Colonic Lymphoid Nodular Hyperplasia in Children: Relationship to Food Hypersensitivity

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Background & Aims: The clinical significance of lymphoid nodular hyperplasia (LNH) of the lower gastrointestinal tract is unclear. The aim of this study was to define the frequency and clinical significance of LNH in pediatric patients undergoing colonoscopy. **Methods:** Two hundred forty-five children (101 male, 144 female; median age, 8.5 years) for whom colonoscopy had been indicated were evaluated during a 3-year period. Apart from ileocolonoscopy with biopsy, all patients underwent routine biochemistry, serum total and specific IgE, and/or skin prick tests for food allergens. Patients with LNH underwent elimination diet and subsequent food challenges. **Results:** LNH was observed in 73 of 245 (30%) consecutive colonoscopies. LNH was the only abnormal finding in 52 of the 73 cases (71%). In 43 of these 52 patients a diagnosis of cow's milk or multiple food hypersensitivity was made. Food allergy was significantly more common than in patients without LNH (83% vs 31%; $P < .0001$). The patients with LNH and food hypersensitivity presented hematochezia ($P < .0001$), elevated serum anti–β-lactoglobulin IgG ($P < .0001$), anemia ($P < .005$), and failure to thrive ($P < .03$) more frequently than those without LNH. In the LNH patients histologic examination showed a higher number of lymphoid follicles throughout the colon and the terminal ileum and an increased number of lamina propria and intraepithelial eosinophils. **Conclusions:** The presence of LNH in the colon and/or terminal ileum is a frequent finding in symptomatic children undergoing colonoscopy. Unless associated with other specific endoscopic or histologic lesions, LNH is related to a condition of delayed-type food hypersensitivity.

For many years lymphoid nodular hyperplasia (LNH) of the terminal ileum and colon has been considered a mucosal response to nonspecific stimuli, most often infections, and consequently has been regarded as a pathophysiologic phenomenon during infancy and childhood.[1] The most frequent alternative interpretation was based on the evidence of an association between LNH and immunodeficiency.[2,3] More recently, LNH has been associated with cow's milk protein hypersensitivity[4–7] and with the very controversial "autistic enterocolitis."[8,9] However, the frequency of LNH in children undergoing colonoscopy for whatever indication has never been reported. In this study we report the endoscopic and histologic findings in consecutive pediatric patients undergoing colonoscopy, with particular attention to the frequency of LNH and its clinical significance.

Patients and Methods

Patients

All patients who underwent diagnostic colonoscopy in 2 pediatric tertiary referral centers located in northern and southern Italy were prospectively enrolled in the study. Patients were recruited during the 3-year period between January 2002–December 2004. The major indications for colonoscopy were the following: severe chronic or recurrent abdominal pain (n = 205), chronic constipation refractory to laxative therapy (n = 111), iron deficiency anemia (n = 91), bloody diarrhea (n = 70), unexplained growth retardation or short stature (n = 45), occult blood loss/hematochezia (n = 40), persistent or recurrent fever (n = 32), chronic diarrhea (n = 30), chronic vomiting (n = 8), and autism (n = 1). Bloody diarrhea was defined as a high frequency of evacuations with unformed stools mixed with blood, whereas hematochezia was defined as evacuations of blood alone.

Patients who had already been evaluated with colonoscopy for the same problem elsewhere, patients with known gastrointestinal disease (eg, IBD), and patients who were taking steroids or were on an exclusion diet for any reason were excluded from the study.

