Cryptogenic multifocal ulcerative stenosing enteritis (CMUSE) diagnosed by retrograde motorized spiral enteroscopy

M. Belhassine[1], C. Dragean[2], H. Dano[3], T. G. Moreels[1]

(1) Department of Gastroenterology, Cliniques universitaires Saint Luc, Brussels, Belgium; (2) Department of Radiology, Cliniques universitaires Saint Luc, Brussels, Belgium; (3) Deparment of Anatomopathology, Cliniques universitaires Saint Luc, Brussels, Belgium.

Abstract

We present the case of a 59-years-old woman with a history of abdominal pain and iron-deficiency anemia. Upper and lower gastrointestinal endoscopy turned out negative and further investigation with wireless videocapsule showed an inflammatory stricture in the middle of the small bowel with retention of the videocapsule. Treatment with budesonide was initiated and allowed the spontaneous evacuation of the videocapsule. Retrograde motorized spiral enteroscopy was performed and confirmed an ulcerative stricture 60 cm proximal to the ileocaecal valve. Clinical, iconographic, endoscopic and histological results were compatible with a rare entity described as cryptogenic multifocal ulcerative stenosing enteritis (CMUSE). After the diagnosis budesonide was replaced by azathioprine 100 mg/d as an immunosuppressor. However, azathioprine induced mild pancreatitis and a second course of budesonide was started again. Clinical evolution was favorable. (Acta gastroenterol. belg., **2022,** 85, **527-530**).

Keywords: CMUSE; motorized spiral enteroscopy; inflammatory bowel disease.

Introduction

Ulcerations and strictures of the small bowel are challenging for several reasons. First, the small bowel is a long and tortuous segment of the digestive tract that remains difficult to explore endoscopically. The newly released motorized spiral enteroscope allows deeper enteroscopy as compared to the other available models of device-assisted enteroscopy (1). Secondly, intestinal strictures and ulcerations may correspond to a wide differential diagnosis including Crohn's disease, NSAID-associated enteritis, cytomegaly virus infection, non-Hodgkin lymphoma, tuberculosis and also radiation-induced enteritis. Cryptogenic multifocal ulcerative stenosing enteritis (CMUSE) is a rare pathological finding that has been described recently thanks to new emerging enteroscopy techniques (2). The medical treatment of CMUSE might be challenging and the debate is still ongoing.

Case history

A 59-year-old woman was referred with a long history of postprandial abdominal pain and cramps leading to vomiting. Fasting helped to remain asymptomatic. Stools were normal without signs of rectal blood loss. The medical history was unremarkable: no surgical intervention, no smoking and only sporadic alcohol consumption. She was on lipid-lowering medication and an oral iron supplement. The use of NSAIDs was denied.

Physical examination was unremarkable. Blood analysis revealed iron-deficiency anemia with hemoglobin of 9.5g/dl (N>11,7) and ferritin level 4 mcg/l (N>10). Platelet count was increased to 475000/mm^3 (N 150000-400000) probably secondary to iron deficiency. There was no inflammatory syndrome, no renal impairment and white blood cell count was normal.

Faeces occult blood test turned out positive.

Digestive endoscopic investigation consisting of conventional upper and lower endoscopy was negative and was followed by a wireless videocapsule to exclude occult bleeding in the small bowel.

Wireless videocapsule revealed multiple substenoses at the level of the jejunum and finally the videocapsule remained entrapped at the level of an ulcerative stricture at 5h03 from the ingestion (Figure 1. A).The patient didn't have any obstructive symptom. The diagnosis of videocapsule's retention was made from the stenosis image and the absence of release after 7h30 of recording. Upper gastrointestinal enteroscopy (both simple balloon and motorized) were tried but failed reaching the videocapsule due to jejunal tortuous position. The device was visible on the abdominal X-ray performed during enteroscopy.

A treatment course with low resorption steroids (budesonide) was initiated in order to reduce intestinal inflammation and abdominal X-ray confirmed the expulsion of the videocapsule one month later.

