Perforated duodenal ulcer in a pediatric patient with eosinophilic gastroenteritis

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C DESLANDRES, P RUSSO, P GOULD, P HARDY. Perforated duodenal ulcer in a pediatric patient with eosinophilic gastroenteritis. Can J Gastroenterol 1997;11(3):208-212. An 11-year-old boy with eosinophilic gastroenteritis treated by an elimination diet alone presented with a perforated gastroduodenal ulcer subsequent to blunt trauma to the abdomen. Peripheral eosinophilia, chronic iron deficiency, chronic hypoalbuminemia and severe failure to thrive had been present since age 2 years. Immunological 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*

Perforation d'un ulcère duodénal chez un patient atteint de gastroenteropathie éosinophilique

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.

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

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TABLE 1
Complete blood cell counts and differential of the presented patient

Age (years/months)	WBC ($x10^6$/L)	Hemoglobin (g/L)	MCV (fL)	Eosinophils ($x10^6$/L)	ESR (mm/h)	BUN (mg/dL) normal 6-20	SGOT (U/L) normal <33	SGPT (U/L) normal <26	Iron (μg/dL) normal 50-180
2/3	15,000	81	64	1800					
3/5	9300	75	66	186					
3/10	12,100	103	82	847					
4/7	7700	107	85	154					
9/4	11,500	94	66.7	345	6	19	22	9	35
11/9*	28,700	83	58.1	574	8				
11/9†	8200	134	66.5	1230					
12/8	7000	85	70.2	630					

**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*

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 admitted 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 15,000x10^6/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 formula. At age 3 years failure to thrive was evident. A small bowel follow-through showed slightly edematous folds of the proximal jejunum. Despite the soy formula hypoalbuminemia (29 g/L) and occult blood loss in his stools persisted. At that time a small bowel biopsy was performed but no abnormality was detected. Results from a 72 h stool collection for fat were normal. Caloric intake was low. By age 3 years his calorie count was evaluated at 610 cal/day; caloric needs for that age are 1400 cal/day.

At age 3.5 a chromium-labelled albumin excretion test in stools confirmed protein losing enteropathy (5.2% excretion of ^{51}Cr albumin, nitrogen 2%). A 24 h urine collection demonstrated normal proteinuria. Barium enema performed at age 3 years 5 months was normal. The terminal ileum was nodular (nodularity thought to be from lymphoid nodular hyperplasia).

Because his condition remained unchanged at age 3 years 10 months he underwent an exploratory laparotomy to search for a Meckel's diverticulum or another source of gastrointestinal bleeding. The terminal ileum was identified, and the entire small bowel eviscerated through the wound. No Meckel's diverticulum was found. The serosal surfaces of the bowel appeared normal, and there was no evidence of mesenteric disease. The colon appeared to be perfectly normal on inspection and palpation. However, the small bowel had mucosal nodules, one of which was biopsed and appeared to consist of lymphoid hyperplasia with a significant amount of eosinophils.

At age 4 years eight months he was admitted for initiation of an elimination diet which consisted of a no gluten, bovine products, soy and eggs. His bone age was delayed at three years and his serum albumin was still low (29 g/L). No clinical or biochemical improvement was noted.

At age 9 years 5 months corticotherapy was recommended to the parents but not instituted. On reevaluation, anemia (hemoglobin 102 g/L, mean cell volume 69 fL), hypoalbuminemia (20 g/L) and occult blood positive stools were all present. His bone age was significantly delayed (age 6.5 to 7 years).

