

A Case of Cryptogenic Multifocal Ulcerous Stenosing Enteritis: Differential Diagnosis from Crohn's Disease

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Abstract

Cryptogenic multifocal ulcerous stenosing enteritis is a rare idiopathic disease of the small bowel. Its origin and pathophysiology have not been established. Clinicopathologic features include unexplained small bowel strictures with superficial ulceration, chronic or relapsing occlusion episodes. A 44-year-old man complained of recurrent colicky abdominal pain and dizziness. Laboratory tests indicated iron-deficiency anemia. There was no evidence of bleeding on esophagogastroduodenoscopic and colonofiberscopic examination. With capsule endoscopy, multiple mucosal ulcers were visualized in the jejunoileal area. A small-bowel series revealed severe strictures and the capsule was retained in the stenotic focus without obstructive symptoms. Small bowel segmental resection with end-to-end anastomosis was performed, and the histologic examination indicated cryptogenic multifocal ulcerous stenosing enteritis. After surgery, the patient's symptoms were completely resolved and his anemia was corrected. Cryptogenic multifocal ulcerous stenosing enteritis should be considered in cases of chronic or recurrent occlusion events and multiple small intestinal ulcers and strictures of unknown origin.

Key words

Cryptogenic multifocal ulcerous stenosing enteritis – Crohn's disease – small intestine – capsule endoscopy.

Introduction

Cryptogenic multifocal ulcerous stenosing enteritis (CMUSE) is a rare disease characterized by repeated

colicky episodes and multiple small intestinal strictures with superficial ulcerations. It usually responds favorably to glucocorticosteroids [1, 2]. CMUSE is sometimes confused with other diseases involving the small bowel, especially Crohn's disease [3]. Diagnosis is established by pathological evaluation after surgery or by double balloon endoscopic biopsy.

We report a patient with prolonged repetitive colicky pain and anemia who was diagnosed with CMUSE by surgical resection of the small bowel.

Case report

A 44-year-old man suffered from intermittent colicky abdominal pain and dizziness for 27 years. At age 17 he had visited a hospital for dizziness and abdominal pain, and was diagnosed with iron-deficiency anemia. Esophagogastroduodenoscopy, colonofiberscopy and small-bowel series did not reveal any abnormalities and the cause of anemia was not determined. Since that time, although he had intermittent bouts of dizziness and abdominal pain, he had not undergone any further evaluation.

Twelve months ago, the patient underwent a general check-up for abdominal pain, dizziness and weight loss of 6 kg during the previous two months. Laboratory tests indicated iron-deficiency anemia, and there was no evidence of bleeding on repeated endoscopic examination.

Eight months ago, the patient was admitted to our hospital for continued dizziness and intermittent colicky pain. Laboratory findings showed anemia and malnutrition. The patient's body mass index was 19.7 kg/m². His hemoglobin was 4.5 g/dL, serum protein was 4.8 g/dL and serum albumin 2.8 g/dL. Stool occult blood screen was positive. Liver function tests, vitamin B₁₂, folate, and thyroid function tests were normal. The patient's erythrocyte sedimentation rate was 10 mm/hr, C-reactive protein was 0.1 mg/dl and anti-*Saccaromyces cerevisiae* antibody (ASCA) screen was negative. He had no perianal lesions. An abdominopelvic computed tomography scan revealed prominent jejunal loop segmental dilatation with no distal visible obstructive pathology. Capsule endoscopy was performed to evaluate

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the suspected small bowel lesions. Multiple mucosal erosions and shallow longitudinal ulcers were visualized in jejunoileal lesions (Fig. 1), and the capsule was retained without obstructive symptoms.

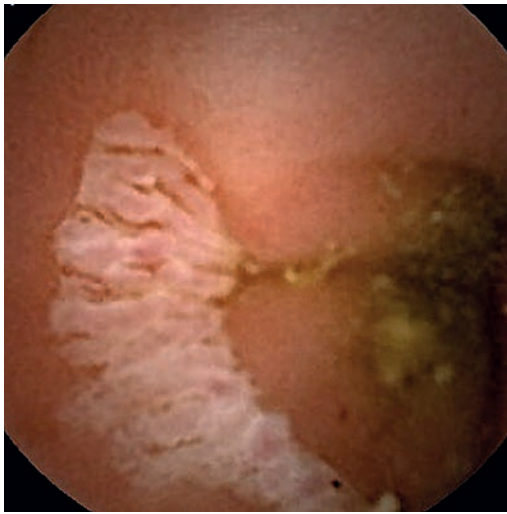


Fig 1. Capsule endoscopy findings. It showed multiple mucosal erosions and shallow longitudinal ulcers in jejunoileal lesions.

A small-bowel series for the evaluation of stenosis showed two foci of segmental narrowing and bird beak-like narrowing of the jejunum in the right lower abdomen (Figs. 2A, B). The capsule was floating in the dilated site. We diagnosed the patient with Crohn's disease and started 5-aminosalicylates (4 g/day) with prednisolone (30 mg/day). His general condition and symptoms improved. However, two months after the withdrawal of prednisolone, the patient's abdominal pain worsened and his hemoglobin was 4.9 g/dL despite a sufficient iron supply.