An accurate personal and family history was taken from all patients, who then underwent a detailed physical examination followed by routine biochemistry and allergology testing, including total (paper radioimmunosorbent test) and specific (radioallergosorbent test [RAST]) IgE and/or skin prick tests to food allergens, as well as serum anti–β-lactoglobulin IgG as previously described.[10,11]

Endoscopy and Histology

After general anesthesia or conscious sedation with meperidine/pethidine 1 mg/kg intravenous and midazolam 0.05–0.1 mg/kg intravenous, colonoscopies were performed with standard pediatric or adult videocolonoscopes ([Olympus, Hamburg, Germany]; or [Fujinon, Willich, Germany], or [Pentax, Milan, Italy].) with a maximum outer diameter of 10.9 mm. The terminal ileum was reached and explored whenever possible. Any endoscopic abnormalities were noted and recorded on tape or compact disk for off-line revision. To be recognized as

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such, LNH as well as any other endoscopic abnormalities had to be agreed on by at least 2 experienced observers in both centers. A lymphoid nodule was defined as an extruding follicle with a diameter of ≤2 mm, and LNH was defined as a cluster of ≤10 of such extruding lymphoid nodules. The diameter of the follicles was evaluated with the biopsy forceps (a standard biopsy forceps with an open-cup diameter of 4–5 mm). Mucosal extrusions with a diameter less than or equal to half the diameter of the biopsy forceps' open cup were considered.

One or 2 endoscopic biopsies were taken from the terminal ileum and from each colon segment (cecum, ascending, transverse, descending, sigmoid, and rectum). In addition, 2–5 more biopsies were taken from areas in which LNH or other endoscopic lesions were noted. Mucosa specimens were oriented on strips of Millipore filter paper, fixed in 10% formalin, embedded in paraffin wax, and subsequently stained with hematoxylin-eosin, periodic acid-Schiff, and Masson trichrome. All histologic examinations were performed by experienced pathologists unaware of the clinical and laboratory data of the patients. Morphometric studies were performed with a Leica interactive image analyzer (model Q500 MC; Leica, Heerbrugg, Switzerland), and intraepithelial as well as lamina propria eosinophils and lymphocytes were counted as previously described.[10] The presence of lymphoid nodules with or without germinal centers was also assessed.

Other Investigations

Depending on the individual clinical and laboratory data, the diagnostic work-up included one or more of the following tests: screening for celiac disease (antiendomysial and/or antitransglutaminase IgA antibodies, total IgA antibodies), fecal occult blood test, stool examination and culture for parasites, bacteria and viruses, chest radiography, esophagogastroduodenoscopy with biopsy, radionuclide scan with blood granulocytes, small bowel barium enema, abdominal ultrasonography, and computed tomography scan of the abdomen. The final diagnoses were based on standard recognized criteria, and the patients were followed up for 12–36 months (median, 18 months) to confirm the diagnoses.

Relationship Between Lymphoid Nodular Hyperplasia and Food Hypersensitivity

To assess a possible relationship between LNH and food hypersensitivity, all patients without a definitive diagnosis and with LNH as the sole abnormality commenced an elimination diet based on our previous experience,[12,13] with the exclusion of cow's milk and its derivatives, wheat, fish, tomato, egg, cocoa, and soy. After 8 weeks, all the patients whose symptoms had improved on elimination diet underwent food challenges, and the diagnosis of food hypersensitivity (to cow's milk protein or another or multiple foods) was confirmed only when the earlier symptoms reappeared on food challenge.

The challenges were performed by using different procedures in the 2 centers participating in the study. In the southern Italy center of Palermo, a double-blind, placebo-controlled cow's milk challenge was begun in the hospital according to the procedure previously described.[10,11] The children were randomly assigned to receive cow's milk or placebo. If no clinical reactions were observed within 12 hours after the beginning of the challenge, the patient was discharged, and the challenge was continued at home with bottles coded A or B. Ass' milk, previously introduced into the diet of the patients without causing any clinical reactions, was used as a placebo when performing the double-blind, placebo-controlled challenge. The test meal consisted of ass' milk containing low-lactose cow's milk powder; the full dose of the test meal was reached after 24 hours when the cow's milk protein content was equal to a daily dose of 500 mL of cow's milk. Vanillin sugar was added to the test meals to avoid identification by taste. During the 2-week challenge period, the parents recorded any clinical symptoms, and the patients were re-examined in hospital for any adverse reactions. The challenge was stopped when a clinical reaction occurred. The challenges for foods other than cow's milk were performed in an open fashion as described elsewhere.[12]

In the northern Italy center of Brescia, the food challenges were performed in an open fashion after 8 weeks of the elimination diet described above. Lactose-free cow's milk was reintroduced cautiously, and the dose was increased to reach a normal dietary intake within 48 hours. During the following 4 weeks, the children and/or their parents kept written diaries to record any symptoms, and the patients were evaluated in hospital at weekly intervals. The reappearance of the earlier symptoms was considered a positive result.

