Clinical Case Report

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Crohn's disease mistaken for long-standing idiopathic mesenteric panniculitis

A case report and management algorithm

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Abstract

Background: Mesenteric panniculitis (MP) is mostly an associated sign of an intra-abdominal or systemic inflammatory primary disease. Nevertheless, etiological and differential diagnosis of idiopathic MP can be challenging when an associate primary cause is not in the foreground. Methods: We report here the case of an isolated small bowel Crohn's disease, long time considered as idiopathic MP.

Results: This patient presented to our department with a 10-year history of acute abdominal symptoms evolving with flare-up and remission. A diagnosis of idiopathic MP was made based on compatible CT-scan features along with normal laboratory tests and upper and lower bowel endoscopies. As symptoms recurred, a steroid course was proposed which dramatically improved his condition for years. Finally, an explorative laparoscopy was performed because of concern of malignancy when he returned to our unit with a steroid refractory flare-up and weight loss, along with MP nodes growing up to 10 mm. Crohn's disease was eventually diagnosed, based on histopathological middle-gut bowel resection and numerous granulomas in mesenteric nodes without necrosis.

Conclusion: This case emphasizes the importance of excluding inflammatory intestinal lesions before making the diagnosis of idiopathic MP (fecal calprotectin, magnetic resonance enterography, wireless capsule endoscopy).

Abbreviations: CD = Crohn's disease, CT = computed tomographic, MP = mesenteric panniculitis, MRE = magnetic resonance enterography.

Keywords: case report, Crohn, mesenteric panniculitis, mesenteritis, middle-gut, misty mesentery

1. Introduction

Mesenteric panniculitis (MP) is strictly defined on histological examination. However, it is increasingly suspected on computed tomographic (CT) scan reports and invasive confirmation is useless in most cases. Except infrequently when it arises from a benign idiopathic cause, MP is mostly an associate insignificant sign of an intraabdominal or systemic inflammatory primary disease. Nevertheless, etiological and differential diagnosis of idiopathic MP can be challenging when an associate primary cause is not in the foreground. Especially when abdominal or systemic symptoms are present, diagnostic work up should ensure that a secondary MP is not missed including lymphoma, peritoneal tuberculosis and Crohn's disease (CD). For this latter reason, digestive endoscopies are usually recommended as a diagnostic etiological step.

We describe here a case of isolated small bowel CD long time considered as idiopathic MP, presenting with compatible steroid responsive symptoms and CT-scan features along with confusingly normal upper and lower bowel endoscopies. After a discussion of chronic bowel and mesenteric fat inflammatory diseases pathophysiological similarities, we propose an etiological diagnosis algorithm, which aims at distinguishing idiopathic MP from MP secondary to malignant and nonmalignant conditions, then including screening of mid-gut lesions. This article was written according to CARE guidelines[1] and informed consent was obtained.

2. Case report

2.1. An idiopathic MP diagnosis after a long-standing mild flare ups disease course

A 40-year-old male, nonsmoker patient complained of digestive symptoms since 2000, with intermittent pain in the upper right side of the abdomen (timeline, Fig. 1). His condition evolved with flare-ups followed by periods of remission. Pain flares were associated with mild diarrhea, but no blood, no mucus, and no fever. Repeated laboratory tests including white blood cell count, hemoglobin, platelets, C-reactive protein, aminotransferases, bilirubin, and lipase were within normal limits, as were

