Perforated duodenal ulcer in a pediatric patient with eosinophilic gastroenteritis

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Diffuse eosinophilic gastroenteritis (EGE) was first described by Kaijser in 1937 (1). EGE is characterized by various gastrointestinal symptoms, peripheral eosinophilia and eosinophilic infiltration of the gastrointestinal tract without granuloma formation or vasculitis (2-7). This uncommon inflammatory disorder is further characterized by tissue eosinophilia unexplained by intestinal parasitic infestations, neoplasia, vasculitis or other known causes (8,9). EGE is an idiopathic disorder with a male predominance generally affecting persons between age 10 and 50 years (7). Half of the affected patients have an atopic history (10).

According to the classification of Klein et al (11), EGE may be divided into three subgroups depending on its primary involvement: mucosal, muscular or serosal. Symptoms of EGE vary and include intermittent nausea, vomiting, abdominal pain, diarrhea, gastrointestinal bleeding, weight loss or stunting of growth, gastrointestinal obstruction, ascites and perforation or fistula. We present a pediatric case with EGE and an upper intestinal perforation, and a literature review of this rare complication.

CASE PRESENTATION

The male patient was born at 37 weeks gestation after an uncomplicated pregnancy. Birth weight was 2.4 kg (less than fifth percentile). Both parents were Chinese. His mother was 150 cm tall and father was 155 cm tall. Family history was negative. The patient had been treated for chronic iron deficiency and chronic hypoalbuminemia since age 2 years. Immuno-allergological work-up revealed food allergies documented by skin tests.

A review of the literature since 1966 revealed only six other cases of perforation of the gastrointestinal tract, one of whom was also a child.

Key Words: Child, Eosinophilic gastroenteritis, Perforated duodenal ulcer

RÉSUMÉ : Un garçon de 11 ans présentant une gastroenteropathie éosinophilique, et traité uniquement par un régime d’exclusion, s’est présenté avec une perforation d’un ulcère duodénal faisant suite à un traumatisme abdominal fermé. Une éosinophilie périphérique, une insuffisance chronique de fer, une hypoalbuminémie chronique et un retard de croissance sévère étaient présents depuis l’âge de 2 ans. Un bilan immunologique avait mis en évidence des allergies alimentaires documentées par des tests cutanés. Une revue de la littérature depuis 1966 a révélé seulement six autres cas de perforation du tractus gastro-intestinal, parmi lesquels, un concernait également un enfant.

Perforation d’un ulcère duodénal chez un patient atteint de gastroenteropathie éosinophilique
noncontributory. The patient was noted to be anemic at the
time of an elective inguinal hernia repair around age
1.5 years at another institution. He was subsequently ad-
mitted to the authors’ institution for evaluation of a microcytic
anemic (hemoglobin 74 g/L, mean cell volume 62 fL) and
hypoalbuminemia (27 g/L) at age 28 months. White blood
cell count was increased to 15,000×10^6/L with peripheral
eosinophilia (12%) (Table 1). Both height and weight were
below the 10th centile. Review of systems revealed bilateral
periorbital edema upon awakening. Occult blood loss in his
stools had been noted on an out-patient basis. A clinical
diagnosis of milk protein enteropathy was proposed, and he
was started on iron supplements and switched to a soy for-
mal on inspection and palpation. However, the small bowel
appeared normal, and there was no evidence of
mesenteric disease. The colon appeared to be perfectly nor-
mal cortisol, insulin, thyroxine and thyroid-stimulating hor-
mones, and T lymphocyte count, and positive skin tests for milk,
beef, peanut and egg white. Endocrine work-up showed nor-
mal cortisol, insulin, thyroxine and thyroid-stimulating hor-
mone. A barium enema double contrast was repeated at age
3 years and his serum albumin was still low (29 g/L). No clini-
cal or biochemical improvement was noted.

At age 9 and showed no signs of inflammatory bowel disease (the
examination was normal).

At age 11 years 9 months he presented with epigastric
pain and abdominal guarding following a kick to his abdo-
men. Abdominal x-ray showed free air with perforated vis-
cus. Preoperative hemoglobin was 83 g/L. Surgical explora-
tion revealed a perforation at the pyloroduodenal junction,
which was repaired with a Graham patch. The perforation
measured 5 mm and was surrounded by edematous and fi-
brotic inflammatory tissue. The initial impression was that of
a chronic pyloric duodenal bulb ulcer with perforation. There
was also a thickened mass of bowel surrounded by
diffuse purulent peritonitis. No biopsies were performed. No
postoperative complications were noted, and he was dis-
charged with cimetidine.