Dietary Assessment

To ensure that the children observed a correct elimination diet, the parents were asked to record the amount and type of food their children had eaten each day. These diaries were analyzed at the end of the study to evaluate adherence to the diet and the quantity of milk consumed.

Statistical Analysis

Frequency analysis was performed with the Fisher test. Student t test or Bonferroni test (where appropriate) was used for means comparisons.

Ethical Considerations

The parents of the patients were informed about the study and gave their written consent. The study protocol was approved by the Ethics Committee of both centers involved in the study.

Results

During the study period, 428 patients exhibited 1 or more of the symptoms listed in the Patients and Methods section, but 180 had been previously evaluated and diagnosed. In accordance with the inclusion criteria, they were consequently excluded. The remaining 248 consecutive patients were initially included in the study and underwent colonoscopy. Three patients were subsequently excluded because they did not complete the colonoscopy (1 case) or were lost during the follow-up (2 cases). Thus a total of 245 children (101 male, 144 female; age range, 2 months–13 years, median, 8.5 years) were enrolled. Table 1 shows the final diagnoses according to the colonoscopy findings, histologic examination of the mucosa of the ileum and colon, and the clinical follow-up. A diagnosis of IBD was made in 65 patients (27%), whereas allergic colitis was diagnosed in 25 cases (10%). Less common findings included colonic juvenile polyps (6 cases), angiodysplasia of the colon (3 cases), and primary lymphangiectasis (1 case). Isolated LNH without any other endoscopic lesions was seen in 52 patients (21%) (Figure 1).

Table 1. Number and Percentage of Final Diagnoses According to the Colonoscopy and Mucosa Histology Findings in the 245 Patients Who Completed the Study

	Center of Palermo (N = 142)	Center of Brescia (N = 103)	Total (N = 245)
Crohn's disease	26	11	37
Ulcerative colitis	14	6	20
Indeterminate colitis	6	2	8
Allergic colitis	14	11	25
Other findings	5	5	10
Isolated LNH	30	22	52
Normal colonoscopy	47	46	93

NOTE. No patient had more than 1 gastrointestinal disease.

Colonoscopy did not show any pathologic findings in 93 patients (38%). The final diagnoses in these patients were irritable bowel syndrome (n = 4), chronic constipation caused by food allergy (n = 35), and chronic idiopathic constipation (n = 54). These diagnoses were confirmed in all cases during follow-up.

Apart from the 52 patients with isolated LNH, this finding was also seen in another 21 patients with IBD: 12 with ulcerative colitis, 8 with Crohn's disease, and 1 with determinate colitis. Overall, LNH was observed in 73 of 245 consecutive colonoscopies (30%) and was an isolated finding in 52 of these 73 (71%). The patients with isolated LNH had undergone colonoscopy for the presence of 1 or more of the following symptoms: hematochezia (n = 31), abdominal pain (n = 26), constipation (n = 22), anemia (n = 22), failure to thrive or weight loss (n = 12), chronic diarrhea (n = 6), vomiting (n = 4), and fever (n = 2). In these patients, stool examinations for culture and parasites were negative.

LNH as the sole endoscopic finding was localized in the colon and terminal ileum in 17 cases, exclusively in the terminal ileum in 13 cases, in the rectosigmoid region only in 13 cases, and in the left and right colon in 9 cases.

