

Ischemic colitis in a young patient with a history of COVID-19 infections: atypical case

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Abstract

As extrapulmonary manifestations of Coronavirus, it has been described patients developing gastrointestinal disorders that replace typical respiratory symptoms or others that debut with intestinal ischemia shortly after infection, however, the association between COVID-19 and ischemic colitis remains unclear. We present a young patient with three previous infections by COVID-19 and chronic consumption of isotretinoin, who developed ischemic colitis and a torpid evolution. It is concluded that Coronavirus infections could represent a risk factor for colonic ischemia and that isotretinoin increases the probability of complications; however, more evidence is needed.

Keywords: Colitis. Ischemic. COVID-19. Isotretinoin.

Introduction

Defining ischemic colitis is simple when approached from grammar and geography, because separating the two words that make up the term, ischemia has as meanings the stagnation or cessation of blood toward a certain tissue, and by colitis we can land at a specific location within the abdominal area that is framed within the framework of the colon, understanding it in a general way as a decrease in the colonic blood supply, with nuances about its origin and complications that will be detailed later¹.

It is described that this decreased or insufficient blood flow is usually temporary and that while the body continues to need the same amount of volume in the gastrointestinal system, it is impossible for the colon to successfully execute the physiological demands, causing inflammation of the mucosa, ulcerative and hemorrhagic lesions,² and inevitably cell death or necrosis,

which devastates from the superficial mucosa, as it is the layer with the greatest metabolic activity, to the complete transmural thickness³.

The classic or typical presentation of colon ischemia is composed of a sudden onset of abdominal cramp-like pain that usually begins in the left lower quadrant, accompanied by superficial tenderness, hematochezia, an urgency to evacuate, and evidence of peritoneal or ileal irritation; it is usually a pathology limited to a single segment, which for anatomical reasons commonly involves the portion of the left hemicolon where the splenic angle is located, but since it is not exclusive, cases of ischemia in the right region or pancolonic have also been reported, both associated with poor prognosis⁴.

It is known as the most common type of intestinal ischemia, with an annual incidence rounded to 23 cases/100,000 people¹, more frequently in older adult

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patients, females, who have comorbidities such as having been diagnosed with atherosclerosis, systemic arterial hypertension, atrial fibrillation, diabetes mellitus, previous CMV, or *Escherichia coli* infection, as well as being under renal replacement treatment and consumption of drugs such as NSAIDs, antidiarrheals, opioids, tricyclic antidepressants, and immunomodulators⁵.

In addition, for a little more than 3 years, due to the SARS-COV 2 pandemic, few but interesting cases have been described about extrapulmonary manifestations of Coronavirus viral infection, mainly during the active phase of the disease, that is, patients who instead of suffering from an acute respiratory condition presented with gastrointestinal manifestations such as loss of appetite, vomiting, pain, bloating, diarrhea, manure, and hematochezia⁶, with a few other reports that propose associating this respiratory condition as a risk factor for intestinal ischemia, as cited by Uhlenhopp et al.⁵ who have detailed the association between this viral infection and ischemic colitis up to 3 weeks before presenting the picture, in both cases described without observing associated respiratory affection.

The pathophysiology that could explain this interaction is described as secondary to the entry of the virus into the cells, when the infection causes the release of cytokines and chemokines through the angiotensin-converting enzyme 2 receptor, which is highly expressed in the cells of the gastrointestinal tract, favoring acute intestinal inflammation; in addition, RNA of the virus has been found in fecal samples from patients with COVID-19, indicative of the potential of the virus to invade the gastrointestinal tract⁷.

The case that will be shared below represents multiple singularities due to probabilities, risk factors, and clinical presentation, being described with the sole objective of sharing its peculiarities for purely theoretical and educational purposes.

