Gastrointestinal Tract

ORIGINAL ARTICLE

Multi-modal conservative management of intra-abdominal collections in fistulising Crohn's disease

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ABSTRACT

Background and Objectives: The management of intra-abdominal collections in fistulising Crohn's disease (CD) has traditionally involved surgery. However, conservative management is a potential alternative. In this study, we report our experience with multi-modal conservative management of intra-abdominal collections secondary to perforating CD. **Methods:** Medical records of CD patients with a history of intra-abdominal collections or fistulas over the past five years were reviewed retrospectively. Patients were included if they were initially managed conservatively using any combination of antibiotics, exclusive enteral nutrition (EEN), percutaneous drainage of collections, endoscopic dilatation of associated strictures and medical therapy for IBD with steroids, immunomodulators and/or biologics. **Results:** Eleven participants were included. All participants had penetrating CD affecting the terminal ileum. Nine participants had intra-abdominal collection on cross-sectional imaging whilst the remaining two participants had fistulising disease and sepsis without a discrete collection. Eight participants completed a 6–8 weeks course of EEN. All participants were treated with antibiotics and a thiopurine. Steroids were used in eight participants and biological agents in six. Six participants underwent endoscopic dilatation of small bowel strictures. After a median follow up of 20 months [range: 3–210] nine participants had evidence of adequate clinical, biochemical, radiological and endoscopic improvement. Complete resolution of abscess was seen in 4/7 participants and a significant reduction in abscess size was seen in 2/7. Two participants had complete endoscopic and histological remission and complete resolution of abscess. Both participants with fistulising disease (without a collection) had evidence of healed fistula tract on progress imaging and endoscopy. Two participants underwent surgery after failure of initial conservative management. **Conclusion:** Intra-abdominal collections in fistulising CD can be managed successfully in appropriately selected patients using a multi-modal approach incorporating antibiotics, EEN, endoscopic dilatations of culprit strictures and optimised medical management using steroids (for induction of remission), immunomodulators and biologics.

Key words: Crohn's disease, inflammatory bowel disease, intra-abdominal collection, intra-abdominal abscess, fistulising Crohn's disease, conservative management, exclusive enteral nutrition, biologics

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Received: 30 October 2023; Revised: 15 December 2023; Accepted: 18 December 2023
https://doi.org/10.54844/git.2023.481

INTRODUCTION

Intra-abdominal collections +/- sepsis are a common complication of fistulising Crohn's disease (CD) with 7%–34% of patients affected during the course of their illness.[1,2] Fistula formation is a consequence of active chronic inflammation in patients with inadequately controlled Crohn's disease, often in the context of associated strictures. Chronic inflammation leads to epithelial injury which subsequently results in differentiation of intra-epithelial cell into mesenchymal-like cells. These cells have the potential to migrate and form fistula tracts and result in extra-luminal collections.[3] The terminal ileum is the most commonly affected site, with such patients often presenting with right iliac fossa pain as well as fevers.[4]

Percutaneous drainage and surgery are the current mainstay of therapy in CD patients with intra-abdominal collection. Whilst percutaneous drainage is less invasive than surgery, studies have shown that a high percentage of patients will subsequently require surgical intervention. A meta-analysis of 6 studies including 333 patients has shown that up to 70% of patients who underwent percutaneous drainage ultimately required surgery.[5] Surgery after successful non-operative management (*i.e.*, antibiotics +/- percutaneous drainage) has been shown to provide good long-term outcomes.[6] On the other hand, Lee *et al.* reported successful outcome in two third of patients using a combination of antibiotics and steroids without the need for invasive interventions.[7]

Treatment of the underlying inflammation is important in preventing ongoing epithelial injury which is a driver of fistula formation and micro-perforation. Another important driver of perforating complications in CD patients is stricture formation due to fibro-stenosis. Endoscopic treatment has been shown to be safe and effective.[3] Endoscopic balloon dilatation has a clinical efficacy rate of 88% and a complication rate of 2.8%.[6]

In view of the pathogenesis of fistulising CD and the fact that ongoing active chronic inflammation and strictures are major drivers of fistula formation and perforation, optimal management requires a comprehensive approach treating infection, addressing inflammation, stricture management as well as enhancing patients' nutritional status. Here, we report our experience using a multi-modal conservative approach to manage complicated perforating disease using antibiotics, exclusive enteral nutrition (EEN) and percutaneous drainage in the acute phase of sepsis followed by immunomodulators, biologics and endoscopic intervention after resolution of sepsis.