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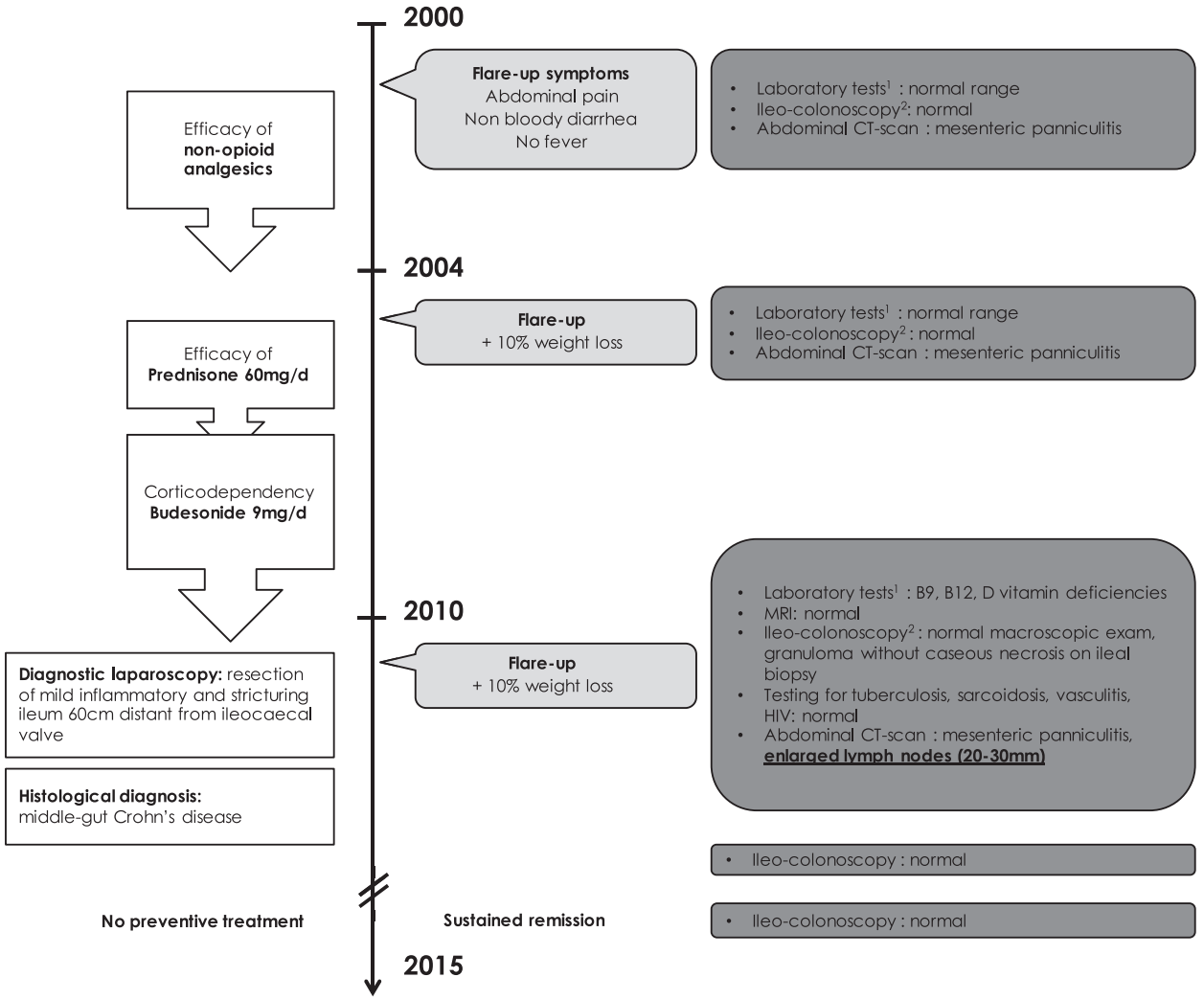

Figure 1. Timeline of symptoms, interventions, and outcome. [1]Laboratory tests include white blood cell count, hemoglobin, platelets, C-reactive protein, aminotransferases, bilirubin, and lipase. [2]Ileo-colonoscopy includes systematic ileal and colonic biopsies. CT = computed tomodensitometry, HIV = human immunodeficiency virus, MRE = magnetic resonance enterography.

colonoscopies with systematic ileum and colonic biopsies. CT-scan found heterogeneous increased attenuation of mesenteric fat (misty mesentery, foggy appearance) surrounding lymph nodes of less than 10 mm (short-axis) and exerting a mass effect on adjacent structures with no invasion of adjacent tissue (Fig. 2) consistent with a diagnosis of MP. After a multidisciplinary discussion and review of the clinical picture, the bowel histology specimens and abdominal CT scans, a diagnosis of idiopathic MP was retained since no sign of inflammatory bowel disease or malignancy had been identified. Nonopioid analgesics were prescribed.