Since initial presentation the patient had little to no gastrointestinal symptoms. The patient had no diarrhea, no nausea and no vomiting. Abdominal pains were also never a major complaint; they were noted at age 4 as being bilateral lower abdominal pains on and off. Thus, the patient's major problem was severe failure to thrive, chronic anemia and hypoalbuminemia. Immune work-up over these years included normal immunoglobulins (A, E, D, M, G), normal B and T lymphocyte count, and positive skin tests for milk, beef, peanut and egg white. Endocrine work-up showed normal cortisol, insulin, thyroxine and thyroid-stimulating hormone. A barium enema double contrast was repeated 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 abdomen. Abdominal x-ray showed free air with perforated viscus. Preoperative hemoglobin was 83 g/L. Surgical exploration 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 fibrotic 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 discharged with cimetidine.

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

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

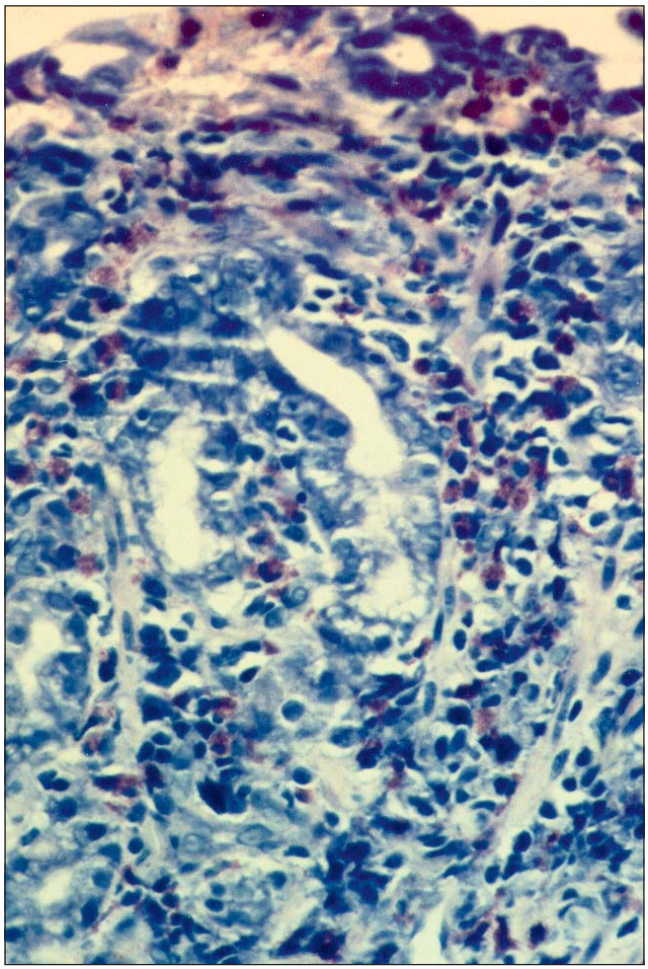

Figure 1) Endoscopic antral biopsy from patient six weeks after surgery for perforated duodenal ulcer. Fairly dense eosinophilic infiltrate of the lamina propria is noted

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

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

**Before onset of symptoms in relation to gut perforation*

philia may be focal, necessitating multiple biopsies for confirmation of the diagnosis (10). Pathologically, the local eosinophilic infiltrates are often associated with tissue edema, shortening of villi, epithelial necrosis and peripheral eosinophilia (8,9,17).

EGE is nearly always limited to the gut but involvement of other organs, including the liver (18), gallbladder, spleen, bladder (19,20) and pancreas (21), has been reported in adults. Thus, the clinical presentation of EGE depends on the primary site of involvement (16). Patients with mucosal disease present with intermittent nausea, vomiting, abdominal pain and diarrhea. Bleeding is occasionally seen. When severe disease is present weight loss or edema from protein-losing enteropathy may predominate. Symptoms may be correlated with ingestion of certain foods. In EGE involving the muscularis, intestinal obstruction is a frequent presentation, most often in the distal stomach. In EGE's serosal form (22,23) ascites containing a high eosinophil count is noted. When the inflammation is transmural, pain, perforation, obstruction, bleeding or fistulas may be seen. However, free bowel perforation is, in fact, a very rare complication of EGE.

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, particulary 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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