METHODS

Case records of all patients undergoing treatment for IBD at Concord Repatriation General Hospital between 2017 and 2022 were reviewed. Patients were included if they had a confirmed diagnosis of CD, had evidence of intra-abdominal collection and/or fistulisation on cross sectional imaging, and were initially managed conservatively. Patients were excluded if they were planned for surgical intervention at index presentation. Patients were treated with broad-spectrum antibiotics with gram negative and anaerobic cover. EEN diet was used for a duration of 6–8 weeks. Steroids, immunomodulators and / or biological agents were used after adequate control of infection (defined as resolution of the systemic manifestations of sepsis and decrease in inflammatory markers +/- reduction in abscess size). Endoscopic balloon dilatation was performed in patients with culprit strictures.

Blood tests including inflammatory markers, albumin, and electrolytes were performed daily or every second day for inpatients. Patients also had blood tests on routine outpatient follow-up. Magnetic resonance enterography (MRE), computed tomography (CT) scan, or intestinal US (IUS) was performed to monitor response to treatment. Patients were closely followed up by a dietitian whilst on EEN diet.

Data on disease characteristics, efficacy, safety, and demographics were collected retrospectively from patients' medical records. Continuous variables were reported as the median and the inter-quartile range (IQR) and categorical variables as the number (percent). Treatment failure was defined as persistence or recurrence of abscess requiring surgical intervention.

RESULTS

Eleven participants were identified (Table 1 and Table 2). Participants were predominantly male (90%) with a median age of 23 years (IQR 7) and median disease duration of three years (IQR 5). All participants had penetrating CD affecting the terminal ileum. Nine participants (82%) had intra-abdominal collection on cross-sectional imaging whilst the remaining two participants had fistulising disease and sepsis without a discrete collection. Two participants had multiple abscesses while the rest of the participants had a solitary abscess. The median collection size was 4.4 cm (SD 2.6) in largest dimension. 7/11 participants had a new diagnosis of CD while the remaining four had known CD at the time of presentation.

EEN was offered to 9/11 participants. Eight participants were compliant with a 6–8 weeks course of EEN. One participant discontinued EEN after 1–2 weeks due to intolerance. All participants were treated

Table 1: Patient characteristics

Patient characteristics	Total number of patients = 11	
Male gender	10	
Median age [IQR]	23 [7]	
Race		
Caucasian	7	
Asian	4	
Median disease duration [IQR]	3 years [5]	
Fistula without collection	2	
Multiple collections	2	
Median collection size (cm) [+/- SD]	4.4 (+/- 2.6)	
	Before presentation with abscess/fistula	After presentation with abscess/fistula
Thiopurine use (total = 11)	2	11
Tioguanine	0	7
Azathioprine	1	3
[6-mercaptopurine	1	1
Biologic therapy (total = 6)	2	6
Vedolizumab	0	2
Ustekinumab	0	3
Infliximab	0	1
Adalimumab	2	0