To relieve the patient's symptoms and improve diagnosis and treatment, we performed surgery and resected about 15 cm of the distal jejunum with end-to-end anastomosis. The gross specimen showed a dilated proximal bowel segment 5.0 cm in diameter. The mesenteric adipose tissue

was focally and minimally adherent to the serosa without any fibrous adhesion band, creeping fat, or enlarged lymph nodes. The mucosal surface was diffusely hyperemic. There were multiple geographic erosions and ulcers with multifocal petechial hemorrhages. Two fibrous stenotic sites were noted without obstruction (Fig. 3). The capsule was found in the proximal stenotic area. Microscopically, superficial and non-granulomatous ulcers were observed. The mucosa on both sides of the ulcers was normal. No villous atrophy, lymphocytic vasculitis, microorganisms, giant cell granulomas, cytomegalopathy, or viral inclusions were observed (Fig. 4). The patient was diagnosed with CMUSE.

After surgery, his abdominal pain resolved, hemoglobin level was 14.6 g/dL, and serum albumin was 4.4 g/dL. The patient has gained about 10 kg over a period of four months. He has had no further symptoms related to CMUSE during 6 months of subsequent follow-up.

Discussion

Diseases such as CMUSE, Crohn's disease, ulcerative jejunoileitis, nonsteroidal anti-inflammatory drugs-induced enteropathy, tuberculosis and some types of infectious enteritis cause small bowel ulceration and stenosis [3]. Occasionally, these diseases are confused with each other because they present with similar symptoms and because the diagnosis of small bowel disease is difficult. Therefore, final diagnosis tends to take a long time from the recognition of the first symptoms. Recently, with the development of capsule endoscopy and double balloon enteroscopy, the diagnosis and understanding of these entities has improved.

CMUSE was first described by Debray et al in 1964 [1]. This rare disease is characterized by chronic and recurrent bouts resulting from multiple small intestinal strictures and superficial ulceration affecting the mucosa and submucosa. CMUSE is not associated with biological signs of systemic inflammatory reactions, but usually responds to steroids. CMUSE typically has a relapsing clinical course even after

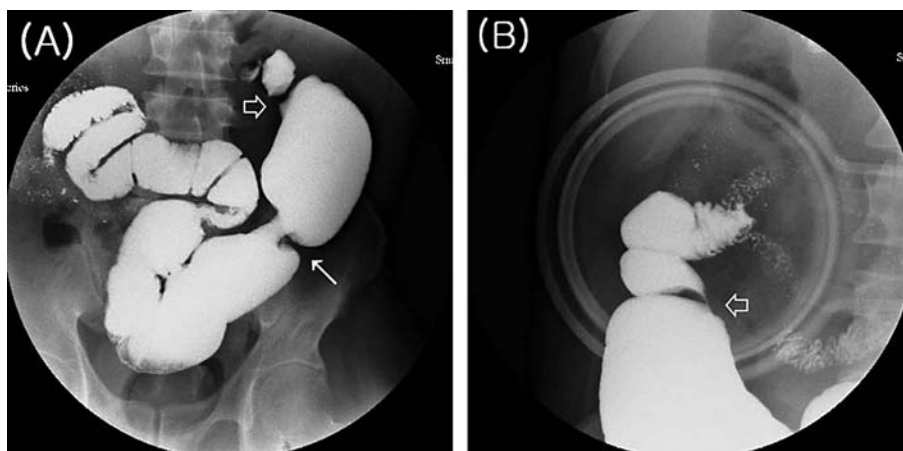


Fig 2. Small-bowel series findings. A) Symmetrical short segment narrowing of the jejunum (thin arrow) in the right lower abdomen. B) Bird beak-like narrowing of the jejunum (arrow) with dilatation of the proximal small bowel loop.

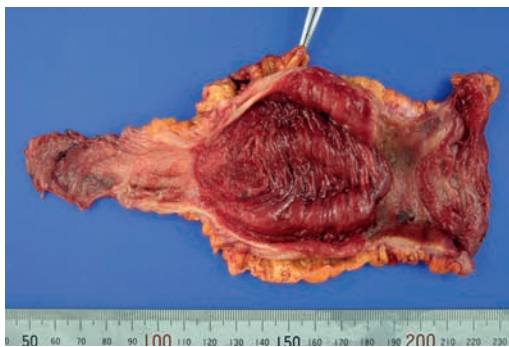


Fig 3. The gross finding of the resected specimen. Multiple geographic erosions and ulcers were observed with two fibrous stenotic foci.

