



Case Study of Complicated Crohn's Disease: Emphasizing the Role of Imaging in Outcome Improvement

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Abstract

Crohn's Disease (CD) is a chronic inflammatory disease of the digestive tract, exhibiting a recurrent-remissive pattern. Its management requires a skilful integration of clinical, biological and imaging methods to obtain disease control. We present the case of a 46-year-old male diagnosed with stenosing CD ten years ago. The initial presentation was due to intestinal occlusion, for which he underwent right hemicolectomy. The colonoscopy performed at six months post-operatively revealed disease recurrence, which imposed the induction of biologic therapy (initially Adalimumab, followed by Infliximab). Complete remission was maintained for ten years as demonstrated by the clinical, paraclinical, colonoscopy and imaging examinations. In February 2023, the patient was admitted for a flare. Abdominal Computed Tomography (CT) revealed the site of inflammation and excluded complications, so the decision was to intensify the Anti-Tumour Necrosis Factor (TNF) therapy. Worsening symptoms led to the patient's readmission, but this time the CT showed inflammatory stenosis of the sigmoid colon and two pericolic air-fluid collection. Multidisciplinary consultation decided for conservatory management with the association of antibiotics and cortisone. Favourable evolution was confirmed by abdominal US, showing the resolution of the pericolic collection. The pathogenic treatment was changed to Ustekinumab, leading to complete remission (clinical, paraclinical and imaging). The presented case demonstrates the prolonged evolution of a patient with complicated CD, for which the multidisciplinary approach was the key to success. High quality imaging is essential for activity monitoring, evaluation of treatment response and diagnosing complications in inflammatory bowel disease patients.

Keywords: Crohn's disease; Abdominal imaging; Abscess; Complicated inflammatory bowel disease; IUS

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Introduction

Crohn's Disease (CD) is a chronic idiopathic Inflammatory Bowel Disease (IBD) affecting the entire digestive tract, with a predilection for the terminal ileum [1,2]. Its complexity extends to the pathology, manifestations, complications, treatment and monitoring of the disease. Long term evolution is characterized by asymptomatic periods (remission) alternating with episodes of recurrent active disease (flare), manifested with diarrhoea, abdominal pain, anorexia and weight loss. Other symptoms result from the acute inflammation of the digestive tract or various extraintestinal localisations, as well as from complicated disease [2]. Imaging findings consistent with active disease include long segments of uniform wall thickening in the small bowel or the colon, as well as the involvement of Lymph Nodes (LN) and mesenteric vessels [1]. Considering the complications, the Montreal classification categorizes the CD into stricturing (stenosis), penetrating (fistula, abscess), perianal disease, or non-stricturing non-penetrating disease [3]. Various societies, including European Crohn's and Colitis Organisation (ECCO), International Bowel Ultrasound Group (IBUS), are focusing their work on strengthening the role of imaging in the follow-up of IBD patients by defining the terminology used to describe the findings of bowel ultrasound (IUS), Magnetic Resonance Imaging (MRI) and Computed Tomography (CT), as well as finding new applications of adjuvant techniques in IBD. The main goal of these societies is to aid clinicians in accurately describing the extent and type of disease, managing therapeutic decisions and creating monitoring protocols, all to reduce the frequency and severity of active disease [4,5]. The therapeutic arsenal is broadening, with many classes of medication and active compounds being researched. Studies on the pathogenic mechanisms allowed for the development of drugs addressing to various targets implied in the inflammatory cascade of CD. Surgical intervention may be necessary in severe cases, consisting in excision of affected bowel segments, abscess drainage or fistula closure [6]. The notions of transmural remission and transmural healing may be used in the future as

therapeutic targets associated with a deeper degree of disease control [7,8]. Disease monitoring includes clinical, biochemical, imaging and invasive methods. A combination of these is required to assess the degree of inflammation and possible complications accurately. Cross-sectional imaging techniques are general abdominal ultrasound, IUS and MRI; the use of CT is limited due to radiation concerns but may be essential in select patients.