SD: standard deviation; cm: centimetre; IQR: interquartile range

with a 10–14 day course of an antibiotic regimen consisting of ceftriaxone and metronidazole or amoxycillin and clavulanic acid. Participants were treated with three to seven days of intravenous antibiotics before switching to an equivalent oral agent. Upon resolution of sepsis, all participants were commenced on a thiopurine. Tioguanine was the most commonly used thiopurine (7/11). Corticosteroids were used in 8/11 participants. Thiopurines and steroids were only commenced after it was deemed safe from infection perspective (*i.e.*, after resolution of all systemic features of sepsis such as fever and tachycardia and a decrease in serum inflammatory markers). Two participants were on anti-TNF agent (adalimumab) prior to presentation with abscess/fistula. However, after presentation with abscess or fistula these patients were switched to a different biologic (ustekinumab and vedolizumab). In total, six participants were on biological agents including ustekinumab (N = 3), vedolizumab (N = 2), and infliximab (N = 1) after presentation with abscess or fistula. Six participants underwent endoscopic dilatation of associated small bowel strictures. One participant underwent three dilatations of a terminal ileal stricture to 16 mm, 18 mm and 20 mm; one participant had three terminal ileal strictures dilated to 15 and 18 mm and subsequently had a repeat dilatation of two strictures to 15 mm. Another participant had two dilatations of a stricture to 15 mm and 18 mm. The remaining three participants required a single dilatation, one to 15 mm and remaining two to 15 mm and 20 mm.

After a median follow up duration of 20 months (range: 3–210), all participants achieved clinical and biochemical improvement with conservative management however two participants ultimately underwent surgical resection (Table 2). The remaining nine participants were managed conservatively. Complete resolution of abscess on progress imaging was seen in 4/7 participants and a significant reduction in abscess size was seen in 2/7. One participant did not have progress imaging but there was clinical and biochemical resolution of sepsis. None of these participants underwent percutaneous drainage. Endoscopic and histological improvement was seen in all participants who underwent repeat endoscopy (N = 7). Two participants had complete endoscopic and histological remission as well as complete resolution of abscess on imaging (Figure 1 and Figure 2). Both participants with fistulising disease without a discreet collection had an excellent response to conservative management with progress MRE and colonoscopy which showed no evidence of an active fistula tract. In terms of reasons for undergoing surgery, one participant had recurrent intra-abdominal collections after initial conservative management (including percutaneous drainage) however his management was significantly compromised by poor adherence to medical therapy and follow up. The second participant re-presented with a large abscess after initial conservative management of a small collection. He underwent percutaneous drainage and medical optimisation before undergoing a right hemi-colectomy.

DISCUSSION

Fistulising CD can lead to small bowel perforation and intra-abdominal abscesses which can result in life-

Table 2: Case by case summary of pre-intervention findings, treatment, and post-intervention patient outcomes

Age	Sex	Disease duration (years)	CRP	Radiological findings	Baseline endoscopic findings	Histology	Treatment						Outcomes			
							Abx	Steroids	EEN	Thiopurine	Biologic	dilatation	CRP	Radiological	Endoscopic	Histologic
28	M	7	32	CT scan: Thickening of TI; abscess in RIF measuring 4.6 × 2.3 × 3.7 cm	2 cm narrowed segment in TI with a 5 mm ulcer; 2 small erosions; no fistula	TI: Inflamed granulation tissue otherwise normal	Yes	Yes	No	Yes	No	No	2	MRE after 2 years: Complete resolution of abscess; mild active TI inflammation	Colonoscopy: 2 small ileal erosions; no stricture or fistula	Mild focal active terminal ileitis
21	M	1	102	Extensive inflammatory change in the RIF involving the proximal ascending colon, caecum, and terminal ileum; small abscess in the right iliac fossa	Moderate terminal ileitis of a 10 cm segment; ICV stricture; CRE balloon dilation from 8 to 18 mm	Mild active inflammation in TI	Yes	Yes	Yes	Yes	No	3 dilatations from 8 to 20 mm	1.3	MRE after one month: Severe ileocolic inflammation (modified MARIA 5) involving 12 cm of TI and 3.5 cm of caecum; fixed TI luminal narrowing; fistula between TI and caecum; resolved abscess	Colonoscopy at 3 months: Partially obstructing ICV stricture, dilated to 20mm; mild distal terminal ileitis SES CD 4	Moderate active inflammation
23	M	1	146	Mural thickening of a 50 cm segment of TI and distal ileum (simplified MARIA 5); multiloculated abscess in distal ileum measuring 3 × 4.7 cm; no stricture	N/A (First colonoscopy was performed 3 months after presentation)	N/A	Yes	No	Yes	Yes	No	No	5	MRE at 8 months: complete resolution of distal ileal abscess; mild active inflammation from TI to mid ileum (simplified MARIA 1)	Normal TI and distal ileum; normal colon	No abnormality
19	M	6	230	CT scan: concentric mural thickening of a 30 segment of TI; 4.2 × 3 × 3.4 cm abscess in RIF near the TI; a second collection at the roof of the bladder measuring 2 × 2.2 × 2.6 cm; no stricture	Moderate stricture in TI with superficial ulceration; dilated to 18, 19 and 20 mm	N/A	Yes	No	Yes	Yes	Yes	One dilatation to 20 mm	34	IUS after one month: Ongoing mural thickening of the distal ileum and TI; significant reduction in size of RIF abscess and some reduction in size of the second abscess at the roof of the bladder	Mild ileitis, mild luminal narrowing (SES CD 5)	Moderate active chronic terminal ileitis
20	M	2	120	Moderate to severe circumferential mural thickening of 23 cm of TI and distal ileum; entero-vesical, entero-enteric and entero-cutaneous fistulae; RIF collection 4 × 3.5 cm	N/A	N/A	Yes	Yes	Yes	Yes	Yes	No	22	N/a	N/A	N/A
38	M	11	3.4	Extensive inflammation involving 30–40 cm	N/A	Acute ileitis, acute proctitis	Yes	No	No	Yes	Yes	No	1.5	MRE at 3 years: No collection; mild	Colonoscopy at 1 year: Ileocolonic	Histological remission