Additional MRI enterography confirmed the presence of an ileal fibrotic stricture extending over 2 cm (Figure 1. B and C). Finally, retrograde motorized spiral enteroscopy was performed in order to obtain biopsies from the stricture. Within 30 minutes after enteroscope insertion, the ileal ulcerative stenosis was reached at 60 cm proximal to the ileocaecal valve, unable to pass

Correspondence to: Maia Belhassine, Cliniques universitaires Saint Luc, Div. Gastro-enterology and Hepatology, Brussels, Belgium.
Email: belhassinemaia@gmail.com

Submission date: 02/07/2021
Acceptance date: 20/07/2021

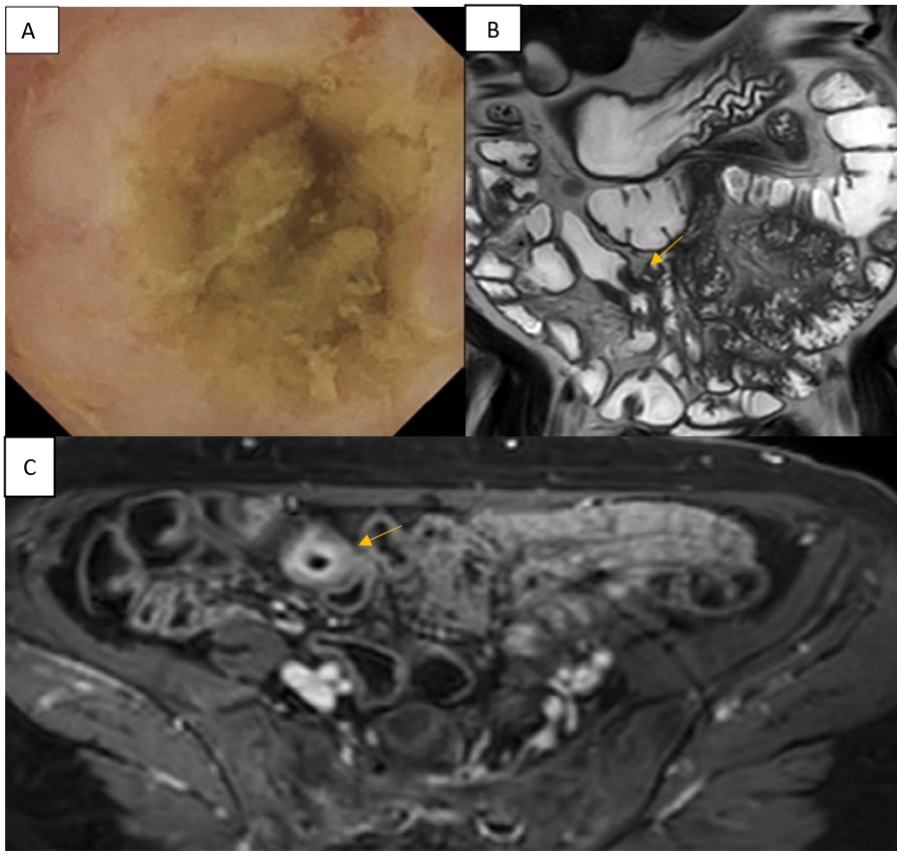

Figure 1. — A: Intestinal stricture retaining the wireless videocapsule. B: Coronal abdominal MRI T2 showing short ileal stenosis (arrow). C: Axial abdominal MRI T1 revealing an inflammatory and fibrotic stricture (arrow).

with the enteroscope. (Figure 2. A, B and C). Biopsies of the stricture identified aspecific superficial inflammatory infiltration with lymphocytes, eosinophils and neutrophils limited to the lamina propria. No virus inclusion, granuloma or vasculitis was identified (Figure 2. D).

Based upon the clinical presentation, radiological and endoscopic findings in the absence of NSAID use nor history of abdominal radiation, the diagnosis of CMUSE was made.

Immunosuppressive therapy with azathioprine was started in a step-up approach and corticosteroids were withdrawn within 6 months.

However, one month later she presented with upper abdominal pain and increased blood lipase levels of 144 UI/L(N<60) with moderate inflammation CRP 83 mg/dl (N<5). Azathioprine-induced pancreatitis was diagnosed and the medication was interrupted. A second course of budesonide was initiated and continued at 3 mg/d with complete clinical remission.