2.2. Steroid dependency

In 2004, the patient had a more severe recurrence with intense abdominal pain and a 10% weight loss in 2 months. Repeated laboratory, endoscopic, and CT findings were similar to the previous scan. Since several steroid responsive idiopathic MP flares have been reported in medical literature and given the worsening of symptoms, the patient was treated with a course of systemic steroids (60 mg per day), which dramatically improved his condition. Faced with a steroid dependency, treatment was then changed to budesonide (9 mg per day), which he continued for several years.

2.3. Concerns of malignancy based on growing nodes

In October 2010, he returned to our gastroenterology unit with a steroid refractory flare-up and weight loss. CT scan retrieved signs consistent with the diagnosis of MP, associated with larger and confluent nodes ranging between 20 and 30 mm in size (Fig. 3). Upper endoscopy and ileo-colonoscopy were normal, but ileum histopathology found a moderate increase of intraepithelial lymphocytes and a granuloma without caseous necrosis. Tuberculin skin test was considered negative and magnetic resonance enterography (MRE) did not find any bowel loop abnormalities. Thus, considering the large size of nodes, an explorative laparoscopy was performed in November 2010 in order to rule out a neoplasm.

2.4. Middle gut Crohn's disease diagnosis reestablishment

Several lymphadenopathies were retrieved in the mesentery as well as a 40 cm mildly inflammatory and stricturing ileum, 60 cm

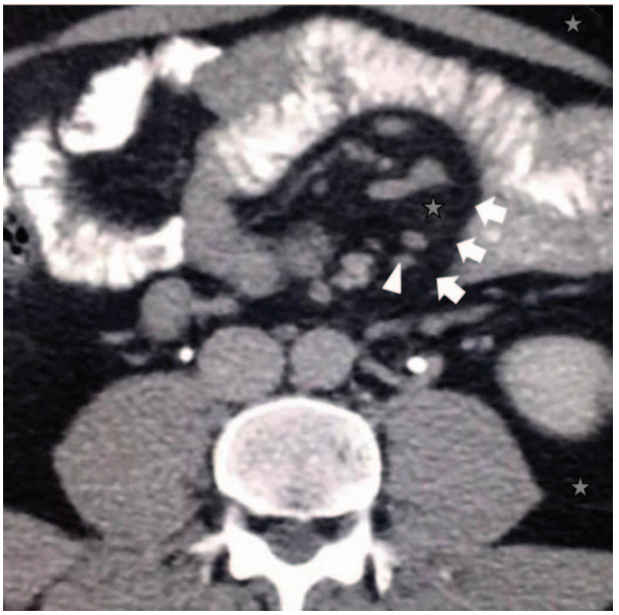

Figure 2. Mild mesenteric panniculitis with subcentimeter nodes. Abdominal computed tomography, axial view. Aspect of mild mesenteric panniculitis: association of hyperattenuation of mesenteric fat (compared to retroperitoneal and subcutaneous fat; gray stars), mass effect on adjacent bowel loops (arrows), subcentimeters lymph nodes (arrowhead).

distant from the ileo-cecal valve (Fig. 4). Near the involved bowel, adjacent signs of fibrofatty mesenteric proliferation and retraction were found. Histopathological analysis found a large, linear, and superficial ulceration associated with crypt abscesses and intervals of normal mucosae in the resected segmental gut, and an epithelioid granuloma in a resected lymph node. These results were consistent with a diagnosis of focal ileum CD revealed by