				segment of TI and distal ileum with entero-enteric fistula and × 3 contained collection Inflammation in ascending and sigmoid colon										residual inflammation in TI; healed ileo-sigmoid fistula	Crohn's disease in remission; inactive ileo-sigmoid fistula	
27	F	5	38	Inflammation of 10 cm terminal ileum and jejunum; enteroenteric fistula	Terminal ileitis	Patchy active inflammation in TI	Yes	Yes	Yes	Yes	Yes	No	3	MRE after one year: Mild terminal ileitis; simplified MARIA 5; tethering of TI and ileal loops; no active disease elsewhere	Endoscopic remission;. no active colitis or ileitis	N/A
19	M	2	155	Severe terminal ileitis and distal ileitis; enteroenteric fistula in the right lower quadrant	Severe inflammation of the ICV with associated stricture; dilated to 15mm; ICV fistula	Moderate terminal ileitis with ulceration	Yes	Yes	No	Yes	Yes	Two dilatations to 15 mm and 20 mm	5	MRE after two years: Significantly improved; sMARIA: 1; no active inflammation; no fistula	Terminal ileal stricture with ulceration. Stricture dilated to 18mm. No fistula opening	Mild terminal ileal inflammation
22	M	1 year	136	30 cm segment of inflamed distal ileum and TI; possible ileocolic fistula. 4.4 × 3 × 2 cm pelvic abscess	Severe stricturing and fistulising Crohn's disease of 10 cm distal ileum; dilated to 15mm; SES CD score 9; ileosigmoid fistula	Active chronic ileitis with ulceration	Yes	Yes	Yes	Yes	No	One dilatation to 15 mm	4	MRE after 1 month: improved but persistent terminal ileitis to 20 cm; significant reduction in size of pelvic abscess to 1.5 × 0.8 × 2 cm; simplified MARIA 4	Mild ileitis with mild stricture not requiring dilatation; SES CD score 4; possible uninflamed ileosigmoid fistula; no active colitis	Mild terminal ileitis; mild colitis of the left colon
25	M	3 years	167	CT scan: 20–30 cm of terminal ileitis with an abscess measuring 4 × 4.5 × 3 cm within the associated mesentery	Severe terminal ileitis (SES CD 9); normal colon	Active chronic inflammation in the TI	Yes	Yes	Yes	AZA	No (Ustekinumab after surgery)	3 strictures dilated to 15 and 18 mm	10	CT scan after two years: Long segment chronic terminal ileitis; right psoas abscess measuring 4.7 × 11 × 4.4 with associated fistula tract	Underwent ileocolic resection after trial of conservative management; initially managed conservatively in October 2021 with recurrence of collection in April 2022 requiring IR drainage and antibiotic therapy before having surgery in July 2022	
55	M	16 years	205	CT July 2022: terminal ileitis; adjacent large collection 10 × 9.7 × 7.7 abutting the bladder dome and inferiorly adhered to abdominal wall	Stricturing distal TI dilated to 15mm; severe ileitis with ulceration in mid TI	Active chronic colitis on ICV bx	Yes	Yes	Yes	TG	Yes	TI stricture dilated to 15 mm	9	US 2 days after percutaneous drainage: significant decrease in abscess size: 3.5 × 5.3 × 1.9	Underwent ileocolic resection after trial of conservative management for 2 months	