In accordance with the study protocol, the patients with isolated LNH were put on an oligoantigenic diet, and on this regimen, symptoms disappeared in 48 of the 52 patients within a median of 5.5 days (range, 2–30 days). These 48 patients

Figure 1. Colonoscopy finding showing dense LNH in the ileum.

underwent cow's milk challenge, and in 43 the symptoms reappeared within a median of 2.5 days (range, 1–10 days). They were then put on an oligoantigenic diet again, and the symptoms resolved once again. Furthermore, open challenges showed hypersensitivity to other foods in 10 patients (wheat 10 cases, egg 6 cases, soy 6 cases, tomato 5 cases, beef 4 cases, cocoa 3 cases, fish 3 cases, and goat's milk 2 cases) as symptoms reappeared 1–7 days after their reintroduction.

Consequently, a diagnosis of cow's milk or multiple-food hypersensitivity was made in 43 of the 52 patients (83%) who exhibited isolated LNH at colonoscopy. None of these patients had biochemical signs of inflammation; all had a normal erythrocyte sedimentation ratio, C-reactive protein and leukocyte count. In all of the 245 study patients, the frequency of food hypersensitivity was 42%, but in patients with isolated LNH, food hypersensitivity was significantly more common than in patients without LNH (83% vs 31%, $P < .0001$). Table 2 shows the clinical characteristics of the patients with LNH and food hypersensitivity (Group A) compared with those with isolated LNH not suffering from food hypersensitivity (Group B) and those with normal colonoscopy and without food hypersensitivity (Group C). In the patients with LNH either related or unrelated to food hypersensitivity, there was a higher frequency of males ($P < .0001$) and an older age (A vs C, $P < .0001$; B vs C, $P < .03$) than in the patients with normal colonoscopy. In comparison with Group C patients, Group A patients exhibited a significant association with the following symptoms: hematochezia (present in 67% of cases, $P < .0001$), anemia (present in 47% of cases, $P < .005$), and failure to thrive (present in 28% of cases, $P < .03$). No other symptoms were associated with the presence of LNH in the Group A patients. Group A was also characterized by a higher frequency of cases with a previous diagnosis of food hypersensitivity (vs Group B, $P < .05$; vs Group C, $P < .0001$). The duration of symptoms before colonoscopy was lower in Group A and in Group B patients than in controls (both groups, $P < .01$ vs Group C). Immunologic assays did not show any difference between the 3 groups as regards serum total IgE levels and number of positive RAST results, but the number of patients with elevated serum IgG anti–β-lactoglobulin was higher in Group A than in Group B ($P < .05$) and Group C ($P < .0001$).

Table 3 shows the histology findings in the study populations. The number of patients with LNH, whether related or unrelated to food hypersensitivity (Groups A and B), exhibiting lymphoid follicles throughout the colon and in the terminal ileum was higher than in the Group C patients, but no differ-
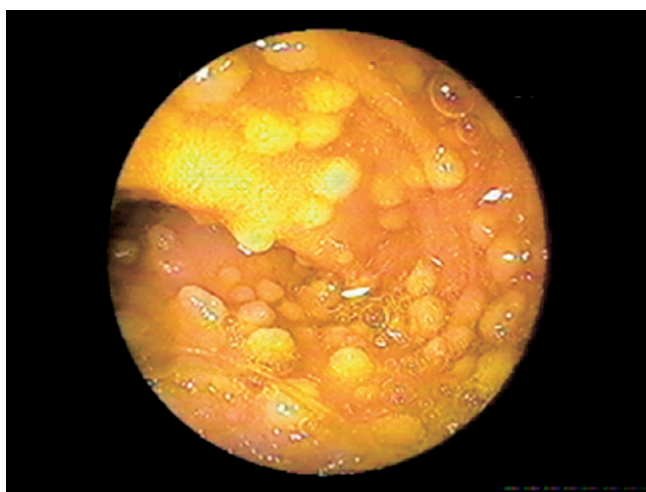
Table 2. Clinical Features of the Patients With Isolated LNH and Food Hypersensitivity (Group A), Compared With the Patients With Isolated LNH Not Suffering From Food Hypersensitivity (Group B) and With the Patients Who Had Normal Colonoscopy and Did Not Suffer From Food Hypersensitivity (Group C)