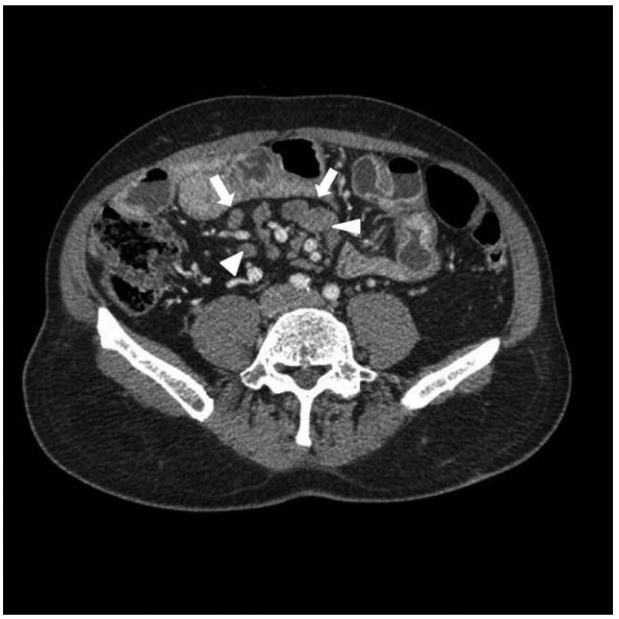

Figure 3. Larger and confluent mesenteric nodes 10 years later. Abdominal computed tomography, axial view. Larger than 10 mm and confluent nodes (arrowheads) into the hyperattenuated mesenteric fat, with mass effect on adjacent bowel (arrows).

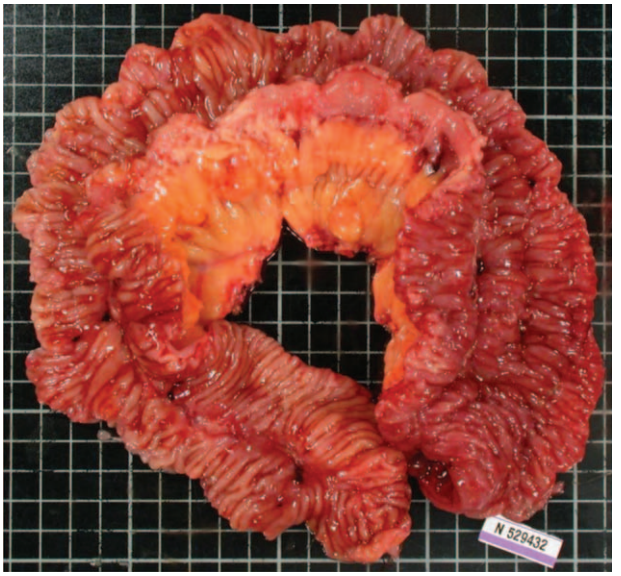

Figure 4. Small bowel resection specimen. The small bowel resection specimen shows multiple mucosal aphthoid ulcerations, some of them responsible for short luminal strictures suggestive of Crohn enteritis.

radiological signs of MP. No medication was introduced after surgery. Ileo-colonoscopies performed at months 6 and 18 were normal. The patient remained asymptomatic with no recurrence of chronic symptoms or flare ups at his last visit in May 2015.

3. Discussion

This case highlights the mesenteric fat features of CD that may mimic MP radiological presentation, reveal the disease, need to rule out middle-gut lesions with a capsule endoscopy on top of MRE, before an idiopathic MP diagnosis. In front of such a clinical case with normal upper and lower endoscopies, fecal calprotectin is a quick and easy test that may help to rule out middle-gut lesions.

To our knowledge, this is the second case of reported association between MP and CD. A first case of CD association with IgG4 sclerosing mesenteritis was recently reported in a 45-year-old Korean patient.[2] Fat abnormalities, especially hypodermal panniculitis (erythema nodosum), are frequently associated features of CD flares. Although it does not reach the radiological and histological criteria for MP, mesenteric fat hyperattenuation is frequently described in tissues nearby inflamed bowel loops.[3] This aspect is related to the mesenteric adipose changes described by Dr Burrill Bernard Crohn as characteristics of the chronic disease to whom he gave his name.[4] Fat hypertrophy, wrapping around inflammatory involved bowel circumference (fat creeping/wrapping sign) is correlated with ulcerations and bowel wall inflammation in CD. Such adipose changes are suspected to be caused by cytokine release from bowel wall and/or adjacent adipose and lymphoid tissue. Indeed, tumor necrosis factor alpha and peroxisome proliferator-activated receptor gamma expression are increased in mesenteric adipocytes adjoining involved inflammatory bowel loops (vs healthy ones), thus suggesting an active role of adipocytokines in the development of intestinal CD lesions, as it is also described in MP.[5]