Case Presentation

We present the case of a 46 years old male patient, ex-smoker, diagnosed with CD for 10 years. The first presentation was due to sub-occlusive syndrome, for which he underwent colonoscopy and entero-MRI. Extended stenosis of the terminal ileum and ascending colon (Figure 1) were detected, which imposed the surgical treatment by right-sided hemicolectomy with ileo-transverse anastomosis. Postoperatively he was started on Metronidazole and Azathioprine. The colonoscopy was repeated six months later and revealed endoscopic relapse (Rutgeerts score i3), necessitating the switch to biologic therapy. He was started on Adalimumab, to which he showed a positive evolution, with remission confirmed by biological and imaging methods. However, at the one-year follow-up, he developed symptoms suggestive of relapse, and in association with the detection of an increased titre of anti-Adalimumab antibodies, the medication had to be changed. The alternative was Infliximab, as in Romania, at that time, the only biologic therapy variants available were anti-Tumour Necrosis Factor (TNF) antibodies. Under maintenance therapy with 400 mg Infliximab every 8 weeks, he maintained a continuous remission, confirmed by clinical scores (CD activity index - CDAI), paraclinical examinations (faecal calprotectin - FC), colonoscopy and imaging (IUS, MRI). In February 2023, he was admitted with a one-week history of diarrheic syndrome (6-8 stools per day), abdominal pain and weight loss of approximately 5 kg in one month, raising the suspicion of a flare. Increased C reactive protein (CRP - 17 mg/dl) and FC (3200 µg/g) were detected, which required further exploration to look for a cause. An abdominal and pelvis CT was performed, which revealed a long segment of uniform wall thickening in the distal two-thirds of the transverse, the descending and sigmoid colon, with corresponding spasm and no signs of occlusion, accompanied by stranding at the level of the correspondent mesocolon (Figure 2). After excluding other causes of disease relapse (for instance, the infection with *Clostridioides difficile*), and as Therapeutic Drug Monitoring (TDM) was not available, the decision was to intensify the treatment with 400 mg Infliximab every 4 weeks. One month later, he presented again in the emergency department due to severe symptomatology, with 10-



Figure 1: Colonoscopy performed at six months post-operatively demonstrates recurrence of Crohn's Disease manifesting as inflammation of the colic mucosa, associated with stenosis of the ascending colon.

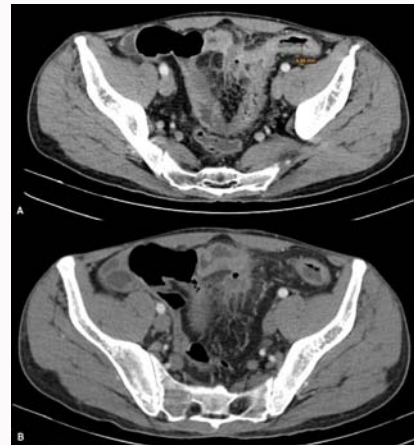


Figure 2: Computed Tomography axial sections venous time showing (A) thickened bowel wall at the descending-sigmoid colon junction, with significant contrast uptake, suggesting inflammatory stenosis at this level. In addition, medially to this segment and in contact with it, there is a gas-fluid collection, with adjacent fat stranding. (B) shows the collection, which is in contact with a small bowel segment, but the images are not specific for a fistula (which remained a suspect, but due to the severity of the symptoms bowel preparation and positive contrast could not be administered to evaluate for extra-intestinal extravasation). Additional findings include engorgement of the vasa recta (the comb sign) and a few enlarged lymph nodes.

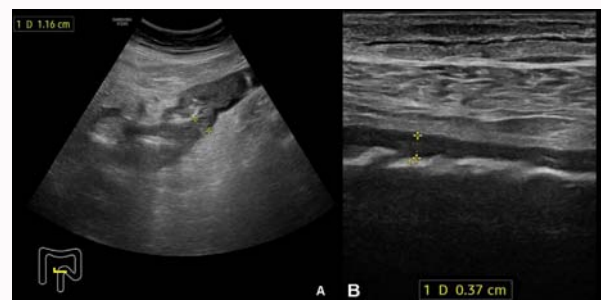


Figure 3: Ultrasound examination of the descending-sigmoid junction. (A) was performed after resolution of the collections, before discharge, showing the thickened colon wall, with loss of stratification and luminal collapse, all suggestive of still active disease. (B) IUS at six months showed resolution of the inflammatory process at this level, with normal thickness of the colon wall.

