CASE REPORT

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Colitis Trouble up High: A Case of Gastroduodenal Ulcerative Colitis and Literature Review

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ABSTRACT

Background & Aims: A few cases of upper gastrointestinal (UGI) inflammation in patients with UC have been reported, most commonly post-colectomy. Based on a case presentation we conducted an analysis of the current literature to identify the prevalence, risk factors and current treatment of UGI UC.

Methods: Case report and review of the literature. An electronic search of five bibliographic databases [Pubmed, Cochrane, DOAJ, Science Direct, and JSTOR], was conducted. A combination of keywords and medical subject headings [MeSH] related to "small intestine" and "inflammation" or "enteritis" and "colectomy" or "post operative complications" or "ileostomy" or "stoma" and "ulcerative colitis" or "inflammatory bowel disease" were used. The manuscripts were analysed for age, gender, extent of colonic and UGI disease, timing of UGI presentation, surgical history, treatment and follow-up.

Results: We present the case of a 59-year-old woman with diffuse UGI inflammation associated with ulcerative colitis (UC) that was refractory to steroid treatment, occurring nine years after a panproctocolectomy for medical treatment failure. Upon initiation of an anti-TNFα agent (adalimumab), she achieved remission. We systematically reviewed the literature to analyse previous reports of patients presenting with UGI UC. To date, 43 cases have been published describing UGI UC with a male to female ratio 5:4 with a mean age of 37.52 years. 85.7% of these patients were post-colectomy secondary to pancolitis. The mean time post-colectomy for UGI UC to occur was 14 months (range 0-12 years). The inflammatory distribution affected the duodenum (74%), ileum (57%), jejunum (31%) and stomach (4%). No standardised treatment strategy is available. Only one other case report reported the successful use of adalimumab to attain remission in UGI UC. The prognosis of these patients was generally good.

Conclusions: This review sheds light on a rare presentation of UC. This highlights the need for further research into the pathogenesis of UC and treatment strategies for patients presenting with UGI UC. Our case further strengthens the use of anti-TNFα, particularly adalimumab for UGI UC and highlights the need for further research into the pathogenesis of inflammatory bowel disease.

Key words:upper gastrointestinal ulcerative colitis – post-colectomy enteritis – ulcerative colitis.

Abbreviations: CRP: C reactive protein; EGD: esophagogastroduodenoscopy; GDUC: gastric and duodenal ulcerative colitis; PPI: proton pump inhibitor; TNFα: tumour necrosis factor alpha; UC: ulcerative colitis; UGI: upper gastrointestinal.

INTRODUCTION

Historically, ulcerative colitis (UC) has been regarded as an inflammatory disease of the colon, with the small bowel being involved in cases of backwash ileitis and post-colectomy pre-pouch ileitis or pouchitis [1, 2]. Over the past few years, a number of case reports have been published describing post-colectomy upper gastrointestinal (UGI) manifestations in patients with established UC, namely gastritis and enteritis [2-4]. This can be severe and even fatal [5]. In this report, we present a case of UGI UC refractory to corticosteroids that responded well to anti-tumour necrosis factor alpha (TNFα) drug (adalimumab) treatment. Additionally, a systematic review of the current literature regarding UGI UC will be discussed with an aim to identify prevalence, risk factors for developing UGI UC and current treatment strategies.

CASE REPORT

A 59-year-old woman with pancolonic UC, who underwent a panproctocolectomy with ileal pouch-anal anastomosis nine years prior, presented with a ten-week history of severe, refractory nausea and vomiting, along with a ten-kilogram weight loss.

She was not on any medications; however, she was previously treated with infliximab, azathioprine and corticosteroids prior to the panproctocolectomy. Mild tenderness was observed in the epigastric region along with raised inflammatory markers [C reactive protein (CRP) 42mg/L, (normal values 0-5)] and platelet count.