Discussion

Small bowel enteroscopy was revolutionized with the introduction of the wireless videocapsule in 2000 followed by double-balloon enteroscopy in 2003 (3). With the development of the motorized spiral enteroscope, unidirectional total enteroscopy is possible nowadays in a relatively short time and allows a thorough diagnostic and therapeutic investigation of the entire small bowel (1). The use of this new type of enteroscope allowed us to diagnose CMUSE in a patient with a long history of meal-related abdominal pain.

The work-up of small intestinal strictures may be challenging as it encompasses a range of possible diagnoses.

CMUSE is a rare inflammatory pathology of the small bowel characterized by web-like ulcerative strictures without systemic inflammation. Less than 100 cases were published worldwide since it was first describe by Debray et al in the early sixties (4). CMUSE's pathophysiology and etiology remain unclear.

An immune-mediated pathogenesis seems plausible as a clinical response is observed to immunomodulatory treatment but a component of vasculitis also seems involved.

CMUSE's diagnostic criteria proposed by Perlemuter et al. includes unexplained small intestinal strictures found in young and middle-aged adults, superficial ulceration limited to mucosa and submucosa, a chronic or relapsing clinical evolution, no biological evidence of inflammation and a beneficial treatment with steroids

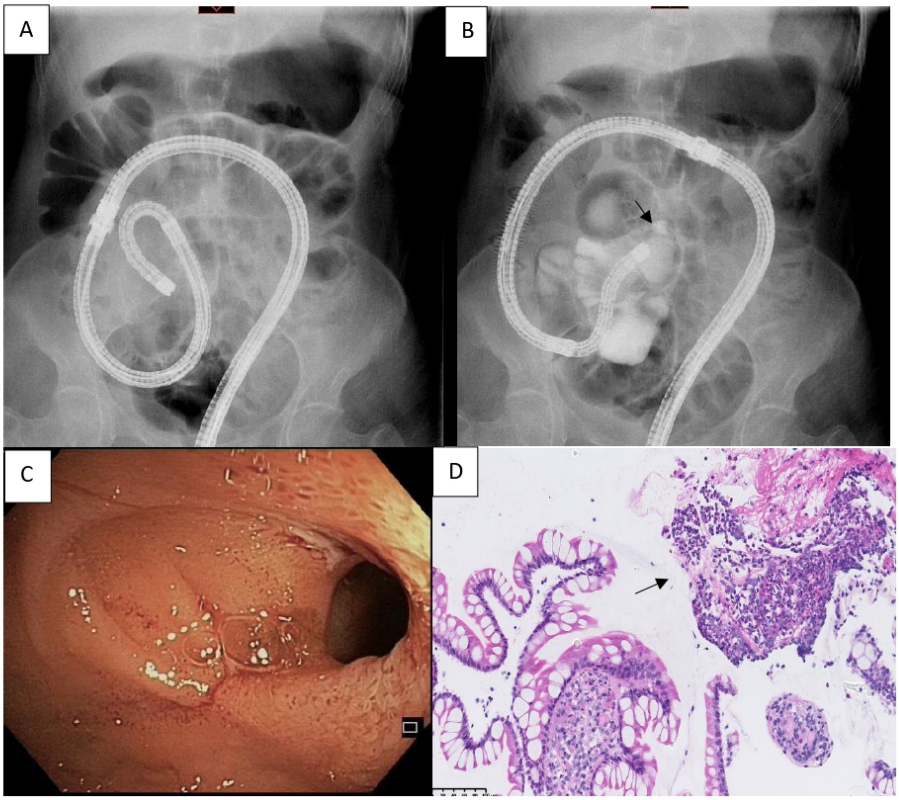

Figure 2. — Hemorrhagic stricture 60 cm above the ileocaecal valve as evidence by fluoroscopic (A and B) and enteroscopic (C) images using the motorized spiral enteroscope. D: Histologic examination (HEX20) with superficial leukocyte fibrinoid membrane (arrow).

(5). The entity is to be differentiated from small bowel Crohn's disease (SBCD).

CMUSE and SBCD are characterized by chronic and relapsing inflammation, with similar digestive symptoms and multiple ulcerations and strictures of the small intestine. Discerning both conditions is challenging but crucial, given that treatment and prognosis of CMUSE differs from SBCD.

Chung et al found out in a Korean retrospective study that 90% of CMUSE patients had been wrongly diagnosed with SBCD (6).

