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Brief Report

BRIEF REPORT

A rare case of epiploic appendagitis in a patient affected by ulcerative colitis on vedolizumab therapy

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Introduction

Epiploic appendagitis (EA) is an acute inflammation of the pedunculated mesenteric fat attached to the colonic surface, distinguished into two forms: primary EA, seemingly elicited by local ischaemic factors; and secondary EA (SEA), elicited by the inflammation of the adjacent organs, with diverticulitis being the most common trigger [1]. Few case series have described the association between SEA and inflammatory bowel disease (IBD); however, information about clinical, laboratory and imaging findings, outcomes, and the impact of IBD-specific therapy were not reported. We first report the case of a woman affected by ulcerative colitis (UC) who developed a SEA during vedolizumab therapy (Figure 1A).

Case presentation

A 64-year-old woman with a 7-year history of extensive UC presented to the outpatient clinic with an acute abdominal pain in the lower left abdominal quadrant, which had started 3 days beforehand and was associated with diarrhoea (five bowel movements/day, Bristol stool scale of 6, blood in trace in <50% of cases) and tenesmus; no other symptoms were associated. Her medical history included breast cancer (successfully treated 5 years earlier), hypertension, type 2 diabetes mellitus, and obesity. She had been receiving vedolizumab for 14 months and was in stable clinical remission up to the previous visit (1 month before); endoscopic assessment 12 months after vedolizumab initiation showed mild endoscopic activity.

The patient presented as severely anxious, diaphoretic, tachycardic, and in pain. Physical examination revealed tenderness of the lower left abdominal quadrant with uncertain rebound tenderness. Laboratory results revealed increased C-reactive protein levels of 14.5 mg/L (normal range < 5 mg/L) and lactic dehydrogenase levels of 583 U/L (<250 U/L). All other values were within the normal range. Urine dipstick test was negative. Infections were ruled out by stool cultures and antigen detection tests. A bowel ultrasound (US) was performed:

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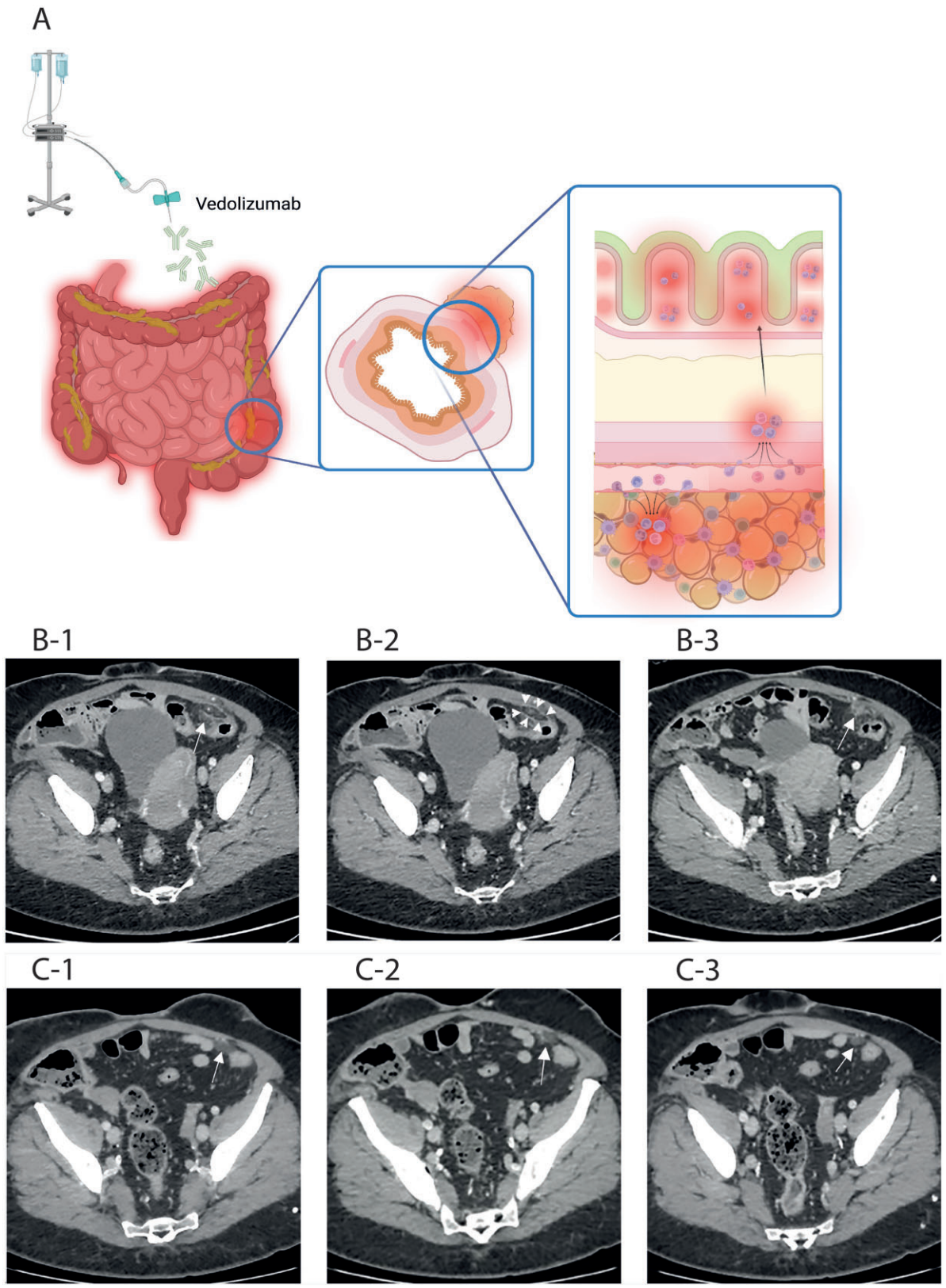