Initial esophagogastroduodenoscopy (EGD) revealed pangastritis and duodenitis with multiple aphthous ulcers and contact bleeding affecting both the first and second parts of the duodenum (Figs. 1, 2). A flexible lower gastrointestinal endoscopy was also performed and both the pouch and ileum were normal. She was prescribed a proton pump inhibitor (PPI), esomeprazole 40 mg daily. A computed tomography (CT) scan of the abdomen and small bowel was normal. Histological evaluation of the UGI biopsies taken revealed moderately severe active and chronic reactive pangastritis with eosinophilia and erosive inflammation associated with active chronic duodenitis with surface erosive inflammation. No granulomata or *Helicobacter pylori* organisms were identified.

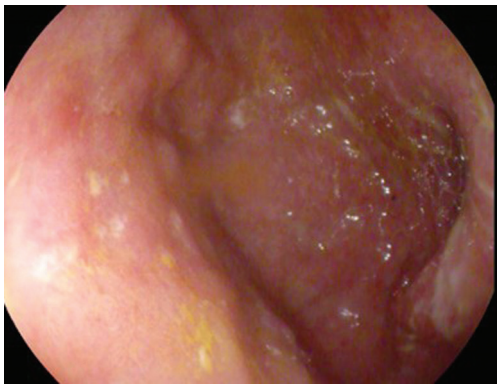

Fig. 1. Endoscopy apperance: Erythema, aphthous ulceration and mucosal oedema in first part of duodenum.

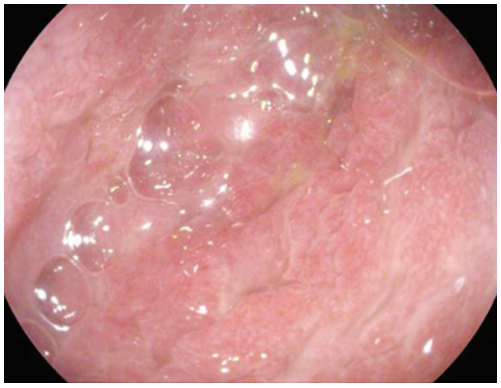

Fig. 2. Endoscopy apperance: Erythema and mucosal oedema in the second part of the duodenum.

Despite receiving high-dose oral PPI, the patient's symptoms persisted, leading to a repeat EGD a few months later which revealed similar macroscopic findings to the previous examination. Histological analysis revealed severe blunting of the villous architecture (Fig. 3) and neutrophilic glandular infiltration associated with a mixed and dense lamina propria inflammatory background (Fig. 4). Extensive ulcerating inflammation was limited to the mucosa. Due to a lack of response to PPI, this was deemed consistent with gastric and duodenal ulcerative colitis (GDUC). In light of these persistent findings, she was started on 40 mg of oral prednisolone, gradually tapered over six weeks. The inflammatory markers returned to normal, her symptoms resolved, and the corticosteroids were subsequently discontinued.

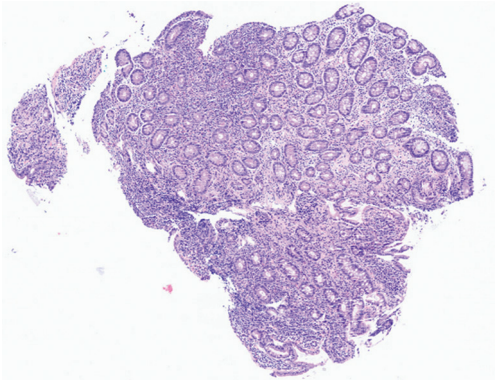

Fig. 3. Histology of the duodenum: blunting of villous architecture and crypt hyperplasia (H&E staining, 50x).