Material and methods

A literature review was conducted in Medline, using MeSH terms. The search strategy used was: (("Colitis, Ischemic" [Mesh]) AND "COVID-19" [Mesh]) and ("COVID-9" [Mesh]) AND "Signs and Symptoms, Digestive" [Mesh]), in addition to keyword searches with "isotretinoin" and "ischemia." A total of 39 results were obtained, including publications of the last 3 years related to pathophysiology, clinical picture, and diagnosis. We used 11 references that met the inclusion criteria.

Case presentation

A 44-year-old female with the following important history: COVID-19 infection on three occasions (2019, 2020, and December 2022), myomectomy (2004), hysterectomy (2020), chronic consumption of isotretinoin due to acne and skin hypersensitivity (since 2022, with intermittent conditions), without allergies or drug addictions described.

On March 1, 2023, she reported starting with symptoms of upper respiratory tract infection (nasal congestion,odynophagia, rhinorrhea, sneezing, headache, and adynamia) without a defined diagnosis, a condition that later led to hyporexia; The next day she presented yellowish watery emesis on six occasions, accompanied by at least three events of diarrhea, nausea and generalized abdominal pain of the colic type that increases with the passing of the days, highlighting the absence of gas channeling, which is why she visits a private doctor, who initiates intravenous hydration, antiemetics, and gastric mucosal protectors that do not condition clinical improvement. Going 4 days later to the Emergency Department at Dalinde Medical Center with a picture of generalized abdominal distension, an attitude limited by the presence of intense abdominal pain that conditions immobility, aperistaltic, with intense pain on superficial and deep palpation and mobilization, neurologically intact, maintaining perfusive blood pressure levels with mean arterial pressure of 78 mm Hg, afebrile (36°), tachycardia (112 ppm), and with a respiratory rate without alterations (14 bpm).

A nasogastric tube was placed that allows pressure gas to escape with at least 250 mL of fecaloid content and when requesting paraclinical studies, alterations in the levels of BUN (45.71 mg/dL), urea (97.8 mg/dL), creatinine (1.44 mg/dL), total leukocytes (10.690 10³/uL), and total neutrophils (10.21 10³/uL) were reported, in addition to hypokalemia of 3.21 mmol/L, elevated prothrombin time (18 s), and partial thromboplastin time just at the limit (35 s). A simple abdominopelvic computed axial tomography scan was also required, showing the presence of gas in the wall of the small intestine and inflammation of the adipose tissue (Fig. 1).

Surgical intervention was performed (Fig. 2) showing a purulent collection in the left hypochondrium that conditioned proximal occlusion secondary to necrotic patch (2 × 2 cm) at a splenic angle, anteroinferior aspect and that caused ischemia in the proximal jejunum (0.5 × 1 cm) due to contiguity (Fig. 3), in addition to multiple fibrin creams in the cavity and devitalized appendix. During surgery (isoperistaltic laterolateral