Abx: antibiotics; CRP: C-reactive protein; EEN: exclusive enteral nutrition; MRE: magnetic resonance enterography; RIF: right iliac fossa; SES CD: simple endoscopic score for Crohn's disease; TI: terminal ileum

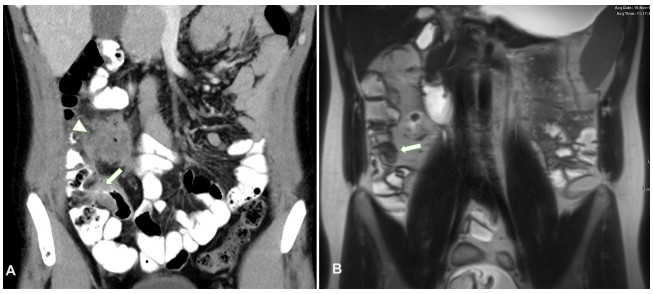

Figure 1. Thickening in the terminal ileum. **A**. Coronal CT with oral and IV contrast demonstrating thickening in the terminal ileum (white arrow) and an abscess superior to it (white arrowhead) from penetrating disease. **B** . MRI coronal T2 weighted sequence 2 years later demonstrating the thickening in the terminal ileum is significantly reduced (white arrow) and there is complete resolution of the previously demonstrated abscess. CT: computerized tomography; MRI: magnetic resonance imaging.

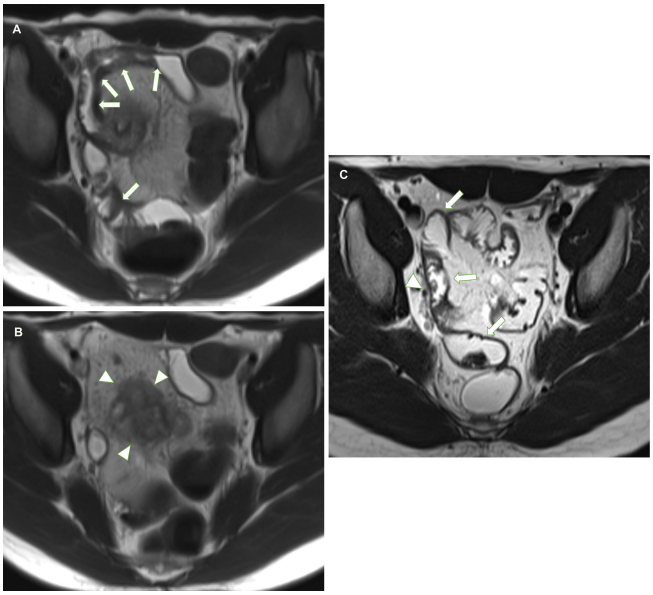

Figure 2. Thickening in multiple loops of distal ileum. **A**. MRI axial T2 weighted sequence showing thickening in multiple loops of distal ileum (white arrows), in one loop clearly more pronounced on the mesenteric side of the bowel wall, characteristic for Crohn's disease. **B**. MRI axial T2 weighted sequence demonstrating a pelvic abscess, just superior to the thickened distal ileal loops (white arrowheads). **C**. 21 months later, MRI axial T2 weighted sequence demonstrating complete resolution of the pelvic abscess. Many of the previously thickened distal loops are now normal (white arrows). MRI: magnetic resonance imaging.