Six weeks later an upper endoscopy revealed a deformed
pylorus with erythema of the antrum and periptyloric area,
and an edematous and hyperemic duodenal bulb with a scar
noted in the duodenal bulb.

Endoscopic biopsies from the antrum (Figure 1) and duo-

### TABLE 1

<table>
<thead>
<tr>
<th>Complete blood cell counts and differential of the presented patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years/months)</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>2/3</td>
</tr>
<tr>
<td>3/5</td>
</tr>
<tr>
<td>3/10</td>
</tr>
<tr>
<td>4/7</td>
</tr>
<tr>
<td>9/4</td>
</tr>
<tr>
<td>11/9*</td>
</tr>
<tr>
<td>11/9†</td>
</tr>
<tr>
<td>12/8</td>
</tr>
</tbody>
</table>

*At age 11 years 9 months the patient was operated for perforated ulcer and received a blood transfusion; †One week postoperation. BUN Blood urea nitrogen; ESR Erythrocyte sedimentation rate; MCV Mean cell volume; SGOT Serum glutamic-pyruvic transaminase; SGPT Serum glutamic-oxaloacetic transaminase; WBC White blood cell count.
denal bulb revealed similar histological changes characterized by a fairly dense, primarily eosinophilic, infiltrate in the lamina propria, with focal invasion of crypt and surface epithelium. *Helicobacter pylori* was not seen on hematoxylin, phloxine and saffron stain nor on Giemsa stain. No ulceration or microabscesses were seen, although in one biopsy focal inflammatory atypia of crypt epithelium and the presence of an eosinophil-rich inflammatory exudate overlying the mucosa were noted.

Corticotherapy was instituted at 2 mg/kg/day. Two months later an upper endoscopy was repeated, mainly to reevaluate the cell atypia described previously. Repeat duodenal and antral biopsies showed partial resolution of the eosinophilic infiltrates, and the atypia was no longer present.

At age 12.5 years he presented with lower gastrointestinal bleeding and a hemoglobin of 98 g/L, compared with 118 g/L three months before. Repeat upper endoscopy revealed two duodenal ulcers, biopsies of which confirmed the presence of a preeminent eosinophilia in the lamina propria. He remained on prednisone 10 mg every other day and restarted cimetidine. A month later albumin decreased to 30 g/L and hemoglobin decreased to 85 g/L (hemoglobin was 102 g/L the previous month). He was restarted on 40 mg/day oral prednisone and slowly weaned. He remained steroid-dependent.

By age 14 years 7 months supplemental nocturnal enteral feedings by nasogastric infusion were finally accepted by the patient and his family to treat his growth failure. In the interim he remained steroid-dependent and required prednisone (15 mg orally every other day). At admission, an upper gastrointestinal and small bowel follow-through showed an irregular duodenal bulb suggestive of scarring. The rest of the examination was normal, specifically the terminal ileum. There was no evidence of thickening folds.

Very poor caloric intake had been a consistent problem. Nocturnal enteral feedings (Isosource; Sandoz Nutrition) resulted initially in a tremendous weight gain. His anemia resolved (hemoglobin 121 g/L), albumin normalized (36 g/L) and growth improved dramatically. Off nasogastric feedings his weight plateaued. Our patient’s final height is 152.5 cm at age 20. His height age is 12.5 years. His genetic potential was evaluated at 160.2±8.5 cm as assessed according to his parents’ height.

DISCUSSION
Since its initial description by Kaijser in 1937 (1), EGE has been widely assumed to be an allergic or immunological disorder. Its pathophysiology, however, remains unknown. Although EGE is often regarded as allergic in origin, trials of elimination diet generally have been unsuccessful. Less than half of all patients described with EGE have a personal or family history of atopy (10). In EGE patients there is no global alteration of immune status (12). Some patients may have an increase in total serum immunoglobulin E, with immunoglobulin E antibodies specific to food antigens (13). Although elimination diet is usually given a trial, rarely will there be a clinical improvement, irrespective of skin test results. Leinbach and Rubin (14) found the results of skin testing in these patients to correlate poorly with their symptoms.

EGE may be found throughout the gastrointestinal tract. The stomach is commonly involved, but the esophagus and colon are usually spared (7). As with Crohn’s disease, the lesions are focal, and the tissue as well as peripheral eosinophilia may fluctuate, sometimes making the diagnosis difficult. As documented by Hoefer et al (7), localization differs between child and adult patients. Adults reportedly have stomach and small bowel involved in 52.1% and 40.8% of cases, respectively, whereas in children the involvement was 25.9% and 66.7%, respectively. In both age groups, the colon tends to be the least involved portion of the gastrointestinal tract. In the pediatric population there is heavy male preponderance, contrasting sharply with adults where sexual distribution is equal (7).

