Aphthous esophageal ulceration: A novel presentation of Crohn's disease?

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PL BECK, PK BLUSTEIN, MA ANDERSEN. Aphthous esophageal ulceration: A novel presentation of Crohn's disease? Can J Gastroenterol 1994;8(2):101-104. Crohn's disease (CD) commonly presents as involvement of the small bowel or colon – the esophagus is rarely involved. The authors describe the case of a 45-year-old woman who presented with odynophagia and was found to have aphthous ulcers of the esophagus. On questioning, she admitted to three to four episodes of nonbloody diarrhea, each lasting less than one week, over the past two years. The patient denied other symptoms of gastrointestinal, collagen-vascular, respiratory or cardiovascular disease. Viral, fungal and bacterial cultures of blood, stool and tissue biopsies were all negative. A small bowel enema showed inflammation of the distal ileum. Colonoscopy revealed patchy areas of inflammation of the colon and distal ileum. Biopsies from the esophagus, duodenum, terminal ileum and colon showed chronic inflammation, lymphoid aggregates, goblet cell hyperplasia (in the colon) and crypt abscesses. Giant cells, granulomas and fissures were not evident in any of the biopsies. The patient failed to respond to a three-week course of omeprazole, but her symptoms resolved within three days of starting prednisone. The exact cause of the esophageal ulcerations is unknown but most likely is CD of the esophagus.

Key Words: Crohn's disease, Esophageal ulcers

Ulcérations œsophagiennes aphteuses : nouvelle présentation de la maladie de Crohn?

RÉSUMÉ : La maladie de Crohn se manifeste généralement par une atteinte de l'intestin grêle ou du côlon, l'œsophage étant rarement affecté. Les auteurs décrivent le cas d'une femme de 45 ans qui s'est présentée avec de l'odynophagie et chez qui des ulcères aphteux de l'œsophage ont été observés. À l'interrogatoire, elle dit avoir présenté à trois ou quatre occasions de la diarrhée non sanguinolente qui a duré moins d'une semaine, au cours des deux années écoulées. La patiente a déclaré n'avoir aucun autre symptôme de maladie digestive, vasculaire-col-

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APHTHOUS ESOPHAGEAL ULCERS are rare. They have been described in Behçet's disease (1-4), ulcerative colitis (UC) (5,6), yersinia enteritis (7), amebiasis (8,9) and Crohn's disease (CD) (10-19). There have been fewer than 60 cases of esophageal ulcers in CD reported in the literature from 1950-93. There are only two reported cases in which odynophagia was the presenting symptom of CD (16,19). Esophageal involvement in CD has been identified in up to 1.8% of adults (9) and 6.5% of pediatric-aged patients with CD (18). Esophageal ulcers containing enveloped virus-like particles have been described in homosexual men (20); in this study, the esophageal ulcers were also commonly associated with a skin rash, oral ulcers and the later development of human immunodeficiency virus (HIV) positivity.

CASE PRESENTATION

A 45-year-old Lebanese woman presented to her family doctor complaining of a four-week history of odynophagia. The pain initially occurred with solids, then with both liquids and solids. She described the pain as a sharp burning sensation that was located from her cricoid cartilage to xiphoid process. She denied abdominal pain, nausea and vomiting. During the six weeks prior to presentation (two weeks

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lagénique, respiratoire ou cardiovasculaire. Les épreuves virales, fongiques et bactériennes de sang, de selles et les biopsies tissulaires se sont toutes révélées négatives. Un lavement pour l'examen du grêle a révélé la présence d'inflammation à l'iléon distal. La colonoscopie a révélé des foyers disséminés d'inflammation du côlon et de l'iléon distal. Les biopsies de l'œsophage, du duodénum, de l'iléon terminal et du côlon ont révélé une inflammation chronique des amas lymphoïdes, de l'hyperplasie sous forme de cellules caliciformes (dans le côlon) et des abcès diverticulaires. Des cellules géantes, des granulomes et des fissures n'ont été notés à aucune des biopsies. La patiente n'a pas répondu à trois semaines de thérapie par oméprazole, mais ses symptômes se sont passés dans les trois jours qui ont suivi l'administration de prednisone. La cause exacte des ulcérations œsophagiennes demeure inconnue, mais est probablement attribuable à une maladie de Crohn au niveau de l'œsophage.