threatening sepsis. Surgery was the mainstay of therapy in the past however non-invasive methods have gained attention in recent times as studies demonstrate positive outcomes.[6,7] The European Crohn's and Colitis Organisation (ECCO) recommends percutaneous image-guided drainage of well-defined abscesses as the primary approach in managing intra-abdominal collections in CD as antibiotic therapy alone may be insufficient to treat large abscesses. These guidelines also support conservative management without surgery following successful percutaneous drainage although a low threshold for surgery is recommended in the event of failure of medical management.[8] In addition, initial conservative management may be associated with less complicated surgery and reduction in resected bowel as well as better long-term outcomes in patients who subsequently require surgery.[6] In our study, 10 out of 11 participants achieved clinical and biochemical +/- radiological and endoscopic improvement with conservative treatment although two patients eventually required surgical intervention. Six out of ten patients had complete resolution of abscess or fistula tract on progress imaging. This includes patients with abscess size > 4 cm. Overall, 9 out of 11 patients avoided surgery to a median follow up of 20 months. Our findings are consistent with previous studies which have shown that medical management is an effective strategy in managing patients with perforating Crohn's disease.[7,9,10] Our results however show higher success rates compared with the previous studies. This is likely due to the comprehensive multimodal approach which targets all aspects of patient care including the acute infection, the chronic inflammation and nutritional needs of the patient.

Previous studies have attempted to identify risk factors associated with failure of conservative management. In a retrospective study of 121 patients with perforating CD who were managed non-operatively, factors that were shown to be associated with future surgery included bowel wall thickness, disease length, bowel obstruction and abscess size.[11] Although the presence of one or more of these factors may indicate more severe disease, there was no clear association between these factors and failure of non-operative management in our cohort of patients. Both of our participants who failed medical management had average disease length and average-sized collections on initial presentation and did not have bowel obstruction. The two patients with the longest disease length (40 cm and 50 cm) both had a favourable response to non-operative management with complete resolution of abscess. One of the two participants had previously failed an anti-tumour necrosis factor biologic (adalimumab) at the time of presentation while non-adherence to medical therapy was likely the main factor in failure of medical therapy in the second participant.

In our patient cohort, the decision by the multidisciplinary team (MDT) to opt for surgical intervention as opposed to conservative management was contingent upon a variety of factors. These included the quantity and size of intra-abdominal collections, the presence and extent of strictures and fistulas. The decision also considered past biologic failures, as well as any previous history of intra-abdominal collections (*i.e.*, patients with recurrent intra-abdominal collections in the setting of Crohn's disease refractory to medical therapy were more likely to be referred for surgery). Other patient-related factors such as the patient's fitness for surgery and their adherence to medication regimen and follow up, also

played a role in the final decision-making process.

Whilst the use of steroids and immunomodulators in the acute phase is limited due to the infection risk, EEN has emerged as a safe adjunctive therapy. EEN has been shown to induce remission in CD patients. In a case series study of 28 patients, EEN was shown to induce complete endoscopic healing at four weeks in the terminal ileum and colon in 44% and 39% of patients respectively.[12] This was shown to be associated with a significant decrease in mucosal cytokine concentrations suggesting that EEN has anti-inflammatory effects. Similarly, use of EEN in CD patients with undrainable intra-abdominal abscesses has been shown to reduce the need for surgery and improve post-operative outcomes.[13] EEN is also effective in inducing remission, promoting fistula closure and reducing abscess size in patients with fistulising CD.[14,15] Therefore, early introduction of EEN is important for optimising nutrition and inducing remission. We successfully used EEN in 72% of our participants. Whilst intolerance can be a barrier to use of EEN in some patients, only one of our patients discontinued EEN for this reason.