12 stools per day, nausea, vomiting, abdominal pain, and weight loss (8 kg in 2 months). Paraclinical tests showed marked inflammation (CRP 31 mg/dl), leucocytosis (17 000/mm³), thrombocytosis (553000/mm³), anaemia (Hb 10.3 mg/dl), hypoalbuminemia (2.8 g/dl). In the context of worsening symptoms even after treatment intensification, a complication was suspected, which indicated the need to repeat the CT examination, revealing two thin-walled fluid collections with gaseous content in the mesosigmoid (measuring 17,4/16/20 mm, respectively 13/10/17 mm in antero-posterior/transverse/cranio-caudal planes), accompanied by traction of the nearby small bowel loops, but without discernible fistulas. The transverse and distal parts of the descending colon showed discontinuous segments of wall thickening, with a normal calibre between these stenotic but permeable regions. Multidisciplinary consultation (gastroenterology, radiology, surgery) decided for conservatory treatment with an antibiotic combination (intravenous ciprofloxacin and metronidazole), associated with corticotherapy with methylprednisolone. The collections were identified by ultrasound as well, in order to permit their follow-up without radiation dose increase. The patient showed a favourable clinical evolution, as well as a reduction of the inflammatory markers.

An abdominal US was performed four weeks later, which showed the resolution of the collections described previously, as well as a slight reduction of the bowel and mesenteric inflammation (Figure 3A). Induction doses of Ustekinumab (390 mg i.v.) were administered with promising results, so the decision was to start maintenance treatment with 90 mg Ustekinumab every 12 weeks. The IUS performed at the six months follow-up demonstrated marked reduction of the intestinal inflammation, with normalisation of the bowel wall thickness (Figure 3B).

Discussion

The presented patient was diagnosed with CD due to intestinal occlusion as a result of complicated disease, which imposed the surgical treatment of the stenosing segment. The long-term disease evolution was also burdened by early postoperative recurrence, loss of response to the anti-TNF therapy and the appearance of stenoses and abscesses. This demonstrates the complexity of CD, emphasising the need for a multidisciplinary team to detect, treat and monitor the disease's evolution. Although the gastroenterologist is at the core of the team, many specialities may be involved in the follow-up of these patients [6]. The clinical aspects of the disease, as well as paraclinical (blood and stool) tests, can detect inflammation of the digestive tract and might be used to assess for the degree of remission or detection of an exacerbation (flare), but they have low sensitivities and specificities [9]. Colonoscopy remains the gold standard procedure for the diagnosis of CD, allowing for macroscopic evaluation of the mucosa and biopsy sampling, but may also be used to assess for endoscopic healing under treatment [6,10,11]. However, its use is limited by its invasiveness and some conditions such as suspicion of toxic megacolon, while also lacking the ability to evaluate transmural or extraintestinal pathological findings. Intense research is being conducted in the field of IBD imaging, with many published guides available on the scanning protocols, the interpretation of findings, reporting systems and scores [10-13]. Cross-sectional imaging's utility in IBD has extended to disease activity monitoring, assessment of response to treatment, detection of complications and accurate description of their type. Each procedure has a series of benefits, but their availability, repeatability, costs and the risk of irradiation are key factors in choosing the appropriate method. Compared to colonoscopy and capsule endoscopy, cross-sectional imaging permits evaluation beyond the mucosa, which is particularly more important in CD due to the transmural damage and extraintestinal inflammatory changes. It can also overcome some of the limitations of the invasive methods, of which strictures and the inability to visualise terminal ileum are the most frequent. However, the aim is not to replace one method with another but the ability to recommend the correct complementary tools to enhance the patient's outcomes. IUS and MRI, in particular with intestinal visualisation (magnetic resonance enterography) are first-line cross-sectional imaging procedures recommended in the evaluation of IBD. On the other hand, CT is a very useful tool that permits fast image acquisition, is widely available and has a reduced cost compared to MRI, but it's use raises worries related to radiation exposure [14]. The American Congress of Radiology have published appropriateness guidelines for specific clinical scenarios in patients with known or suspected CD, aiming to help clinicians in deciding between the available imaging methods. According to these experts, contrast-enhanced CT or CT enterography have been deemed appropriate in all scenarios, which include initial imaging, suspected acute exacerbation and for therapy monitoring. In moderate and severe cases, similar to our patient, in which findings