	Group A (N = 43)	Group B (N = 9)	Group C (N = 58)
Sex (M/F)	35/8	8/1	30/28
Age (y) (mean + SD)	7.5 ± 3.3	6.2 ± 3.6	3.8 ± 2.9
Presenting symptoms[a]	Hematochezia (29), abdominal pain (21), constipation (20), anemia (20), failure to thrive (12), chronic diarrhea (4), vomiting (4)	Abdominal pain (5), fever (2) , hematochezia (2), chronic diarrhea (2), constipation (2), anemia (2)	Abdominal pain (58), constipation (54), anemia (10), failure to thrive (2), chronic diarrhea (4)
Site of LNH	Colon and ileum, 14; terminal ileum, 10; colon, 6; rectosigmoid, 13	Colon and ileum, 3; terminal ileum, 3; colon, 3	No cases showed LNH
Symptom duration before colonoscopy (mo)	3.1 ± 4.1	3.5 ± 3.2	6.4 ± 8.3
Previous history of food hypersensitivity	26/43 cases (60%)	2/9 cases (22%)	8/58 cases (13%)
Elevated serum IgE	8/43 cases (19%)	1/9 cases (11%)	5/58 cases (9%)
Positive RAST results for cow's milk antigens	9/43 cases (21%)	1/9 cases (11%)	5/58 cases (9%)
Elevated serum IgG anti–β-lactoglobulin	30/43 cases (70%)	2/9 cases (22%)	3/58 cases (5%)

NOTE. Group C included only 58 of the 93 patients with negative colonoscopies enrolled in the study, because for this analysis, 35 patients with chronic constipation due to food allergy were excluded from this group. Reference values were total serum IgE <60 KU/L (mean value + 2 standard deviations recorded in age-matched healthy children by our laboratory); skin prick tests: any wheal diameter that exceeded that of the control and was more than one fourth the size of the histamine wheal was regarded as positive; specific IgE for food antigens <4 sorbent units/mL; serum IgG anti–β-lactoglobulin <36% (value with the highest diagnostic accuracy in a large study performed on more than 200 healthy controls and more than 200 CMPI patients).
CMPI, cow's milk protein hypersensitivity; SD, standard deviation.
[a]More than 1 presenting symptom was present in each patient; the number of the patients exhibiting that symptom is given in parentheses.

ence was observed between Groups A and B. Furthermore, the patients with LNH related to food hypersensitivity exhibited a higher mean number of lamina propria and intraepithelial eosinophils than the patients of Group B and Group C in all the colon and ileum sites. In general, there was a progressive reduction in the severity of eosinophilic infiltrate from Group A to Group B and Group C. The rectum and terminal ileum were the regions with the more frequent and marked histology alterations.

In 7 patients with LNH and food allergy, colonoscopy was repeated 3–6 months (median, 4.5 months) after the beginning of the elimination diet. In these cases, the parents had requested a repeat examination, even though the patients were asymptomatic. In all of these 7 patients LNH persisted but with a lesser extension and smaller nodule size than at the first colonoscopy.

Discussion

For several years LNH of the mucosa of the lower gastrointestinal tract has been considered a serendipitous finding without clinical significance or, in a lower percentage of cases, a sign within the spectrum of inflammatory bowel diseases.[14] It has been underlined how small nodular defects (<2 mm in diameter) can be considered a normal variant, but greater changes very probably depend on an infective or chronic bowel inflammatory disease.[15] More recently, Kokkonen et al[4–7] suggested a strong association between LNH at any level of the gut and food hypersensitivity. In particular, they reported that

52% of their patients with LNH of the lower gastrointestinal tract suffered from food allergy.[5] However, to our knowledge, there have been no further studies on the frequency of LNH in a series of consecutive colonoscopies and its relationship with food hypersensitivity.