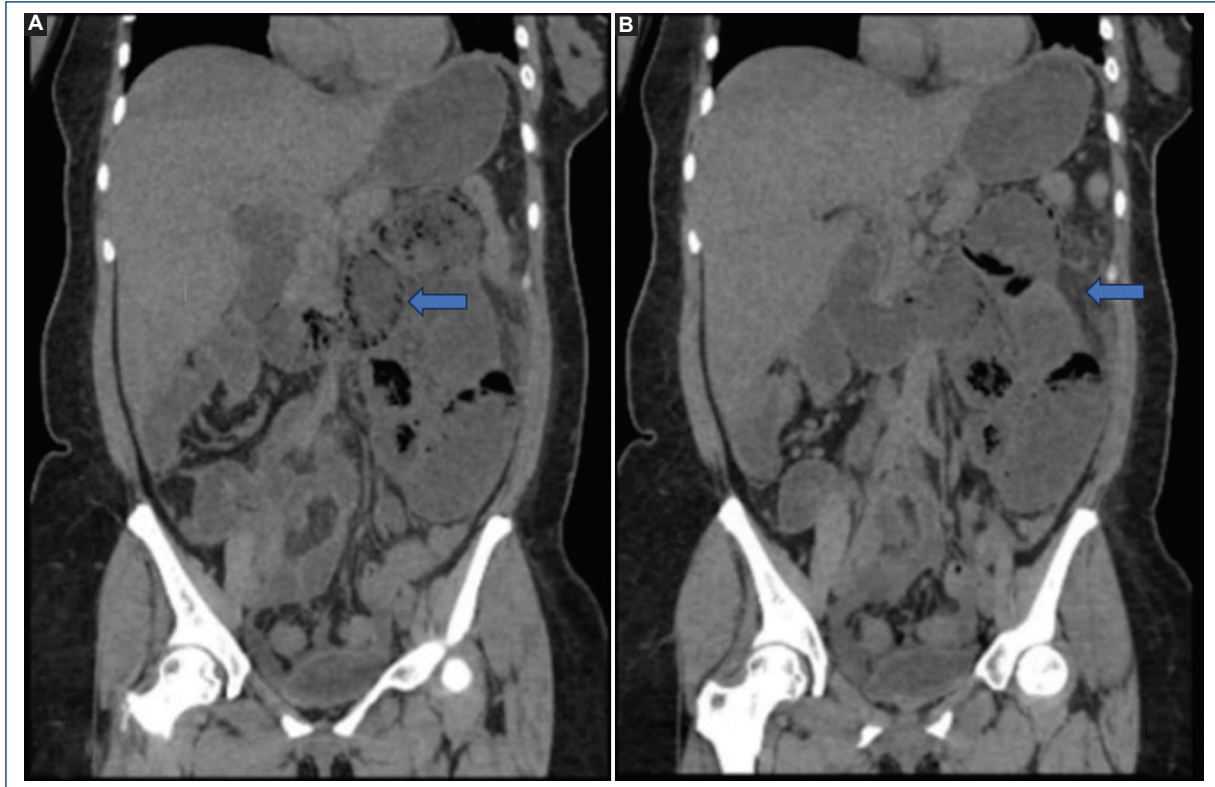


Figure 1. **A:** coronal section of a simple abdominopelvic CT scan showing pneumatosis at the level of the proximal jejunum and **B:** striation of the peri-caecal fat at the level of the splenic angle.

coloanastomosis with jejunal rafia), a culture of peritoneal fibrin tissue was taken, in which *E. coli* infection of 70,000 CFU/mm³ was subsequently reported.

Within the first 7 days, the patient has a favorable evolution, with tolerance of early ambulation, little pain in the surgical wound, and the presence of stools with gas channeling, being until the 8th day of hospitalization, 1 day after starting a liquid diet, which presents a gradual intolerance to the oral route, eight fetid diarrheal bowel movements, all preceded by colic and feverish peak that yields to the antipyretic. The patient went to the second surgical stage where there was a 1 cm anastomosis dehiscence associated with an abscess with very little leakage of intestinal material (Fig. 4). Two days of evolution after the second intervention, culture reports detail 80,000 CFU of multiresistant *E. coli* sensitive to ciprofloxacin, as well as a significant decrease in hemoglobin, so antibiotic treatment and iron supply are adjusted. Subsequently, a frank melanic evacuation and two stools with little blood were reported, paradoxically contrasted with the clinical and emotional improvement of the patient, who was referred to asymptomatic and without alarm data.

During the same early morning, she presented two more evacuations with hematochezia and clots, the first of them with data of mucosal slag, in addition to a decrease in hemoglobin (from 11.1 to 8.9 g/dL) and data of low cardiac output, which dictates transfusion of erythrocyte concentrates, enemas of mesalazine and enterogermina by nasogastric tube.

A second culture of wound secretion was performed, which showed carbapenem-sensitive ESBL *E. coli*, re-adjusting treatment to ertapenem and presenting a patient with a rapid favorable evolution until the day of discharge (03/22/2023).