Figure 1. The clinical data of the case. (A) Concomitant presence of epiploic appendagitis and UC flare. Schematic representing the concomitant occurrence of epiploic appendagitis (with immune cell extravasation into the pericolic fat) and UC flare (with immune infiltration of the intestinal mucosa) in a patient receiving vedolizumab therapy. (B) Radiological finding during the florid phase of epiploic appendagitis. Axial contrast-enhanced CT images show an oval area of 3 cm in diameter close to the sigmoid colon. The lesion had a density equal to that of fat (B-1) with a hyperattenuating rim (arrowheads in B-2) and it was surrounded by inflammatory changes (white arrows in B-1 and B-3). A central focal spot of hyperattenuation was observed inside the lesion (asterisk in B-1). (C) Radiological findings during the resolving phase of epiploic appendagitis. Axial contrast-enhanced CT images, 4 weeks after the completion of medical treatment and symptom resolution, display size reduction of the lesion (compared with Figure 1B) with residual soft-tissue attenuation and disappearance of hyperattenuating rim (white arrows).

although the pain elicited by the probe compression and the patient's body habitus limited the examination, a mildly increased thickness of the sigmoid colon wall (6 mm), with normal echogenicity of intestinal layers, and a slight increase in colour Doppler signals were revealed; the surrounding mesenteric perivisceral fat appeared hypertrophic and hyperechogenic; no abscesses or free fluid were identified. To better define the diagnosis, a computed tomography (CT) scan was performed showing an oval area of 3 cm in diameter close to the sigmoid colon whose density was equal to fat, with a hyperattenuating rim and surrounding inflammatory features; a central focal spot of hyperattenuation was observed inside the lesion (Figure 1B). No diverticula were observed. Comprehensively, these signs supported the diagnosis of EA.

Oral ibuprofen (1,200 mg for 7 days) was prescribed for the treatment of SEA in conjunction with a dose optimization of oral mesalamine (4.8 g/day) plus topical mesalamine (1 g/day suppositories) to treat the UC flare. Symptoms progressively improved and fully resolved within the following 2 weeks, accompanied by inflammatory marker normalization.

One month after symptoms resolution, a CT scan was performed revealing a decreased size of the area with residual soft-tissue attenuation and the disappearance of the hyperattenuating rim (Figure 1C). Henceforth, the patient maintained vedolizumab therapy as scheduled, with clinical benefit.

Discussion and conclusion

We report a rare case of SEA associated with an UC relapse, the first to have occurred in a patient receiving vedolizumab therapy. Our patient experienced an UC clinical relapse associated with elevations of inflammatory markers. Since UC flares do not normally present with acute, localized abdominal pain and rebound tenderness, we suspected a concomitant complication or an alternative affection and decided to perform imaging techniques. Bowel US showed inflammatory involvement of the colon and the surrounding mesenteric perivisceral fatty tissue, but a clear diagnosis could not be established. Indeed, even though US is capable of identifying pathognomonic signs of EA [1], the frequent association with visceral obesity often limits its role for the diagnosis [2]. Consequently, CT scan was necessary. Acute diverticulitis was excluded due to the absence of sigmoid diverticula. Omental infarction was considered unlikely because it is most often localized in the lower or upper right quadrants and due to the absence of other predisposing factors. Although omental infarction could have a similar CT appearance, it lacks the hyperattenuating ring typical of EA. Moreover, the main lesion in EA commonly measures <5 cm and is close to the sigmoid colon, while the area of omental infarction is larger and most frequently localized next to the right colon [3, 4]. Imaging findings and clinical criteria pointed towards the diagnosis of SEA, which we treated with ibuprofen; however, given the concomitant bloody diarrhoea (a key finding in UC but normally absent in EA), we believed a concomitant UC relapse was present and treated the patient accordingly.