Our study showed a 30% frequency of LNH in a large series of consecutive children undergoing colonoscopy. LNH was associated with other endoscopic and/or histologic findings that pointed to a diagnosis of IBD in 28.8% of cases. In the vast majority (83%) of the 52 patients with LNH as the sole endoscopic finding, an appropriate elimination diet followed by food challenge with the offending food(s) led to a diagnosis of food hypersensitivity. Cow's milk was the only causative food protein in three fourths of these cases (33 of 43 patients), whereas multiple hypersensitivity, involving also wheat, egg, soy, and other foods, was observed in the remaining one fourth of patients. Thus, it should be emphasized that a lack of response to a cow's milk–free diet in patients suspected of having food allergy is quite often dependent on a condition of multiple food hypersensitivity, as previously shown in children[11-13] and adults.[16] The consistency of the association between food hypersensitivity and LNH is demonstrated by the fact that a much lower (31%) percentage of patients without colonic and/or ileal LNH had food allergy. Furthermore, in 5 of another 9 patients with isolated LNH, clinical symptoms disappeared on an exclusion diet but did not recur during or after challenge. This behavior, reported in other studies on cow's milk allergy,[17,18] could indicate the existence of a subgroup of

Table 3. Histologic Features in the Patients With LNH and Food Hypersensitivity (Group A), Compared With the Patients With LNH Not Suffering From Food Hypersensitivity (Group B) and With the Patients Who Had Normal Colonoscopy (Group C)

	Group A (N = 43)	Group B (N = 9)	Group C (N = 58)	P value		
				A vs B	A vs C	B vs C
Sigmoid-rectum						
Lymphoid follicles	24/43 (56%)	5/9 (55%)	10/58 (18%)	NS	< .001	< .01
Intraepithelial lymphocytes	3.6 ± 2.1	3.5 ± 2.2	3.2 ± 1.9	NS	NS	NS
Intraepithelial eosinophils	4.1 ± 0.9	2.1 ± 2.0	0.7 ± 0.4	< .0001	< .0001	< .0001
Lamina propria eosinophils	7.4 ± 4.7	3.3 ± 2.8	4.1 ± 2.2	< .0005	< .0001	NS
Transverse colon						
Lymphoid follicles	25/43 (58%)	4/9 (44%)	9/58 (15%)	NS	< .001	< .05
Intraepithelial lymphocytes	3.9 ± 3.1	3.8 ± 4.2	3.1 ± 3.1	NS	NS	NS
Intraepithelial eosinophils	4.9 ± 1.9	2.9 ± 3.6	0.9 ± 0.6	< .0001	< .0005	< .0005
Lamina propria eosinophils	6.9 ± 4.2	3.8 ± 1.9	4.2 ± 3.2	< .0005	< .005	NS
Cecum–right colon						
Lymphoid follicles	30/43 (70%)	5/9 (55%)	12/58 (21%)	NS	< .001	< .01
Intraepithelial lymphocytes	4.6 ± 3.2	3.9 ± 3.2	4.2 ± 2.9	NS	NS	NS
Intraepithelial eosinophils	5.4 ± 2.4	3.1 ± 3.4	0.8 ± 0.8	< .0005	< .0001	< .0005
Lamina propria eosinophils	8.4 ± 3.4	4.1 ± 3.2	3.7 ± 1.9	< .0001	< .0001	NS
Terminal ileum						
Lymphoid follicles	32/43 (75%)	6/9 (66%)	18/58 (31%)	NS	< .001	< .05
Intraepithelial lymphocytes	19.6 ± 14.1	13.4 ± 22.2	13.1 ± 21.9	NS	NS	NS
Intraepithelial eosinophils	6.2 ± 2.9	3.9 ± 3.0	1.1 ± 1.4	< .05	< .0001	< .005
Lamina propria eosinophils	9.4 ± 3.5	4.9 ± 3.6	3.8 ± 3.6	< .0005	< .0001	NS