Discussion

This case represented a diagnostic challenge due to the low suspicion and probability of the same in the context of the patient, as ischaemia in the splenic angle of the colon is a condition frequently associated with elderly patients and various comorbidities, which is why, at first, the abundant diarrhoeal events were the most tangible and evident predisposing factors, but not enough to be able to ratify it.

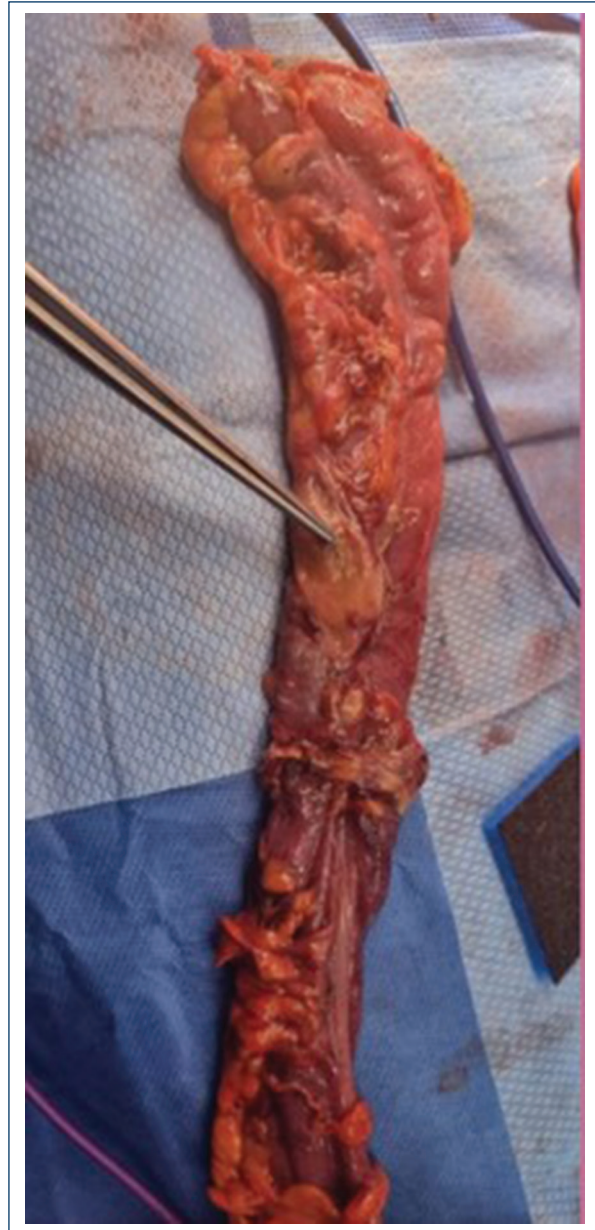


Figure 2. The left hemicolectomy product showed transmurial ischemia marked with dissection forceps.

It was considered possible that the chronic use of isotretinoin, a derivative of retinoic acid that the patient used frequently and chronically as part of her treatment for acne, contained a risk of colonic ischemia as an adverse effect, however, there is inconclusive literature on this matter and with a greater tendency toward a probable relationship with chronic inflammatory disease and ulcer formation⁸, describing cases of young patients with no history of rectal bleeding events that improved after discontinuation of the drug⁹.



Figure 3. Transmurial ischemia was observed at 12 cm Treitz angle in the proximal jejunum.



Figure 4. Resection of previous dehiscence anastomosis and new mechanical colosigmoid end-to-end anastomosis.

Consequently, the association that could exist with Coronavirus infection resonates, finding in the search for case reports such as those published by Tafur¹⁰ in mid 2023, which highlights that of a young patient without comorbidities who began with positive respiratory

symptoms for SARS COV-2 a few days prior to admission, evolving to abdominal alarm data (pain on palpation, decreased peristalsis) with a final diagnosis of acute mesenteric ischaemia, recognised up to the time of surgery and pointed out by the author as an uncommon complication but associated with SARS COV-2 infection, especially from the second and third waves onwards.

