currently there are no compelling data on the use of the patch test [5]. Present study reports a series of 14 exclusively breast fed infants with histologically documented APC and negative response to a maternal oligoantigenic diet. Additionally, we have tested the utility of the patch test in detecting non-IgE-mediated immunogenic mechanisms and the efficacy of AAF when multiple food allergy is suspected.

Cases presentation

Fourteen exclusively breast fed infants, aged 7 days-6 months were admitted to our Paediatric Gastroenterologic Unit with haematochezia probably due to allergic colitis, which did not resolve with an oligoantigenic maternal diet (Table). Growth was good in all but 2 infants. On admission, all patients were exclusively breast fed and mothers were on cow’s milk and soy and/or egg-free diets. The period of allergens avoidance varied from 10 days to 2 months and did not lead to complete resolution of rectal bleeding in any patients. The laboratory findings were normal in all patients except for sideropenic anemia in two patients, peripheral eosinophilia in one patient and mild hypertransaminasemia in two patients. Skin prick tests were performed for food proteins
(cow’s milk, soy, rice, wheat, egg) [6]. Patch tests were performed for the same allergens plus breast milk [7]. The prick tests were negative for all patients. The patch tests were positive for breast milk in all patients, cow’s milk in seven patients, soy in four patients, egg in three patients and rice in two patients. An ileo-colonoscopy (or rectosigmoidoscopy in four patients) with biopsy was performed to confirm the diagnosis (Figure 1). The macroscopic appearance showed LNH of the terminal ileum, left colon and rectum in six patients, in the terminal ileum, colon and rectum in two patients, and exclusively in the terminal ileum in two patients. LNH was defined as a cluster of >10 extruding lymphoid nodules as previously described [8]. Lesions varied from widespread hyperhaemic and edematous rectal mucosa with microerosions in three patients, to erythema with scattered rectosigmoid aftoid erosions in seven patients, to diffuse colonic hyperhaemic and edematous mucosa in five patients. Biopsies taken from the terminal ileum, from each segment of the colon and from areas where endoscopic lesions were identified revealed more than 60 eosinophils per 10 high power field (HPF) in the lamina propria in almost one biopsy specimen in six infants (Figure 2). In all patients, non-specific signs of inflammation, such as edema and lymphoplasmocitic infiltrate, were found and the overall architecture of the mucosa was always conserved. Histologic examination was performed by a pathologist unaware of the clinical and laboratory data of the patients. Given the non responsiveness to the mothers’ avoidance of food allergens and in the absence of an alternative diagnosis, breast feeding was discontinued and exclusive feeding with an aminoacid-based formula was started. The patients showed progressive resolution of rectal bleeding in 48-72 hours and were discharged in good general condition. After one month of elemental diet, they underwent a follow-up rectosigmoidoscopy that showed complete normalization of mucosa in all patients. The infants were followed-up monthly or bi-monthly and checked for possible symptoms during the oligoantigenic diet, that was started after two months of feeding with elemental diet. All the infants tolerated an exclusive diet based on lamb and rice or maize and olive oil [9].
Discussion

Our study confirms the hypothesis that food proteins transferred via breast milk can lead to APC in an early age. The positivity of the patch tests suggest the involvement of a delayed immunogenic mechanism, and the need of AAF prove that responsible antigens cannot be exclusively cow’s milk proteins.

Our case series of fourteen breast fed infants confirms that APC, as previously reported [1-4,10-15], appears in the first months of life with potentially severe clinical features. The prognosis is good with gradual and complete resolution after 72-96 hours of maternal allergen avoidance; long term prognosis is likewise good [1-4,6]. More than 50% of cases reported in literature are exclusively breast-fed infants and this fact initially seemed an unusual finding in the field of food allergy, since breast feeding is thought to be a preventive factor in atopic disease. The presence of cow’s milk proteins in human milk was first shown in 1921 by Shannon et al. These authors hypothesized that breast feeding could be a source of food allergens potentially able to induce an allergic reaction in infants [16]. It has been suggested that an allergic reaction in the first week of life (as seen in our youngest 7-day-old patient) could be due to an intra-uterine sensitization, secondary to transplacentar antigen passage [11]. However, this study did not provide any data to confirm this hypothesis and should be underlined that such an early manifestation of food allergy is extremely rare.