Idiopathic MP is a rare and benign condition whose diagnosis requires ruling out primary causes, as idiopathic symptomatic

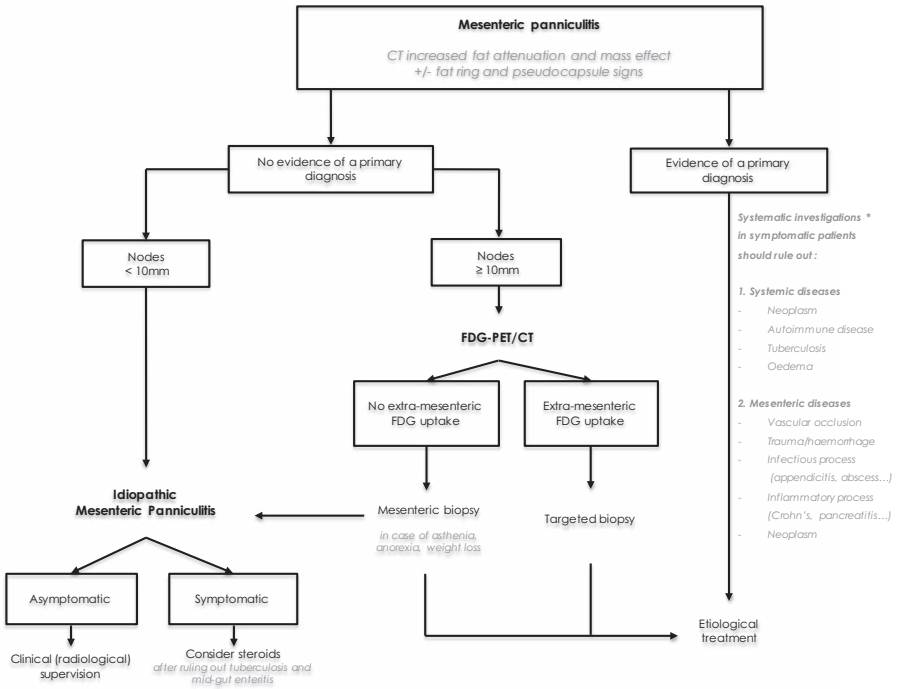

Figure 5. Management algorithm proposal of mesenteric panniculitis. This etiological diagnosis algorithm aims at distinguishing idiopathic MP from MP secondary to malignant and nonmalignant conditions. Systematic investigations are required in symptomatic patients and should rule out mainly lymphoma, tuberculosis, and mid-gut Crohn's disease. *Systematic investigations in symptomatic patients: Clinical examination including skin, peripheral nodes, prostate, and gynecological; full blood count, C-reactive protein, PSA; interferon-gamma release assay or tuberculin skin test; chest x-ray; abdominal contrast-enhanced CT scan review; upper/lower digestive endoscopy (+ fecal calprotectin, MRE and capsule endoscopy in case of normal endoscopies). CT = computed tomodensitometry, MRE = magnetic resonance enterography, PSA = prostate-specific antigen.

cases can report nonspecific abdominal pain or diarrhea as well as fever, abdominal mass, and weight loss. Although MP has a strictly histological definition, suspicious signs are increasingly identified on CT scans and an invasive mesenteric biopsy is unnecessary in most cases since a related primary cause is generally known or easily diagnosed. Thus, MP is now considered as an image-based diagnosis which mostly is regarded as an associate insignificant sign of an intraabdominal or systemic inflammatory primary disease. However, consensus is lacking on the CT definition of MP, leading to confusion toward the disease comprehension and literature analysis. In a recent systematic review, an increased mesenteric fat density (misty mesentery) was the main radiological sign and inclusion criteria in 8 out of 14 studies. A discrete mass effect was reported in 94% cases, when normal fat density halo around nodes or vessels (fat ring sign) and pseudocapsule sign were reported in 64% and 57% of cases.[6,7]