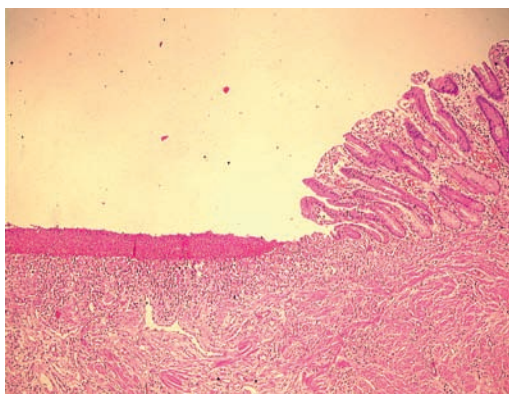


Fig 4. Superficial and non-granulomatous ulcer with relatively well preserved mucosa on side of the ulcer (H&E, 40x).

surgery [1, 2]. To the best of our knowledge, only about 40 cases compatible with CMUSE have been published worldwide [2, 4-6]. In Korea, only three cases have been reported [7, 8]. Chang et al reported two cases of CMUSE in 2007 [7]. One patient had recurrent abdominal pain and melena for 41 months, and was diagnosed with CMUSE by double-balloon endoscopy. In the other case, capsule endoscopy was impacted in the stenotic site of the small bowel and a surgical specimen indicated CMUSE. In 2011, Kim et al described a 25-year old woman with steroid-refractory CMUSE who ultimately underwent four surgeries [8]. The diagnosis of CMUSE should be considered after excluding other diseases causing multifocal small bowel ulcers and stenosis, such as Crohn's disease involving the small intestine, chronic non-granulomatous ulcerative jejunoileitis, lymphoma (especially invading the mucosa only), infections, drug-induced small bowel disease, traumatic injury, and ischemia related to vasculopathy [3, 9]. Capsule endoscopy is noninvasive and useful to detect abnormal small bowel findings and has good patient compliance. However, diagnosis must be confirmed by pathological evaluation of intestinal specimens obtained by double-balloon endoscopic biopsy or surgery. In our case, we first diagnosed our patient with Crohn's disease, since there were multiple somewhat longitudinal ulcers and

strictures seen by capsule endoscopy and he had chronic obstructive symptoms with anemia over a period of 27 years. Furthermore, his symptoms initially responded to glucocorticosteroids.

When diagnosing CMUSE, it is imperative to distinguish CMUSE from Crohn's disease in particular [10]. Compared to Crohn's disease, CMUSE is not associated with clinical or laboratory features of systemic inflammation. Moreover, it is not associated with perianal disease or fistula formation. On pathology, the ulcerations are localized to the mucosa and submucosa, while Crohn's disease shows transmural inflammations and giant cell granulomas. In our case, the patient's inflammatory markers such as ESR and CRP were normal, ASCA was negative and there was no history of perianal lesions. Unfortunately, double balloon endoscopy was not available at our hospital, and we were therefore unable to obtain preoperative pathologic confirmation. Surgery was needed to relieve the patient's recurring abdominal pain and anemia. Histopathologic findings included multiple superficial ulcers mainly affecting the mucosa and submucosa. Fibrosis and inflammatory cell infiltrates extended beyond the ulceration, but the mucosa on both sides of the ulcerations was normal and there was no villous atrophy [2]. In our case, the microscopic examination showed no granulomas, transmural inflammation and fissures, and we therefore ruled out Crohn's disease.

Some authors have suggested that vasculopathy is part of the etiology of CMUSE [2, 11, 12]. However many reported cases showed no evidence of vasculopathy, and Chang et al divided CMUSE into two subcategories, MUSE-I (idiopathic MUSE) and MUSE-V (vasculitis-related MUSE) [7]. Some authors disagree with this classification, and have suggested that any type of vasculitis should be described simply as vasculitis and not CMUSE. The etiology and pathogenesis were recently suggested to be related to the overstimulated production of fibrous tissue and disturbance of collagen degradation in CMUSE [13, 14].

The treatment of CMUSE remains symptomatic. Typically, CMUSE responds to glucocorticosteroids, but steroid dependence often is a result, and a case of steroid-refractory CMUSE was previously reported [8]. In our case, glucocorticoids initially improved the patient's condition, but his symptoms worsened and his anemia with malnutrition was not corrected. Surgery was performed to reach a conclusive diagnosis and to relieve strictures. After surgery, the patient's symptoms were resolved and his laboratory findings normalized. Multiple strictures and stenoses associated with CMUSE commonly require surgery, but with the advancement of double balloon endoscopy, endoscopic balloon dilatation of symptomatic stenoses may be tried first [13,15].

The prognosis of CMUSE remains poorly understood. Our patient had no further symptoms or other complications related to CMUSE over a period of 6 months after surgery. However, CMUSE has a propensity for recurrence of symptoms and strictures even after surgical resection, and therefore we plan to follow up the patient closely.

In **conclusion**, we report a case of CMUSE diagnosed by surgical resection of the small intestine. CMUSE, a rare idiopathic small bowel disease, should be considered during differential diagnosis in patients with small bowel ulcerations and strictures.

Conflicts of interest

None to declare.

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