The gut is functionally immature in the first year of life and intestinal mucosa, which normally prevents the absorption of antigenic peptides, is more permeable in the first 3 months of life, which seem to be important in the pathogenesis of food allergy. The exposure to food antigens in a sensitized infant may lead to hypersensitivity response types I, III and IV (according to Gell and Coombs classification). Some authors suggested that both intestinal immaturity and marked eosinophilic infiltration, which may significantly alter tight junctions, lead to increased intestinal permeability to food proteins [17]. The immune system fails to prevent the infiltration of
inflammatory cells, particularly eosinophils, leading to the destruction of epithelial cells, which are responsible for clinical features [9]. Why the allergic response involves only the distal colonic tract, leading to proctocolitis, is currently unknown. One hypothesis is that the allergen from the mother’s diet is complexed with secretory IgA or another immunologic component of human milk, which is only cleaved from the protein by certain environmental rectosigmoideal factors, such as microbial IgA-proteases [1]. It is thought today that eosinophils may be directly responsible for tissue injury in allergic colitis and it is interesting to note that these cells can bind IgA and undergo degranulation [9]. Eosinophils are often clustered in proximity to the lymphoid aggregate below an epithelial erosion; this observation suggests their role in response to antigen uptake and the possible site of T cell interaction [1]. Odze et al. suggested that the production of PAF by eosinophils may also be important in allergic colitis, since this factor has been shown to induce bowel injury in experimental animal models. Eosinophil-derived mediators can stimulate a secretory response from epithelial cells in vitro; this may represent an important pathway in the development of diarrhea [10].

In this case series, the clinical suspicion of APC was always confirmed by colonoscopic features and biopsies, which showed inflammatory infiltration containing eosinophils and LNH, which is a common finding in food allergies [8,18,19]. After one month of elemental feeding LNH significantly decreased or completely disappeared and colonic mucosa was normal. Positivity of patch tests performed with breast milk of mothers undergoing an oligoantigenic diet suggest that a multiplicity of antigens, and not only cow’s milk proteins, can be transferred to infants, triggering an allergic delayed response. This delayed-type hypersensitivity reaction has already been proposed in a very rare granulomatous variant of APC by Dargent et al [20].

In our series, the oral provocation test was not performed for ethical considerations due to the severity of clinical findings. Rectosigmoidoscopic control was considered more ethically correct to confirm mucosal healing.
Conclusion

In conclusion, APC induced by food proteins, should always be taken into consideration in differential diagnosis of hematochezia, especially in exclusively breast-fed infants. Endoscopy with biopsies are necessary to confirm diagnosis. The most valid allergological test seems to be the patch test with common food allergens and breast milk, a food proteins carrier deriving from the maternal diet. An elemental diet should be prescribed in select cases that are refractory to a maternal oligoantigenic diet and should always lead to complete clinical and endoscopical remission.

Run Title

Food-induced allergic proctocolitis

Key words

allergic proctocolitis, food allergy, breast feeding, patch test

Abreviations

LNH: lymphoid nodular hyperplasia: APC: allergic proctocolitis; HPF: high power field

Competing interest

The authors declare that they have no competing interests.

Authors’ contributions:

SL: Protocol design, editing manuscript, DN: gastroenterology and endoscopy evaluation, editing manuscript, SF: gastroenterology and endoscopy evaluation, editing manuscript, YD: protocol design, editing manuscript., GL: protocol design, editing manuscript, TF¹: protocol design, editing manuscript, SC: protocol design, editing manuscript, TF²: protocol design, allergology evaluation, editing manuscript, AM: tissues processing, histological analysis of biopsies. All authors have read and approved the final version of manuscript.
References


FIGURE LEGEND

Figure 1. Endoscopic findings showing colonic (A), ileal LNH(B) and rectal aphthoid ulcers (C) in a child with dietary protein-induced allergic proctocolitis.

Figure 2. Significant (>60/10 HPF) eosinophilic infiltration of the colonic mucosa in a child with dietary protein-induced allergic proctocolitis.
Additional files provided with this submission:

Additional file 1: table 1 APC.doc, 30K
http://www.biomedcentral.com/imedia/1328094382502095/supp1.doc