are less subtle, a standard abdomen and pelvis CT with i.v. contrast demonstrates a good sensitivity in defining the affected segments and possible complications. Oral negative contrast can increase the accuracy in detecting stenoses, as well as inflammation limited to the mucosa, but it's use is limited by the severity of the exacerbation, as the placement of the nasoduodenal tube and the need for active infusion of oral contrast may be poorly tolerated by the acutely ill [15,16]. In the presented patient, the disease evolution was evaluated by clinical, paraclinical and colonoscopy examinations, as well as by imaging. We favoured the non-invasive methods, respectively IUS and MRI. CT examinations were performed in emergency settings and demonstrated a good sensitivity for detecting disease complications, aiding the clinicians in the management of these conditions. Breakthroughs in understanding CD pathogenesis led to the development of various therapeutic molecules and changes in the therapeutic targets. Endoscopic healing has been classically used as the main objective in these patients, but histological and transmural healing are being proposed as possible targets, with better long-term outcomes and a decrease of complication rates. As there is no consensus on the definitions for transmural response and transmural remission, these terms have been used in a few studies using IUS explorations that demonstrate the reduction of the significant parameters: bowel wall thickness and stratification, colour Doppler intensity and perienteric modifications (fibrofatty proliferation, complications). Other studies suggested that patients can be stratified based on these parameters in groups with simplified, extended and complete response [17,18]. The first presentation of the patient in our centre was due to stenosis as a complication of CD, leading to intestinal occlusion. At that time, the CT performed in emergency settings was able to detect the thickened colon and indicated the need for surgery. However, CT is less specific for differentiating between fibrotic and inflammatory stenoses, two conditions which may be treated differently, the main target being the limitation of bowel excision. The need for surgical sparing has been filled by elastography, performed either by IUS or by MRI, which is useful as a tool for differentiating between fibrotic and inflammatory stenoses [19,20]. At the current presentation, the loss of response to the therapeutic scheme led to the formation of two abscesses, which have been described on the second CT performed. However, there were no signs to suggest the origin of these collections such as extraluminal gas bubbles of tracts originating from the thickened bowel wall. In most cases, CT exploration performed in emergency settings may be sufficient in describing the extra-intestinal fluid collections and also detect extraluminal gas bubbles, which might point to the origin of the perforation or fistulas. In other cases, MRI may be added to increase the accuracy. IUS is a cheap exploration that can be easily performed in most clinical settings for repeated evaluation under antibiotic treatment or after curative surgical procedures.

Our patient underwent a right-sided hemicolectomy ten years before the current presentation due to ileal stenosis as a complication of CD. The post-operative colonoscopy showed early recurrence at the anastomotic site. Many features have been incriminated in the pathology of post-operative flares, including smoking, type and extent of disease and surgical factors [21,22]. The risk of a new flare after surgery increases with time [23], and administration of medication is required to delay it. Pre-operative imaging may be used as a tool to manage CD patients appropriately. Starting from qualitative (presence of complications) or quantitative parameters obtained by ultrasound, CT or MRI, we can create scores that may predict the

patients with a higher risk of postoperative complications or early flares, in whom intensive treatment and frequent re-evaluation should be performed. Currently, in CD, IUS and MRI scores have been imagined and validated for use in assessing disease clinical activity and therapeutic response [11,12,24] but, to our knowledge, no pre-operative score to predict post-operative outcomes have been reported. Similar scores have been imagined however for other diseases, helping practitioners to predict and overcome serious complications, and their methodology may be applied to IBD as well [25]. Artificial Intelligence (AI) is rapidly evolving, changing the medical practice. Machine learning, deep neural networks, support vector machines and other types of AI tools may enhance the role of imaging scores by facilitating measurements, observing patterns and establishing relationships between information and outcomes, becoming real predictive tools. A series of studies have been published regarding the use of AI to assess disease severity, predict the response to treatment and clinical outcomes. These tools may be used as well in research, to create new therapeutic formulations [26-29].

Conclusion

Crohn's disease is a complex condition that demands comprehensive understanding of its pathogenesis, clinical manifestations, complications, and the therapeutic options available. Imaging plays a crucial role in guiding diagnosis, monitoring disease progression, and evaluating treatment efficacy. Therefore, a multidisciplinary team, with a core consisting of a gastroenterologist, surgeon, and radiologist, is essential to enhance disease outcomes.

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