Gastric involvement is usually limited to the antrum or distal half of stomach and occurs with pyloric obstruction, a known complication (12,15). The antral biopsy (10-17) is usually accepted as the preferred site of biopsy for diagnosis in the majority of reported pediatric cases. Tissue eosino-
TABLE 2
Previous reported cases of eosinophilic gastroenteritis (EGE) with perforation of the gastrointestinal tract

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Level of gastrointestinal perforation</th>
<th>Gastrointestinal complaints*</th>
<th>History of allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russell et al (24)</td>
<td>45</td>
<td>Male</td>
<td>Duodenum</td>
<td>Recent onset upper abdominal discomfort</td>
<td>Contact dermatitis</td>
</tr>
<tr>
<td>Hoefer et al (7)</td>
<td>6</td>
<td>Male</td>
<td>Distal ileum</td>
<td>Recurrent abdominal pain, nausea, vomiting, diarrhea</td>
<td>Negative</td>
</tr>
<tr>
<td>Felt-Bersma et al (25)</td>
<td>74</td>
<td>Female</td>
<td>Small bowel (90 cm distal to ligament of Treitz)</td>
<td>Several years: low body weight, frequent loose stools</td>
<td>Occasional pruritus</td>
</tr>
<tr>
<td>Lysey et al (26)</td>
<td>45</td>
<td>Female</td>
<td>Small bowel (100 cm proximal to ileocecal valve)</td>
<td>Recurrent right lower quadrant pains, vomiting, diarrhea, weight loss over three months</td>
<td>Recurrent generalized urticaria in childhood</td>
</tr>
<tr>
<td>Walia et al (27)</td>
<td>60</td>
<td>Female</td>
<td>Proximal small bowel</td>
<td>Perforation while on corticotherapy for EGE</td>
<td>Negative</td>
</tr>
<tr>
<td>Wang et al (28)</td>
<td>60</td>
<td>Male</td>
<td>Small bowel</td>
<td></td>
<td>Negative</td>
</tr>
</tbody>
</table>

*Before onset of symptoms in relation to gut perforation

The majority of reported pediatric cases have involvement predominantly of the muscular layer. Subserol disease appears least associated with historical and immunochemical evidence of allergy, while mucosal layer disease may have an allergic basis (15). We found only six other cases in the adult and pediatric literature with perforation of the gastrointestinal tract in EGE, all of which had more than our bowel layer involved (7,24-28) (Table 2). The only other pediatric patient was reported by Hoefer et al in 1977 (7). That patient presented with perforation of the antimesenteric ileum. Pathology confirmed ileal EGE. Fifteen months after surgical repair that patient presented again with distal ileal perforation. Further treatment was not necessary.

Our patient presented with long-lasting malabsorptive disease. Celiac disease was excluded by a normal D-xylose test and, furthermore, a normal small bowel biopsy. Inflammatory bowel disease with onset in infancy could have been possible. Repeat gastrointestinal tract imaging failed to demonstrate any abnormalities (upper gastrointestinal tract, small bowel follow-through, barium enema). A colonoscopy was never obtained but the patient never presented ‘colitic’ type of symptoms. Cystic fibrosis was excluded by a normal sweat test. No steatorrhea was demonstrated. Chronic parasitic infestations, particular giardiasis, were not demonstrated by either stool examinations or endoscopic biopsies of the duodenum. Gastritis due to H pylori is also in the differential diagnosis. However, no histological evidence of H pylori was observed, and the predominantly eosinophilic nature of the infiltrates is most uncharacteristic of H pylori gastritis.

Our patient’s EGE was a transmural disease of the gastrointestinal tract, which appeared to not affect other digestive organs. He did not respond to elimination diet. Food allergy did not appear to be a contributory factor. The dominating symptoms throughout his life were severe failure to thrive accompanied by delayed bone maturation, hypoalbuminemia from protein-losing enteropathy, iron-deficient anemia and intermittent eosinophilia.

CONCLUSIONS
Free bowel perforation is, thus, a very rare complication of EGE. Only one other pediatric patient has been reported in the literature with such a complication. In our case, a long term malabsorptive state dominated the clinical picture and was associated with failure to thrive. Our patient’s severe transmural disease also led to perforation of his gastrointestinal tract. Various elimination diets were unsuccessful. Corticosteroid therapy combined with supplemental nocturnal enteral feedings helped to control his severe disease.

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