NOTE. Group C included only 58 of the 93 patients with negative colonoscopies enrolled in the study, because for this analysis, 35 patients with chronic constipation due to food allergy were excluded from this group. Presence of lymphoid nodules indicates the number of patients who showed this finding in their biopsy specimens. Intraepithelial lymphocytes and eosinophils were counted in cross sections of 50 crypts randomly selected from each slide; these cell numbers were expressed per 100 deep-crypt epithelial cells. The count of eosinophils in the lamina propria was expressed as a percentage of eosinophils per 1000 lamina propria cells per section (5 sections per biopsy were examined).

patients who have a mild form of food hypersensitivity, or who are developing tolerance and would have probably exhibited symptoms after an extended challenge with higher doses of the offending food. As regards the clinical features, it is interesting to note that the age of the patients with isolated LNH and food hypersensitivity ranged between 3–12 years (mean, 7.5 years). This finding adds further evidence to support our and other previous studies that showed that food hypersensitivity might persist or manifest itself in school-age children[19,20] and in adults.[16] Because clinical symptoms reappeared after a median of 2.5 days after the challenge, it is clear that most patients had a delayed-type reaction to the offending food(s). In agreement with a previous report on the frequency of LNH in patients with hematochezia,[21] we observed that gastrointestinal bleeding was present in 67% of the patients with isolated LNH, a frequency significantly higher than that found in the whole study group (16%). Not unexpectedly, other symptoms associated with the endoscopic evidence of isolated LNH such as anemia and growth deficiency were also part of the clinical spectrum of food hypersensitivity. We observed only 1 patient with autism, abdominal pain, and alternating bowel movements. He exhibited LNH of the rectum without other endoscopic findings and had elevated serum total IgE and positive RAST result for ovalbumin. This patient did not improve on elimination diet, but his parents were not able to ensure a strict adherence to the diet. Obviously, our data do not add anything to the controversial discussion on the significance of intestinal LNH in autistic patients,[8,9,15,22,23] but the hypothesis that food allergy could underlie both these manifestations should be considered.

The humoral as well as the histologic findings also strongly suggest that LNH is a sensitive endoscopic marker of food hypersensitivity, most likely related to a cell-mediated immune response. In fact, although there was no difference in serum IgE levels and the number of positive RAST results between patients with isolated LNH and controls with negative colonoscopy, the patients with elevated serum anti–β-lactoglobulin IgG were significantly more numerous in the LNH group. This is in keeping with previous reports on food allergy with gastrointestinal manifestations[6,24,25] and with the known allergenicity of β-lactoglobulin, which is the main allergen in cow's milk.[26] Furthermore, the histologic evidence of a high number of lymphoid follicles, previously reported in cases of gastrointestinal symptoms caused by food allergy,[4–7,10,12] strongly supports the hypothesis that in most cases LNH is the endoscopic sign of

delayed-type food allergy. Unfortunately, we were unable to perform immunohistochemical studies on the colonic biopsies and thus cannot confirm a previously well-documented finding of an increased density of intraepithelial $\gamma/\delta+$ T cells as a marker of food hypersensitivity.[4,5,17,20,26] Another prominent histologic finding in our study was the increased number of eosinophils in the epithelium and in the lamina propria of the ileal and colonic mucosa. Although this histologic finding is considered more typical of immediate-type hypersensitivity, it has consistently been reported in the gut mucosa of patients with delayed-type models of food allergy, ie, chronic constipation caused by food allergy[10,12,17] and eosinophilic esophagitis.[27-29]

In conclusion, we found that the presence of LNH in the mucosa of the colon and/or terminal ileum is a frequent finding (30%) in children undergoing colonoscopy. Unless associated with other endoscopic lesions, LNH is mostly related to a condition of delayed-type food hypersensitivity and affects mainly preschool or school-age children with hematochezia. We suggest that a diagnosis of food hypersensitivity should be considered in all children with LNH of the colon and/or terminal ileum.

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