In addition, we used thiopurines in all and steroids in two-thirds of our participants after clinical and biochemical resolution of sepsis (defined as the systemic response to bacterial infection manifesting as physiologic, biologic or biochemical abnormalities such as fever, tachycardia, elevated inflammatory markers +/- organ dysfunction). Tioguanine was the most used thiopurine in our cohort of patients as it has been shown to be better tolerated compared to conventional thiopurines.[16] There were no infective complications associated with use of steroids, thiopurines and biological agents in our cohort of patients. These findings are consistent with the outcomes of previous studies which have shown that immunosuppressants can be safely introduced after initial treatment of sepsis.[9,10]

While the ECCO and American College of Gastroenterology (ACG) guidelines recommend image-guided percutaneous drainage for select patients, the guidelines do not specify the criteria for percutaneous drainage *vs.* medical therapy. Some studies have suggested percutaneous drainage for abscesses > 3 cm.[17] In the present study we demonstrate that abscesses greater than 4 cm can be managed successfully with medical management alone. Factors that necessitate prompt percutaneous or surgical drainage include sepsis uncontrolled with antibiotics, severe pain despite oral or parenteral analgesia, and large abscesses that are unlikely to respond to antibiotics alone and/or may require prolonged antibiotic courses. We propose the following approach to management of patients with intrabdominal collections secondary to fistulising CD (Figure 3).

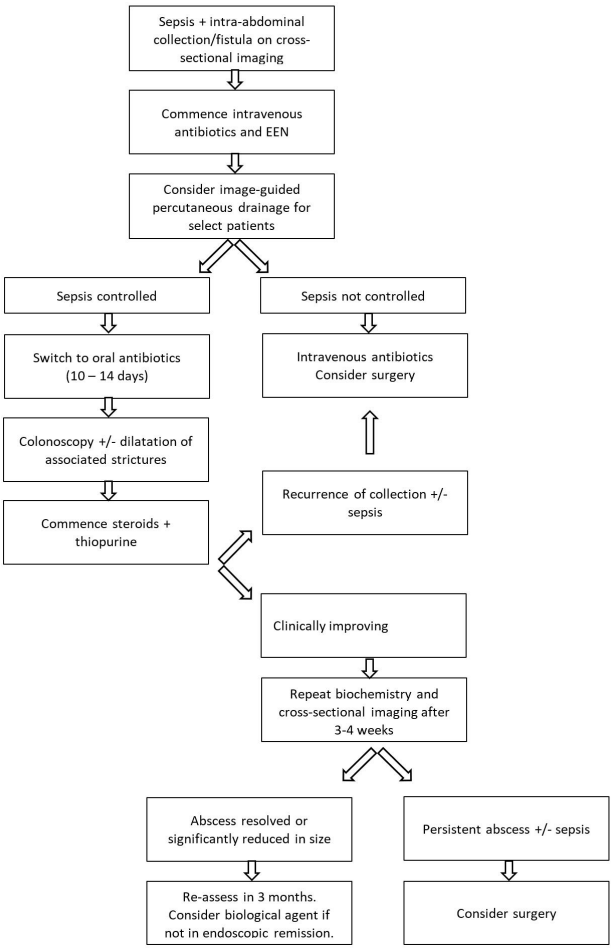

Figure 3. Approach to management of patients with intrabdominal collections secondary to fistulising CD.

Limitations of our study include the small sample size, observational nature of the study, and the focused selection of cases excluding patients who required upfront surgery; therefore, the patient population does not fully represent the broader spectrum of clinical scenarios. Notwithstanding, our findings provide evidence of the utility of a multi-modal conservative approach in managing intra-abdominal collections in fistulising CD.

In conclusion, intra-abdominal collections +/- sepsis in fistulising and perforating CD can be managed conservatively in select patients using a multi-modal approach including percutaneous drainage, antibiotics, EEN, endoscopic dilatations, immunomodulators and biological agents.

DECLARATIONS

Acknowledgment
None.

Author contributions

Shir Ali M contributed to the study design, data collection, analysis and interpretation, literature review and preparation of the manuscript. Leong RW contributed to the study concept and design, study supervision, critical revision of manuscript and final approval of manuscript. Kariyawasam V contributed to the study concept and critical revision of manuscript. Yang J contributed to review and comparison of cross-sectional imaging, and preparation of representative cross-sections for the manuscript. Paramsothy S contributed to the study concept and design, study supervision, critical revision of manuscript and final approval of manuscript. Leong RW and Paramsothy S contributed equally to the development of this manuscript.

Source of funding

None.

Conflicts of interest

The authors report no conflicts of interest

Data sharing statement

No additional data is available.

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