prior to the onset of the odynophagia), she had mild diarrhea. Bowel movements were brown in colour, and she had from three to 10 per day. The patient denied features suggesting gastrointestinal blood loss. She had three or four episodes of similar diarrhea (lasting up to seven days) over the two years prior to the onset of the odynophagia, but had never sought medical attention for it. She denied symptoms of reflux gastroesophageal disease, had never taken antacids or ulcer medications, and denied the use of nonsteroidal anti-inflammatory drugs over the past two years. The patient had no history of other gastrointestinal, respiratory, cardiovascular, neurological or rheumatological problems. Specifically, she denied joint pain or swelling, oral or genital ulcers, dry eyes, dry mouth, hair loss, skin rashes, jaundice and eye problems. Her past medical history was negative except that while living in Lebanon, she received two units of blood in 1980 (10 years before presentation) following a postpartum hemorrhage. Her family history was negative for gastrointestinal, autoimmune, respiratory, neurological and dermatological diseases. There was no family history of tuberculosis and she denied contact with tuberculosis. Her mantoux test was negative 10 years ago on emigration from Lebanon to Canada.

The patient was married and only had one sex partner in the past 20 years. She denied a history of sexually transmitted diseases. She smoked 10 to 15 cigarettes per day and denied street drug use. On presentation, she was not on any medications and denied allergies. She denied fever, chills and rigors,

but complained of a 6.8 kg weight loss over the past month. She felt her weight loss was due to decreased intake secondary to her odynophagia. She also noted a decrease in energy over the past four weeks.

Physical examination on admission to hospital was normal. There were no oral ulcers, skin rashes, joint problems or respiratory problems. Abdominal and rectal exams were normal. Stool was negative for occult blood.

Laboratory data on admission: White blood cell count was 5.8×10^9 (normal, 4 to 10.5×10^9); hemoglobin, 88 g/L (normal, 120 to 160); mean corpuscular volume, 65.7 (normal, 80 to 100); retic count, 6%; platelets, 372×10^9 (normal, 150 to 400×10^9). Serum ferritin was less than 5 µg/L (normal, 10 to 250); serum iron, 2 µmol/L (normal, 7 to 29); and total iron-binding capacity, 48 µmol/L (normal, 41 to 77). Serum folate was 23.9 nmol/L (normal, greater than 5.7); red blood cell folate, 1241 nmol/L (normal, greater than 396); and serum vitamin B₁₂, 376 pmol/L (normal, greater than 197). Mantoux test was negative and anergy screen was normal. Electrolytes, liver enzymes, lipase, albumin and calcium were all normal. Her erythrocyte sedimentation rate, antinuclear antibody titre, rheumatoid factor, C3, C4 and hemoglobin electrophoresis were all normal. Human lymphocyte antigen screen was negative for the B5, B12 and B27 antigens. Stool studies, including occult blood, culture, ova and parasites, acid fast bacilli (AFB) and viral cultures, were repeated four times over a four-week period and were normal. Chest and plain abdominal radiographs were normal. HIV serology,

repeated twice over a one-year period, was negative both times.

Gastroscopy revealed numerous aphthous ulcers throughout the esophagus (Figure 1). The stomach appeared normal. The duodenum had patchy areas of erythema and inflammation in the first and second segments. Biopsies of the esophageal lesions showed acute and chronic inflammatory changes (Figure 2). The inflammatory cell infiltrate primarily was made up of macrophages and lymphocytes. No granulomas, giant cells or fissures were noted. Electron microscopy failed to identify bacterial or viral particles. Bacterial, AFB, fungal and viral cultures of the esophageal biopsies were negative. Fungal and AFB stains were negative. Biopsies from the stomach were normal. Duodenum biopsies showed mild nonspecific, acute and chronic inflammatory changes.

The patient was started on a course of omeprazole (20 mg orally per day) and discharged home. Omeprazole was continued for three weeks, at which time it was discontinued due to her continued severe odynophagia and persistent nonbloody diarrhea. She required readmission to hospital due to odynophagia and dehydration. Endoscopy and biopsies repeated at that time exhibited no change in the macroscopic or microscopic appearance of the lesions. Again, tissue cultures and stains for AFB and fungi were negative. A small bowel enema and a double contrast barium enema were done, and showed inflammatory changes in distal ileum suggestive of CD (Figure 3). The esophageal ulcerations were not visible on the upper gastrointestinal series. Colonoscopy showed patchy areas of erythema and inflammation in the colon and distal ileum. Biopsies from the colon and ileum showed acute and chronic inflammatory changes. The inflammatory cell infiltrate primarily consisted of macrophages, lymphocytes and some neutrophils. Mild goblet cell hyperplasia, lymphoid aggregates and crypt abscesses were noted. Granulomas, giant cells and fissures were not seen. AFB and fungal stains were negative.