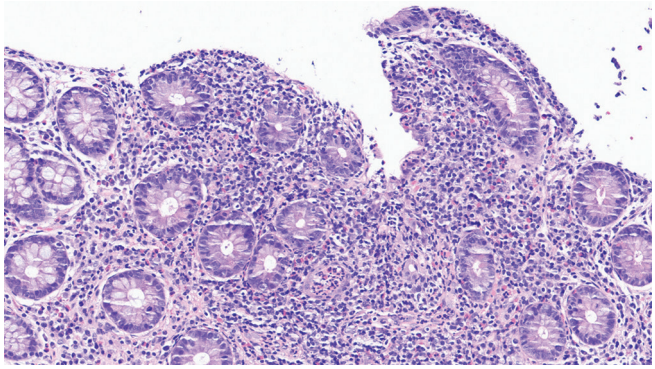

Fig. 4. Histology of the duodenum: Neutrophilic glandular infiltration in keeping with active inflammation, associated with a mixed and dense lamina propria inflammatory background (H&E staining, 200x).

However, a month after stopping the corticosteroid treatment, she experienced a recurrence of symptoms resembling the initial presentation. Repeat EGD showed similar macro- and microscopic findings to the first endoscopy consistent with the presumed GDUC. The patient was re-prescribed a course of oral prednisolone; however, since upon reaching the 10 mg dose symptoms recurred, a decision was made to initiate a steroid-sparing biological agent. Adalimumab, an anti-TNFα drug, was chosen and initiated. Steroids were successfully discontinued following the

induction period of adalimumab treatment, and the patient did not experience a recurrence of symptoms. The patient gained weight and has been symptom free for the past year. Inflammatory markers remain within normal limits.

REVIEW OF THE LITERATURE

Only a few case reports have been published describing such small bowel inflammation in UC. Therefore, an electronic search of five bibliographic databases - Pubmed, Cochrane, DOAJ, Science Direct, and JSTOR - was conducted. A combination of keywords and medical subject headings [MeSH] related to "small intestine" and "inflammation" or "enteritis" and "colectomy" or "post operative complications" or "ileostomy" or "stoma" and "ulcerative colitis" or "inflammatory bowel disease" were used. Referenced papers not published in English were excluded from the study.

Two literature reviews published in 2009 and 2019 were identified, along with three other manuscripts [2, 4, 5, 6, 11]. The full texts were reviewed and data extracted. Referenced papers not fully available in English text were excluded from the study.

The manuscripts were analysed for age, gender, extent of colonic and UGI disease, timing of UGI presentation, surgical history, treatment and follow-up (Table I).

To date, 43 cases have been published describing UGI UC with a male to female ratio 5:4 with a mean age of 37.52 years (IQ range 27 years). The majority (88%) of these patients were post-colectomy secondary to pancolitis, while 9.3% had left-sided disease. The mean time post-colectomy for UGI UC to occur is 14 months (range 0-12 years). The prognosis of these patients was generally good; however, severe complications including haemorrhage, perforation and death have been reported (2, 5). Table II summarises the findings.

The inflammatory distribution affected the duodenum (74%), ileum (57%), jejunum (31%) and stomach (4%). The majority of patients with reported changes in the stomach had a pangastritis pattern, with only one case describing isolated antral inflammation.

In the literature review, 28% of patients were found to be off treatment on follow-up. However, the majority required long-term steroid-sparing agents. Unfortunately, duration of follow-up was not consistently reported. The most frequently described treatments for UGI UC in the literature include intravenous and oral corticosteroids, 5-aminosalicylates (5-ASA), thiopurines and calcineurin-inhibitors, though treatment has not yet been standardised. Other steroid sparing agents, particularly TNFα-inhibitors, have been found to be effective in treating UGI UC, despite probable initial lack of response during the pancolitis phase pre-colectomy (2, 5, 6).