Another important piece of information that arises from the search is the increase in D-dimer or fibrinogen levels, in patients with documented acute mesenteric ischaemia related to Coronavirus, reported in most of the sources consulted¹⁰⁻¹², showing a state of hypercoagulability and thrombosis that could not be confirmed in the patient as these parameters were not requested, although the alteration of coagulation times, specifically prothrombin time, urea and creatinine, coincides with the findings of Uhlenhopp et al.⁵, Tafur¹⁰ and Chan et al.¹², confirming that the presence of intravascular thrombosis is not indispensable for the association of both conditions.

Now, it is true that due to the time elapsed between the three confirmed infections and the reason for his admission, it is unlikely that there was a direct association, but this does not exclude the importance that these had as risk factors for the establishment of sequelae in the gastric system, since on the one hand, it has been proven that reinfection with SARS COV-2 contributes to a significant increase in the percentage of probability of suffering future gastrointestinal disorders, with the number of reinfections being directly proportional to the increase in risk, with the highest probability after three or more infections¹³.

On the other hand, bibliography was found that points to the damage caused to the intestinal microbiota in patients with Coronavirus infection, reducing the quantity and diversity of anti-inflammatory bacteria in the acute phase and predisposing to long-term complications (diarrhoea, abdominal pain, among others) included in the Post COVID-19 Syndrome¹⁴.

In view of the above, it is considered that since the patient had respiratory symptoms compatible with Coronavirus infection a few days before her hospitalisation, even in the absence of a confirmatory diagnosis, on this occasion she may have had a fourth SARS COV-2 infection with consecutive gastrointestinal manifestations and acute mesenteric ischaemia, as described above, although in most of these cases the presence of infection in the upper airways was confirmed, in one of them in situ viral detection in the intestinal mucosa was required due to negative results

in PCR tests and imaging studies¹¹, while in another case three weeks had elapsed since the positive result in the rapid test until the ischaemic intestinal symptoms⁵, although it was still associated with COVID due to the similarity in the clinical presentation.

Having said this, a new question arises when contemplating its unexpected evolution and the dehiscence of the anastomosis after the first intervention stands out, for which two alternatives are contemplated, both the probable failure of the suture material and the technique used. This, together with the fact that viability was never checked with indocyanine green, a fluorescent dye useful for assessing tissue irrigation¹⁵, which would have been a useful technique for reducing the risk of complications, because although the tissue was apparently viable, its perfusion was not faithfully guaranteed.

Three possible causes are proposed, the first of them due to an underlying infectious picture due to the history of a positive wound secretion culture for *E. coli* ESBL; however, during his stay stool cultures were not taken that could corroborate the theory, in addition to the fact that there were no clear clinical data of infection in his post-operative time. Hence, due to lack of evidence, it is not confirmed.

The second conjecture is anchored in the possibility that, due to the mechanical movement inherent in the resection and performance of the new anastomosis, with the circular stapler direct lesions have been caused to the mucosa of the colosigmoid wall that later manifested themselves in isolation with the bloody evacuations, an issue that at the moment seems to be one of the most meaningful.

Finally, without being able to prove the association as a causal factor but not ruling it out outright, it is true that isotretinoin could have played a relevant role in the entire condition and specifically within the last days of the patient's hospital stay since doubts regarding a predisposition for the formation of ulcers and even for inflammatory disease allow us to elucidate the probability that there has been a transient ischemic process after the second anastomosis that will set the stage for the aforementioned outcome.

Conclusions

Certain questions remain in limbo with their respective answers, as well as the real cause of the appearance of this ischemic picture in a patient without comorbidities described as true antecedents for her, however, it is concluded that, by probability, it

is most likely that there has been a favorable scenario for the establishment of ischemic due to the three previous COVID-19 infections, which together with the presence of severe diarrhea for multiple days, and isotretinoin, condition the outcome already described. The uniqueness of the case has kept the team that authored this review in constant search for answers and more information is expected to be provided soon.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text.

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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