

Cryptogenic Multifocal Ulcerous Stenosing Enteritis (CMUSE): A Tale of Three Decades

Ayaskanta Singh, MBBS, MD, DM¹, Manoj Kumar Sahu, MBBS, MD, DM¹,
Manas Kumar Panigrahi, MBBS, MD, DM², and Debasis Misra, MBBS, MD, DM¹

¹Department of Gastroenterology and Hepatobiliary Sciences, Siksha O. Anusandhan University Institute of Medical Sciences and SUM Hospital, Bhubaneswar, India

²Department of Gastroenterology, All India Institute of Medical Sciences, Bhubaneswar, India

ABSTRACT

We present a patient who, over the course of 35 years, presented with repeated episodes of ileus and melena and was misdiagnosed several times, leading to several surgeries. Macroscopic and microscopic features of his resected intestine were compatible with cryptogenic multifocal ulcerous stenosis enteritis (CMUSE), but additional angioectatic lesions were also noted. The patient responded dramatically to hormonal therapy consisting of ethinylestradiol and norethisterone. To our knowledge, this is the first reported case of CMUSE that has shown response to hormonal therapy. We suggest that this is a variant of CMUSE in which vasculopathy plays a role in the pathogenesis.

INTRODUCTION

Cryptogenic multifocal ulcerous stenosing enteritis (CMUSE) affects the small bowel exclusively and is characterized by repeated bouts of small bowel obstruction due to strictures and gastrointestinal bleeds (GIBs) due to superficial ulcerations.¹ Chronic nonspecific ulcers of the small intestine (CNSU) is a term recognized by Japanese gastroenterologists that describes a similar disease entity.² It is an extremely rare and underdiagnosed disease. CMUSE is frequently misdiagnosed with other diseases involving the small bowel, especially Crohn's disease.³ Diagnosis is established by pathological evaluation after surgery or by double-balloon enteroscopy or capsule endoscopy.

CASE REPORT

As a teenager in 1982, our patient, now 52 years old, presented with intermittent colicky pain, constipation, and abdominal distension. He also had intermittent bouts of melena, during which his hemoglobin dropped to ~6 g/dL, requiring multiple blood transfusions. There was no history of any nonsteroidal anti-inflammatory drug (NSAID) intake. Multiple gastroduodenoscopies revealed duodenal ulcers, for which proton pump inhibitors were prescribed on regular basis.

These symptoms persisted for 7 years, but during an episode of small bowel obstruction and GIB he underwent a laparotomy at a local hospital where jejunal ulcerations were identified and resection anastomosis was done. Biopsy of the resected specimen showed nonspecific ulcers. After surgery, however, there was no symptomatic relief. He was extensively evaluated during this period. Gastroduodenoscopy, colonoscopy, abdominal computed tomography, and Meckel's scans were all normal.

ACG Case Rep J 2017;4:e44. doi:10.14309/crj.2017.44. Published online: March 15, 2017.

Correspondence: Ayaskanta Singh, Department of Gastroenterology, IMS and SUM Hospital, Bhubaneswar, India (ayaskantice@gmail.com).



Copyright: © 2017 Singh et al. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0>.

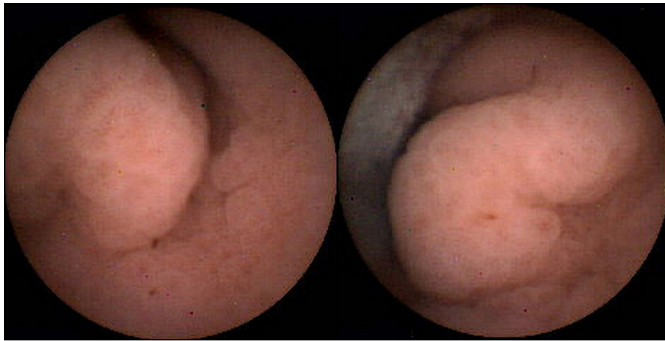


Figure 1. Capsule endoscopy showing superficial jejunal ulcer with stricture.

For the next 10 years, the patient underwent several abdominal surgeries with no clinical improvement. He consulted several gastroenterologists. Barium studies revealed small bowel strictures and ulcerations. Small bowel tuberculosis (TB) was suspected, and antitubercular drugs were given empirically. As the patient didn't respond, Crohn's disease became the leading diagnosis. He received corticosteroids, mesalamine, and azathioprine for a prolonged period. His small bowel symptoms didn't improve, but he developed complications of steroids such as cataracts and uncontrolled diabetes. He also developed features of chronic diarrhea and hypoproteinemia.