Table I. Summary of cases reported and patient characteristics

Case No.	Gender	Age (years)	Onset of UGI UC post-colectomy if done (days)	Extent of UGI UC	Maximal therapy	Follow-up
1	M	23	14	J, I	CS and Ciclosporin	Off treatment
2	F	61	30	S, D, I	CS	Off treatment
3	M	52	116	D, I	CS	AZA
4	F	29	2,190	A, D	Oral 5-ASA	Oral 5-ASA
5	M	young	4,380	D	Oral 5-ASA	Oral 5-ASA
6	M	46	730	I	CS	Oral 5-ASA
7	M	38	150	D, J	CS and AZA	Off treatment
8	M	31	N/A	D	CS	Off treatment
9	F	30	210	D	CS	Off treatment
10	M	36	3285	D	Oral 5-ASA	Oral 5-ASA
11	F	3	365	D	CS	Off treatment
12	F	17	270	D, J	CS	Off treatment
13	F	58	180	D,J	CS, Ciclosporin, AZA	CS, Ciclosporin, AZA
14	M	17	8	D, I	CS	Off treatment
15	M	37	30	S, J, I	CS	Passed away
16	F	46	N/A	D	Oral 5-ASA, CS	Oral 5-ASA
17	M	17	N/A	S, D	CS, Gammaglobulin	Off treatment
18	M	16	N/A	S, D, J	CS and AZA	AZA
19	F	22	N/A	D, J	CS and AZA	AZA
20	M	31	N/A	D	CS	N/A
21	F	30	13	D	CS	N/A
22	F	51	120	D, I, P	CS	Off treatment
23	M	23	90	S, D, I, P	CS, AZA	AZA
24	F	29	120	S, D, I, P	CS, AZA, Allopurinol, Certolizumab, MTX	AZA, Allopurinol, Certolizumab, MTX

Table I (continued)

25	M	30	810	S, D, I, P	CS, AZA	AZA
26	M	57	810	S,D, I	CS, AZA	AZA
27	F	43	90	S,D, I	CS, Tacrolimus	Tacrolimus
28	M	56	120	D, I, P	CS, AZA	AZA
29	F	56	26	D, I, P	CS	Passed away
30	F	47	120	D, J	CS, Tacrolimus	Tacrolimus
31	M	19	12	S, D, I	CS, IFX	IFX
32	F	25	9	D, J, I, P	CS	N/A
33	M	44	10	D	Oral 5-ASA	Off treatment
34	F	25	N/A	D	CS	Off treatment
35	F	56	90	I	CS, IFX, Ciclosporin, USM	USM
36	F	25	28	S, J, I	IFX GCV	IFX
37	F	65	90	S, J, I	IFX + GCV	IFX
38	M	45	248	S, I	IFX	IFX
39	M	55	25	J, I	GLM	GLM
40	M	25	34	S, J, I	IFX	IFX
41	M	55	33	S, I	GLM	GLM
42	M	85	12	S, I	IFX	IFX
43	M	20	None	I	Oral 5-ASA, CS	ADA, 6-MP

J: jejunum; I: ileum; S: stomach; D: duodenum; P: pouch; CS: corticosteroids; 5-ASA: 5-aminosalicylate; AZA: azathioprine; MTX: methotrexate, IFX: infliximab; USM: ustekinumab; GLM: golimumab; GCV: ganciclovir; ADA: adalimumab, 6-MP: 6-mercaptopurine; N/A: not available.

This can be observed in our case, as our patient responded well to adalimumab. TNFα-inhibitors may, in fact, be the first treatment of choice as reported in the study carried out by Horio Y et al. [6] where all seven patients with UGI UC treated with infliximab or golimumab responded well. Ustekinumab may also be an option for those failing infliximab as described by Guo C et al in a case report published in 2024 [7].

Additionally, two patients were noted to have passed away. Notably, one died from disseminated intravascular coagulation and multi-organ failure secondary to sepsis and the other from recurrence of cancer and peritoneal dissemination [2, 12].

DISCUSSION

To date, apart from our patient discussed above, only one reported case of GDUC has shown successful treatment outcomes with adalimumab. In this case, adalimumab was combined with 6-mercaptopurine and the patient, although presenting with pancolitis, did not need surgical intervention [11].