A recent retrospective study identified that hematochezia was more common in CMUSE patients while diarrhea was more prevalent in SBCD patients. Also, patients with CMUSE presented more intestinal strictures and they lack the typical Crohn-related extra-intestinal manifestations. Moreover, intestinal ulcers are superficial and circumferential whereas they are transmural and longitudinal in SBCD (7).

Enteroscopy allows to correctly assess the typical circumferential ulcerative strictures and allows histological examination, while CT and MRI often miss short strictures.

Wireless capsule should be considered carefully as retention may occur, as shown in the current case and was already reported in literature despite prior MRI underestimating the short strictures (8).

Treatment is based on immunosuppressive therapy. CMUSE can respond to glucocorticoid therapy even tough relapse during step-down therapy is frequently observed and corticosteroid dependance may occur (9).

Also the potentially beneficial effect of other immunosuppressive therapy such as azathioprine and anti-TNF-alpha has been reported. A recent case report showed the beneficial effect of anti-TNF -alpha therapy in steroid-refractory CMUSE avoiding surgical resection of small intestine with the risk of short bowel syndrome (10). Endoscopic balloon dilatation of the strictures can be considered but does not provide long term clinical remission (2). While enteroscopy development is rapidly evolving, it occupies a predominant place in the diagnosis and therapeutic approach of CMUSE. Since motorized spiral enteroscopy allows quick deep and even total enteroscopy via an integrated motor which rotates the cover tube that is surrounded with soft spiral-shaped fins softly following the mucosa, it seems a very useful tool to further elucidate the work-up of the rare entity CMUSE.

References

1. BEYNA T., ARVANITAKIS M., SCHNEIDER M., GERGES C., HOELLERICH J., DEVIERE J "et al." Total motorized spiral enteroscopy: first prospective clinical feasibility trial. *Gastrointest Endosc* 2021;**93**:1362-1370.

2. OOMS H., DE SCHEPPER H.U., MOREELS T.G. Case series of Cryptogenic Multifocal Ulcerating Stenosing Enteritis (CMUSE). *Acta Gastroenterol Belg*, 2017; **80**: 361-364.
3. MOREELS T.G. History of endoscopic devices for the exploration of the small bowel. *Acta Gastroenterol Belg,* 2009; **72**: 335-337.
4. DEBRAY C., BESANCON F., HARDOUIN J.P., MARTIN E., MARCHE C., KHOURY K. Cryptogenetic Plurifocal Ulcerative Stenosing Enteritis. *Arch Mal Appar Dig Mal Nutr*, 1964; **53**: 193-206.
5. PERLEMUTER G., CHAUSSADE S., SOUBRANE O., DEGOY A., LOUVEL A., BARBET P *et al.* Multifocal stenosing ulcerations of the small intestine revealing vasculitis associated with C2 deficiency. *Gastroenterology*, 1996; **110**(5): 1628-32.
6. CHUNG S.H., PARK S.U., CHEON J.H., KIM E.R., BYEON J.S., YE B.D *et al.* Clinical Characteristics and Treatment Outcomes of Cryptogenic Multifocal Ulcerous Stenosing Enteritis in Korea. *Dig Dis Sci*, 2015; **60**(9): 2740-5.
7. CHEN D., LIU W., ZHENG W., WU D., QIAN J. Retrospective study of the differential diagnosis between cryptogenic multifocal ulcerous stenosing enteritis and small bowel Crohn's disease. *BMC Gastroenterol*, 2020; 20(1): 252.
8. TACHECI I., RYSKA A., REJCHRT S., KOPACOVA M., HORAVA V., BURES J. Spontaneous disintegration of a retained video capsule in a patient with cryptogenic multifocal ulcerous stenosing enteritis: a rare complication. *Endoscopy*, 2008; **40** Suppl 2: E104-5.
9. KIM C.W., YU C.S., YOON YS., YOON S.N., LIM S.B., KIM JC. Steroid-refractory cryptogenic multifocal ulcerous stenosing enteritis. *Am J Surg,* 2011; **202**(5): e48-51.
10. DE SCHEPPER H., MACKEN E., VAN MARCK V., SPINHOVEN M., PELCKMANS, P., MOREELS, T. Infliximab induces remission in cryptogenic multifocal ulcerous stenosing enteritis: first case. *World J Gastroenterol*, 2013; 19: 1661-1664.