Capsule endoscopy showed a stricture along with superficial ulceration of the mucosa in the mid-jejunal area (Figure 1). The capsule became lodged in the stricture and was retrieved using an enteroscope. Diagnostic laparotomy, adhesiolysis,

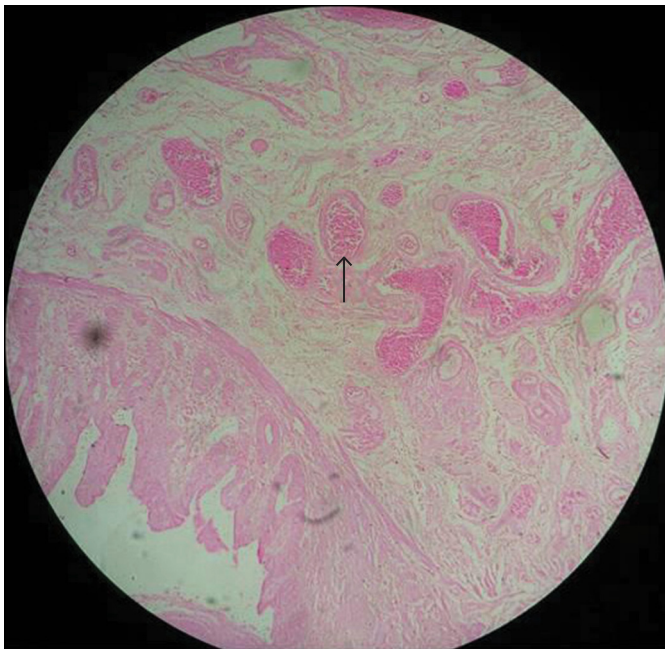


Figure 2. Histology showing superficial mucosal ulcerations, inflammatory infiltrates, and angioectasia (arrow).

on-table enteroscopy, and resection anastomosis of distal ileal segment were performed in 2005. The resected ileal segment showed multiple, superficial, circular and linear ulcers and sharply demarcated ulcers with normal surrounding mucosa. The microscopy showed nonspecific ulcerations and a few angioectasia (Figure 2). The ectasias on pathology did not show any evidence of obliteration or hypertrophy, which is inconsistent with diagnoses of Crohn's disease or TB.

Thus, from the clinical features, endoscopic pictures, and biopsy evaluation, a diagnosis of CMUSE was made. The patient was kept on a nonresidual diet, medium chain triglycerides, high protein, and dietary supplementations. His obstructive symptoms improved and hypoproteinemia was corrected. Periodic GIBs persisted, however, for which he received blood transfusions as before. Five years later, hormonal therapy consisting of ethinyl estradiol and norethisterone successfully addressed his angioectasias stopped his GIBs. For the past 7 years he has been on hormonal therapy and a nonresidual diet, and he is symptom-free. As a complication of hormonal therapy, however, he developed gynecomastia and loss in libido, so the therapy was stopped. The melena reappeared, and the hormonal therapy resumed.

DISCUSSION

Exclusive small bowel disease always poses a diagnostic dilemma as most of the small intestine is not easily assessable. Enteroscopy and capsule endoscopy are uncovering new specific diseases, many of which had been traditionally characterized as Crohn's disease or intestinal TB or NSAIDS enteropathy. CMUSE was first described in 1964.¹ Clinicopathological features of CMUSE have been summarized as unexplained small intestinal strictures found in adolescent and middle-aged subjects, superficial ulceration of the mucosa and submucosa, chronic or relapsing clinical course, a lack of biological signs of systemic inflammatory reaction, and beneficial effect of systemic glucocorticosteroids.

Japanese gastroenterologists, however, who prefer the term CNSU, believe that these patients do not respond to steroid therapy.² This is an extremely rare condition, with approximately 40 cases compatible with CMUSE published worldwide.^{2,4-5} Only 12 cases of CMUSE were reported in France between 1965 and 1993.³ Most of the reported cases have a very prolonged disease course interspersed with relapses and remission, and most of the patients undergo multiple surgeries. Matsumoto et al.² reported a single case of CMUSE followed for 40 years since 1963, and that patient underwent several resections of the small bowel.

