Food Hypersensitivity as a Cause of Rectal Bleeding in Adults

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Background & Aims: Rectal bleeding and lymphonodular hyperplasia (LNH) in children can be caused by food hypersensitivity (FH). Our aim was to verify whether similar clinical and endoscopy presentations in adults can be due to FH. Methods: Consecutive adult patients with rectal bleeding were enrolled. All underwent routine assays, colonoscopy, and histology study. Results: Ten of 64 (15%) patients showed LNH as the unique sign at colonoscopy. An oligoantigenic diet resolved the rectal bleeding in 9 patients, and the reintroduction of several foods caused symptom reappearance. Double-blind placebo-controlled challenges with cow’s milk and wheat protein confirmed the FH; symptoms reappeared 1–96 hours after the challenge. None of the patients were positive for IgE-mediated assays. In patients with LNH and FH, histology of the ileum and colon mucosa showed a higher number of lymphoid follicles and intraepithelial and lamina propria eosinophils compared with the other patients with rectal bleeding. Conclusions: Recurrent rectal bleeding can be caused by FH in adult patients. Endoscopic evidence of LNH characterizes these cases.

Rectal bleeding caused by allergic proctitis is a clinical manifestation of food hypersensitivity (FH) in infants. However, in a recent article we showed that rectal bleeding related to a condition of FH can occur also in school-age children. In these older children the main endoscopic characteristic was the presence of lymphonodular hyperplasia (LNH) of the colon and/or the ileum. Others described LNH as an endoscopic marker of cow’s milk allergy in children.

This prospective study showed that rectal bleeding and intestinal LNH can be caused by FH in adult patients.

Patients and Methods

Consecutive patients with rectal bleeding and referred to our Institute between January and December 2005 were enrolled. Rectal bleeding was defined as evacuation of blood alone or of unformed stools mixed with blood.

Inclusion criterion was a history of recurrent rectal bleeding lasting more than 3 months, with a frequency ≥1 episode per week. Exclusion criteria were (1) treatment with steroids or an exclusion diet for whatever reason and (2) presence of concomitant symptoms or laboratory results suggesting an inflammatory bowel disease.

Routine biochemistry and allergology tests were performed as described.

Endoscopy and Histology

Colonoscopies were performed as far as the terminal ileum. Any endoscopic abnormalities were noted and recorded for off-line reappraisal. LNH was defined as a cluster of ≥10 extruding lymphoid nodules as previously described. Biopsies were taken from the terminal ileum, from each segment of the colon, and from areas where endoscopic lesions were noted. Histologic examination was performed by a pathologist unaware of the clinical and laboratory data of the patients. Intraepithelial and lamina propria eosinophils and lymphocytes were counted.

Other Investigations

The diagnostic work-up could have included screening for celiac disease, serum immunoglobulin, stool examination and culture, serum anti-human immunodeficiency virus antibodies, chest radiography, esophagogastroduodenoscopy with biopsy, small-bowel follow-through study, abdominal ultrasonography, and computed tomography scan. The patients were followed up for a median of 25 months to confirm the diagnoses.

Evaluation of the Relationship Between Lymphonodular Hyperplasia and Food Hypersensitivity

To assess a possible relationship between LNH, rectal bleeding, and FH, all patients with LNH as the sole abnormality and without a definitive diagnosis commenced an oligoantigenic diet containing rice, lamb, carrots, olive oil, salt, and sugar. After 4 weeks, the subjects remaining asymptomatic on this regimen were introduced to new foods singly, with at least 8 days between the introduction of each new food. Tolerated foods were kept in the diet. After the introduction of a new food if the patients observed the reappearance of rectal bleeding, this food was excluded from the diet. If the symptom disappeared again, a second challenge was performed after at least 2 months to confirm FH. The first challenge was performed at home in an open fashion. The second challenge was performed at home by using the double-blind pla-
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dian age, 40.5 years; range, 18–79 years; 34 male/30 female) completed the study. The final diagnoses in these patients were hemorrhoids (N = 20), anal fissures (N = 5), large tubular adenoma (N = 10), large villous adenoma (N = 6), colon carcinoma (N = 5), angiodysplasia of the colon (N = 2), ulcerative proctitis (N = 6), and LNH (N = 10). LNH was in the terminal loop of the ileum and in the rectum in 4 patients, in the terminal ileum, colon, and rectum in 5, and exclusively in the terminal ileum in 2 (Figure 1). All these patients exhibited erythema and edema of the rectal mucosa, with presence of bright red blood after endoscope touching.