Especially when abdominal or systemic symptoms are present, to differentiate idiopathic MP from other GI or systemic conditions can be challenging. Diagnostic work up should ensure that a secondary MP is not missed including lymphoma, peritoneal tuberculosis, and middle gut CD. In this case report, exclusion of inflammatory bowel disease and tuberculosis relied on a tuberculin skin test and upper/lower GI endoscopies before consideration for steroids and laparoscopy. Fecal calprotectin, MRE and capsule endoscopy have good reported sensitivity and specificity for detecting small bowel CD activity. In this setting however, capsule endoscopy may have a slight increased value in diagnosing superficial lesions in such a location.[8] In our case report, capsule endoscopy was not proposed as MRE was performed once, and fecal calprotectin was not easily available in our center in 2010. In this case report, this may explain why diagnosis was not established before surgery.

Although still debated, recent radiological series of MP indicates a significant association with neoplastic conditions (mostly lymphoma, melanoma, colorectal, and prostate cancers). Such underlying causes should be suspected in the presence of lymph nodes larger than 10 mm (short axis).[9,10] In this case, 18F-FDG-PET/CT can help detect a superficial FDG-up-taking lesion before a more invasive (radioguided or surgical) mesenteric biopsy, although this is generally advised to confirm a diagnosis of malignancy.[11]

This case emphasizes how challenging the etiological diagnosis of MP can be when a primary cause is not in the foreground. In this context, we propose a management algorithm in Fig. 5 to avoid unnecessary explorations and misdiagnosed intraabdominal inflammatory process such as tuberculosis, CD, or malignancies. Especially when upper and lower GI endoscopies are normal, we suggest performing repeated fecal calprotectin test and MRE and/or wireless capsule endoscopy to rule out mid-gut inflammatory lesions before making diagnosis of idiopathic MP.

References

[1] Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case report guideline development. J Clin Epidemiol 2014;67:46–51.
[2] Kim EJ, Kim EY, Song JE, et al. A case of IgG4-related sclerosing mesenteritis associated with Crohn's disease. Korean J Gastroenterol 2014;63:176–82.
[3] Magro F, Langner C, Driessen A, et al. European consensus on the histopathology of inflammatory bowel disease. J Crohns Colitis 2013;7:827–51.

[4] Crohn BB, Ginzburg L, Oppenheimer GD. Landmark article Oct 15, 1932. Regional ileitis. A pathological and clinical entity. By Burril B. Crohn, Leon Ginzburg, and Gordon D. Oppenheimer. JAMA 1984; 251:73–9.
[5] Schaffler A, Scholmerich J, Buchler C. Mechanisms of disease: adipocytokines and visceral adipose tissue—emerging role in intestinal and mesenteric diseases. Nat Clin Pract Gastroenterol Hepatol 2005; 2:103–11.
[6] Halligan S, Plumb A, Taylor S. Mesenteric panniculitis: systematic review of cross-sectional imaging findings and risk of subsequent malignancy. Eur Radiol 2016;DOI: 10.1007/s00330-016-4298-2.
[7] Coulier B. Mesenteric panniculitis. Part 1: MDCT—pictorial review. JBR-BTR 2011;94:229–40.
[8] Jensen MD, Nathan T, Rafaelsen SR, et al. Diagnostic accuracy of capsule endoscopy for small bowel Crohn's disease is superior to that of MR enterography or CT enterography. Clin Gastroenterol Hepatol 2011;9:124–9.
[9] Corwin MT, Smith AJ, Karam AR, et al. Incidentally detected misty mesentery on CT: risk of malignancy correlates with mesenteric lymph node size. J Comput Assist Tomogr 2012;36:26–9.
[10] van Putte-Katier N, van Bommel EF, Elgersma OE, et al. Mesenteric panniculitis: prevalence, clinicoradiological presentation and 5-year follow-up. Br J Radiol 2014;87:20140451.
[11] Nakatani K, Nakamoto Y, Togashi K. FDG-PET/CT assessment of misty mesentery: feasibility for distinguishing viable mesenteric malignancy from stable conditions. Eur J Radiol 2013;82:e380–5.