Over the years, the improvement in clinical awareness and in diagnostic detection of EA has increased the rate of conservative approaches, limiting useless surgery procedures. EA is usually a benign, self-limiting condition, often recovering with medical therapy, mainly non-steroidal anti-inflammatory drugs (NSAIDs) [1]. Despite being generally contraindicated in IBD patients, the lack of alternative medical approaches led us to decide in favour of their use. The simultaneous UC relapse required mesalamine optimization as well.

Two questions arise from our case: Did the colonic inflammation, in an UC patient experiencing a clinical relapse, induce EA, or was EA to induce the UC flare? And in the event that a definite diagnosis would not be obtained, could the optimization of UC therapy alone have induced symptom recovery? Large population studies are needed to investigate whether a meaningful association between EA and IBD relapse exists, and mechanistic studies are required to elucidate the potential ties between these conditions. Mesalamine, exerting a gut-selective anti-inflammatory action [5], could theoretically represent an alternative to NSAIDs for the management of EA, but evidence is lacking.

A conceivable uncertainty exists as to whether and how vedolizumab contributes to the pathophysiology or treatment of EA. Being a gut-selective agent with 'anti-inflammatory' properties [6], vedolizumab might help in the treatment of EA. Vedolizumab prevents lymphocytes homing in on the gut by selectively blocking $\alpha 4\beta 7$-MAdCAM1 interactions [7], but whether these same receptors also mediate lymphocyte extravasation in epiploic appendages is unknown. Vedolizumab effects on T helper type 2 (Th2) and Th17 cells are primarily responsible for reducing mucosal inflammation [8], but actions on other leukocyte subpopulations are also assumed. Accordingly, vedolizumab effects on innate immune [9] and T regulatory cells [10] might potentially play a detrimental role in promoting epiploon inflammation.

The occurrence of EA in an IBD patient is an apparently rare condition, which may be associated with a clinical relapse. Exclusion of other causes using a CT scan is crucial to promptly adapt medical therapies to achieve symptomatic control and resolution of inflammation.

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Conflict of Interest

D.P. received speaker fees and/or advisory board fees from AbbVie, MSD, Takeda, Janssen, and Pfizer. G.P. received consultancy fees from Alphasigma and Janssen. A.A. received consulting and/or advisory board fees from AbbVie, Allergan, Amgen, Arena, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Roche, Samsung Bioepis, Sandoz, and Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Arena, Biogen, Bristol-Myers Squibb, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mitsubishi-Tanabe, Novartis, Pfizer, Roche, Sandoz, Samsung Bioepis, and Takeda; and research grants from MSD, Pfizer, Takeda, and Biogen. The remaining authors declare that there are no conflicts of interest in the study.

References

1. Giannis D, Matenoglou E, Sidiropoulou MS *et al.* Epiploic appendagitis: pathogenesis, clinical findings and imaging clues of a misdiagnosed mimicker. *Ann Transl Med* 2019;**7**:814.
2. Nugent JP, Ouellette HA, O'Leary DP *et al.* Epiploic appendagitis: 7-year experience and relationship with visceral obesity. *Abdom Radiol* 2018;**43**:1552–7.

3. Singh AK, Gervais DA, Hahn PF *et al.* Acute epiploic appendagitis and its mimics. *Radiographics* 2005;**25**:1521–34.
4. Thoeni RF, Cello JP. CT imaging of colitis. *Radiology* 2006;**240**:623–38.
5. Harbord M, Eliakim R, Bettenworth D *et al.*; European Crohn's and Colitis Organisation [ECCO]. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 2: Current management. *J Crohns Colitis* 2017;**11**:769–84.
6. Luzentales-Simpson M, Pang YCF, Zhang A *et al.* Vedolizumab: potential mechanisms of action for reducing pathological inflammation in inflammatory bowel diseases. *Front Cell Dev Biol* 2021;**9**:120.
7. Neurath MF. Targeting immune cell circuits and trafficking in inflammatory bowel disease. *Nat Immunol* 2019;**20**:970–9.
8. Fischer A, Zundler S, Atreya R *et al.* Differential effects of α4β7 and GPR15 on homing of effector and regulatory T cells from patients with UC to the inflamed gut in vivo. *Gut* 2016;**65**:1642–64.
9. Zeissig S, Rosati E, Dowds CM *et al.* Vedolizumab is associated with changes in innate rather than adaptive immunity in patients with inflammatory bowel disease. *Gut* 2019;**68**:25–39.
10. Zhang HL, Zheng YJ, Pan YD *et al.* Regulatory T-cell depletion in the gut caused by integrin β7 deficiency exacerbates DSS colitis by evoking aberrant innate immunity. *Mucosal Immunol* 2016;**9**:391–400.