UC has traditionally been considered a disease primarily affecting the colorectum. However, emerging evidence suggests a shift in this perspective. While the involvement of the terminal ileum, known as "backwash ileitis," has been well-documented, the association of UC with the rest of the small bowel has not been widely recognized [7].

The association between UGI involvement and UC may often go unnoticed due to the limited availability of literature describing this connection. Initially, the clinical suspicion may be Crohn's disease. This is further compounded by the fact that patients with UGI UC typically present with common symptoms such as dyspepsia, abdominal pain, high output ileostomy, nausea, and vomiting [2, 3]. Moreover, the lack of established criteria for diagnosing UGI UC increases this diagnostic challenge.

Characteristic findings indicative of UGI UC include diffuse superficial erosions and granular changes affecting both the stomach and the small bowel. Histologically, these lesions demonstrate inflammatory cell infiltration and the

Table II. Features which may help distinguish between Crohn's disease and ulcerative colitis

Endoscopic findings	Crohn's disease	Ulcerative folitis
	Deep linear/serpentine ulcers/erosions	Erythema & granularity
	Nodularity	Mucosal friability
	Fistulas/Strictures	Aphthous erosions
Histopathological findings	Granulomas	Variable neutrophilic and eosinophilic infiltration in the lamina propria
	Focal cryptitis	Cryptitis and crypt abscesses
		Diffuse mucosal lymphoplasmacytic infiltration

presence of crypt abscesses, resembling the patterns observed in colonic UC [2, 3, 8]. Table II illustrates endoscopic and histological features that help in differentiating between CD and UC [9].

When diagnosing UGI UC, it is crucial to exclude other potential causes of widespread enteritis, such as ischemia, infections (particularly cytomegalovirus and *Helicobacter pylori*), drug-induced reactions (especially non-steroidal anti-inflammatories), and immunological factors (such as coeliac disease) [1, 10].

The underlying pathogenesis and triggers of UGI UC remain unknown. It is hypothesised that the occurrence of UGI involvement may be related to changes in bacterial exposure and inflammatory mediators post-surgery [4, 10], but further research is required to establish and comprehend this association. In addition, Hori et al. [6] highlighted that inflammation associated with UC might not be limited to the colorectum alone. They emphasised that UGI involvement could potentially go unnoticed due to the presence of active pancolitis and the use of medications aimed at treating colonic UC [6]. Given these findings, it raises the question of whether an EGD should be considered for all patients at the time of diagnosis, especially in those who have upper gastrointestinal symptoms, an approach that is now recommended for CD patients [11].

Anti-TNFα drugs, particularly infliximab and adalimumab, should be considered early in patients presenting with UGI UC. This prevents prolongation of symptomatology, significant side-effects from repeated courses of corticosteroids or from drugs such as thiopurines, avoidance of polypharmacy and achievement of remission without having to move from one drug to the next, something which could be seen in some previous case reports.

CONCLUSIONS

The occurrence of UGI UC draws attention to a significant gap in our understanding of the pathogenesis of not only UC but also IBD in general. Although various medications have been employed in the management of UGI UC, the treatment algorithm and follow-up protocols remain poorly defined. Further research is necessary to elucidate the factors and changes leading to these conditions, including the interplay between the initial microbiome, its alterations post-surgery, and its interaction with the patient's immunological and genetic makeup. This case also underscores the importance of patient and physician awareness regarding these potential scenarios, both during the pre-colectomy consent process and for patients who develop symptoms post-colectomy. Consequently, this case provides valuable additional insights into the successful management of this condition through subcutaneous treatment, offering a potentially more convenient option for patients.

Conflicts of interest: None to declare.

Authors' contribution: S.C. collected the data for the work and initially drafted the manuscript. F.V. collected the data for the manuscript. M.S. and P.E. revised the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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