Our patient meets the diagnostic criteria for CMUSE/CNSU, but he is unique, however, because of the presence of angioectasia in the histological specimen of the small bowel.⁶ Some suggestions indicate that this disease is a type of

atypical “vasculitis,” although many have refuted this hypothesis.³ Complement (C2) deficiency has been associated with systemic vasculitis and CMUSE.⁷ The genetic basis of the disease was evaluated in a pair of affected siblings, and mutation in the cytosolic phospholipase A2 gene was recognized.⁸ Despite these evidences, the exact pathogenesis is still unclear. We suggest that this patient may represent a variant of CMUSE where vascular lesions (angioectasia) play a role and these patients may respond to hormonal therapy. To our knowledge, this is the first reported case where hormonal therapy has been tried and has been successful in decreasing gastrointestinal blood loss and controlling disease morbidity. The treatment of CMUSE remains symptomatic. Enteral and parenteral nutrition along with iron supplementation have been tried before and are transiently effective.⁹ Our patient responded to nonresidual diet and medium chain triglycerides. The response to corticosteroids is disappointing, and most patients undergo multiple surgeries. In one case, anti-tumor necrosis factor therapy (infliximab) was successful in inducing remission in a steroid-refractory case of CMUSE.¹⁰

In conclusion, not all cases of small bowel disease are Crohn’s disease, TB, or NSAID enteropathy. Although CMUSE is a rare clinical entity, more extensive imaging of the small bowel provided by double-balloon enteroscopy and capsule endoscopy may increase detection and diagnosis. Better understanding regarding the underlying pathology may help identify and treat this condition.

DISCLOSURES

Author contributions: A. Singh collected the data, and wrote and edited the manuscript. MK Sahu collected the data, wrote and edited the manuscript, and is the article guarantor. MK Panigrahi wrote the manuscript and reviewed the literature. D. Misra edited the manuscript.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received November 20, 2016; Accepted February 2, 2017

REFERENCES

1. Debray C, Besancon F, Hardouin JP, Martin E, Marche C, Khoury K. [Cryptogenetic plurifocal ulcerative stenosing enteritis]. *Arch Mal Appar Dig Mal Nutr.* 1964;53:193-206.
2. Matsumoto T, Iida M, Matsui T, Yao T. Chronic nonspecific multiple ulcers of the small intestine: A proposal of the entity from Japanese gastroenterologists to Western enteroscopists. *Gastrointest Endosc.* 2007;66(3 Suppl):S99-S107.
3. Perlemuter G, Guillemin L, Legman P, Weiss L, Couturier D, Chaussade S. Cryptogenetic multifocal ulcerous stenosing enteritis: An atypical type of vasculitis or a disease mimicking vasculitis. *Gut.* 2001;48:333-8.
4. Spencer H, Kitsanta P, Riley S. Cryptogenetic multifocal ulcerous stenosing enteritis. *J R Soc Med.* 2004;97:538-40.
5. Fraile G, Norman F, Reguero ME, Defargues V, Redondo C. Cryptogenetic multifocal ulcerous stenosing enteritis (CMUSE) in a man with a diagnosis of X-linked reticulate pigmentary disorder (PDR). *Scand J Gastroenterol.* 2008;43:506-10.
6. Yao T, Iida M, Matsumoto T. Chronic hemorrhagic ulcers of the small intestine or chronic nonspecific multiple ulcers of the small intestine. In: Yao T, Iida M, editors. *Diseases of the small intestine.* Tokyo: Igaku-Shoin; 2004:176-86.
7. Perlemuter G, Chaussade S, Soubrane O, et al. Multifocal stenosing ulcerations of the small intestine revealing vasculitis associated with C2 deficiency. *Gastroenterology.* 1996;110(5):1628-32.
8. Brooke MA, Longhurst HJ, Plagnol V, et al. Cryptogenetic multifocal ulcerating stenosing enteritis associated with homozygous deletion mutations in cytosolic phospholipase A2- α . *Gut.* 2014;63(1):96-104.
9. Kohoutová D, Bártová J, Tachecí I, Rejchrt S, Repák R, Kopáčková M, Bureš J. Cryptogenetic multifocal ulcerous stenosing enteritis: A review of the literature. *Gastroenterol Res Pract.* 2013;2013:918031.
10. De Schepper H, Macken E, Van Marck V, Spinhoven M, Pelckmans P, Moreels T. Infliximab induces remission in cryptogenetic multifocal ulcerous stenosing enteritis: First case. *World J Gastroenterol.* 2013;19(10):1661-4.