A course of prednisone (45 mg

Figure 1) Aphthous ulcerations of the esophagus noted on initial gastroscopy. The ulcers were present throughout the esophagus

Figure 2) Histological appearance of one of the esophageal ulcers. The inflammatory cell infiltrate primarily consisted of macrophages, lymphocytes and fibroblasts. Both light and electron microscopy failed to identify an infectious agent in multiple biopsies from the esophagus, duodenum, ileum and colon

orally per day) was then started. Three days later, the patient was asymptomatic and returned to a full diet. The prednisone was tapered over a period of six weeks. Gastroscopy after six weeks of therapy showed no signs of inflammation or ulceration of the esophagus, stomach or proximal duodenum. She has been followed for two years and has been asymptomatic.

DISCUSSION

The exact etiology of the esophageal ulcers in this case is unknown. The lack of other symptoms and laboratory data to suggest an infectious or a collagen-vascular cause, the presence of diarrhea, and chronic inflammation of the duodenum, distal ileum and colon all point to CD. Esophagitis in Behçet's disease is rare and is usually not due to aphthous ulcers (1). Of 26 reported cases of esophagitis in Behçet's disease, 42% had ileocolonic ulcerations (1). The presented case did not have a history of rheumatological or eye problems, and denied skin rashes, and oral and genital ulcers. The diagnostic criteria of Behçet's disease include: major criteria of buccal ulcerations, genital ulcerations, eye lesions and skin lesions; and minor criteria of arthritis, a positive family history, thrombophlebitis, and lesions involving the gastrointestinal, cardiovascular and neurological systems (21). A minimum of three

Figure 3) Radiograph following a small bowel enema. Note the inflammatory changes in the distal ileum (arrows)

major and two minor criteria are required for the diagnosis; thus, this case does not fulfil the diagnostic criteria

(21). Further, there were no features to suggest infectious or collagen-vascular disorders.

Esophageal ulceration in UC occurs rarely and is usually associated with longstanding severe disease (5,6). In the presented case, the findings on colonoscopy, barium enema and histological examination were not suggestive of UC.

Esophageal involvement in CD is usually associated with advanced ileocolonic disease and an increased prevalence of the extraintestinal manifestations of CD (10,15). As aforementioned, esophageal ulceration due to CD has been reported in two individuals who had no other evidence of CD on presentation with esophageal symptoms (16,19). Geboes *et al* (10) followed 500 patients with biopsy-proven CD and found esophageal ulcers in nine patients (1.8%), which probably was an underestimate of the involvement of the esophagus because less than 20% of the patients had upper endoscopy (10). In this same study, six of the nine patients with esophageal ulcers also had aphthoid oral lesions (10).

Giant cells and granulomas were not found in any of the biopsies in our case. However, in a review of 53 cases of esophageal CD reported from 1950-88, granulomas were found in only 12 cases, five of which required several sections (10,22).

CD involvement of the esophagus most commonly presents as strictures and fistulas which are thought to be due to longstanding esophageal involvement (10,16,23,24). Two patients with esophageal CD, when followed for six and 14 years, developed severe strictures and fistulas (16).

The presented patient's odynophagia failed to improve on omeprazole but resolved within three days of starting 40 mg/day prednisone. Esophageal ulcerations in patients with biopsy-proven CD have been found to resolve completely and rapidly to 30 to 50 mg/day prednisone (10).

Esophageal ulcers usually occur late in the course of CD. However, in one of the two cases in which esopha-

geal involvement was the presenting feature, four years lapsed from presentation to ileocolonic involvement (16).

CONCLUSIONS

In summary, esophageal involvement can be the presenting feature of CD and, if untreated, esophageal Crohn's can lead to debilitating complications such as fistulation, perforation and stricture. The symptom complex of odynophagia and dysphagia in Crohn's with esophageal involvement appears to respond rapidly and completely to corticosteroids. There has not been a clearly documented case of recurring esophageal CD. Thus, it is essential to note that esophageal ulcers can be the presenting feature of CD or can occur at any time throughout the disease course, and that corticosteroids are very effective in treating this potentially debilitating manifestation of this disease.

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