Patients with LNH underwent a complete work-up; none were positive for celiac disease-specific antibodies (anti–tissue transglutaminase and endomysial antibody) and had a reduction in the villi/crypts ratio in the duodenal mucosa. All other differential diagnoses were excluded.

All patients with LNH received the above described oligoantigenic diet for 4 weeks. During this period 9 patients remained asymptomatic. In these 9 patients, subsequent open challenge determined the reappearance of rectal bleeding associated with abdominal pain and bowel habit change (Table 1).

The subsequent DBPC challenge determined the reappearance of rectal bleeding, abdominal pain, and bowel habit change but did not show any symptoms when the 9 patients assumed placebo.

The patients with rectal bleeding caused by FH were younger than the other 54 included in the study (28 ± 10 versus 58 ± 21 years; P < .0001), exhibited a higher frequency of self-reported food intolerance (5 of 9 versus 3 of 54; P = .02), and had undergone a higher number of previous endoscopic examinations (between 2 and 4 colonoscopies) (P = .04); there was no difference as regards the duration of the symptoms (4.2 ± 1.9 versus 2.3 ± 3.3 years). The immunologic assays did not show positive IgE-mediated assays (radioallergosorbents, prick tests) in the FH patients. Five patients were positive for serum IgG anti-gliadin antibodies and underwent HLA determination, although they had a normal duodenal histology. Only one of these was positive for DQ2 or DQ8 haplotypes.

The histology showed that FH patients had a higher number of lymphoid follicles and intraepithelial and lamina propria eosinophils than the other patients studied in the ileum and in each segment of the colon-rectum. No patients exhibited histologic features suggestive of inflammatory bowel disease.

Table 1. List of Foods That Caused Symptom Reappearance at the Time of the Open Challenge, Time of the Reaction After Food Assumption, and Kind of Symptoms Reappearing in 9 Patients Who Were Asymptomatic on Oligoantigenic Diet

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Food causing symptoms</th>
<th>Time of the reaction (h)</th>
<th>Symptoms at the challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa, beef, legumes, soy, oranges, fish, peas, cauliflowers, bananas</td>
<td>1</td>
<td>Rectal bleeding, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>2</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa, beef, legumes, soy, oranges, fish, peas, cauliflowers</td>
<td>48</td>
<td>Rectal bleeding, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>3</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa, beef, legumes, soy, oranges, fish</td>
<td>4</td>
<td>Rectal bleeding, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>4</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa, beef, legumes, soy, oranges</td>
<td>96</td>
<td>Rectal bleeding, abdominal pain, constipation</td>
</tr>
<tr>
<td>5</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa, beef, legumes</td>
<td>1</td>
<td>Rectal bleeding, abdominal pain</td>
</tr>
<tr>
<td>6</td>
<td>Cow’s milk, wheat, eggs, tomatoes, cocoa</td>
<td>24</td>
<td>Rectal bleeding, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>7</td>
<td>Cow’s milk, wheat</td>
<td>6</td>
<td>Rectal bleeding, abdominal pain</td>
</tr>
<tr>
<td>8</td>
<td>Cow’s milk, wheat</td>
<td>1</td>
<td>Rectal bleeding, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>9</td>
<td>Cow’s milk, wheat</td>
<td>1</td>
<td>Rectal bleeding, abdominal pain</td>
</tr>
</tbody>
</table>

Figure 1. Colonoscopic finding showing dense LNH in the left colon.
During follow-up the patients with FH continued to follow an elimination diet with the exclusion of the foods that caused rectal bleeding, and none experienced new episodes. Occasional ingestion of the eliminated foods always caused the recurrence of the rectal bleeding associated with abdominal pain. After 12–15 months all these patients underwent a second colonoscopy; the recordings of the endoscopy examinations showed a reduction in the number and size of the LNH clusters.

Discussion

Allergic proctitis is a quite common manifestation in infants with cow’s milk allergy. Furthermore, it can occur in school-age children who frequently exhibited LNH of the colon, which is now considered a possible marker of FH in children. Undergone multiple investigations in the past (a mean of 2.2), LNH often accompanied the rectal bleeding. All these patients had known history of interest in FH, and this could have determined a selection bias.


References


