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Uncanny Association between Microscopic and Clostridium Difficile Colitis—A Case Report

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Abstract

Clostridium difficile colitis leads to bowel injury, increasing the risk for microscopic colitis, whereas people with any inflammatory disease are prone to infections. A complete evaluation, including a colonoscopy, should be performed in undiagnosed cases. Finally, upon diagnosis of microscopic colitis, discontinuation of offending medicines should be promptly done. Use of antibiotics other than Vancomycin administered orally will only lead to partial or no response. Lastly, if the suspicion for the Clostridium difficile diarrhea is high, further testing should be done even if initial lab work is negative.

Keywords

Clostridium Difficile, Microscopic Colitis, Escitalopram

1. Introduction

Bile salt diarrhea in patients with cholecystectomy, SIBO for patients with diabetes or anastomotic surgeries, chronic pancreatitis in type 1 diabetics, and giardiasis in patients living near water bodies are reasonable considerations [1]. Furthermore, celiac disease and inflammatory bowel disease based on family history are things that can be explored [2]. Rarely in immunocompromised/immunosuppressed people, immune checkpoint inhibitors, mycophenolate, cytomegalovirus, or malakoplakia have been associated with diarrhea as well [3]. Recently, more data is available for a possible allergy-mediated process, with eosinophilic colitis emerging as a relatively unknown cause of diarrhea in the past [4]. Furthermore, drugs can be associated with diarrhea, including oral iron, non-steroidal anti-inflammatory drugs, and magnesium supplements [5].

Chronic diarrhea is often ignored or deemed to be in the setting of IBS-D, especially in women with anxiety, depression, or fibromyalgia [6]. However, this case explores the need to evaluate the causes of chronic diarrhea with the patient's medical, surgical, and personal history taken into consideration.

After empiric treatment for years, a colonoscopy was performed during an acute exacerbation of chronic diarrhea, leading to a diagnosis of microscopic colitis, which led to the rightful discontinuation of SSRI, which has been a studied risk factor [7]. On top of that the patient had *C. difficile* diarrhea which was initially missed due to a negative antigen test but given high suspicion, PCR was ordered correctly identifying at least colonization prompting treatment given the clinical setting [8].

There have been cases with a to-and-fro relationship between microscopic colitis and *C. difficile* diarrhea, with one as a risk factor for the other and vice versa [9]. But any pre-existing inflammatory colon condition predisposes *C. difficile*, and any recurrent *C. difficile* should raise suspicion of an underlying condition [8].

2. Case

A 47-year-old female with a medical history significant for anxiety, migraines, and chronic loose stools/diarrhea following a cholecystectomy 15 - 20 years ago, presented with worsening diarrhea. The patient initially presented to the clinic with complaints of sinusitis. She was prescribed a 5-day course of Augmentin, which did not alleviate her symptoms. Subsequently, she received another 7-day course of Augmentin. During this time, she developed diarrhea, which persisted despite completing the antibiotic regimen. A CT abdomen/pelvis revealed pancolitis. Stool culture was negative.

For the loose stools, she received a course of ciprofloxacin and metronidazole in an outpatient setting as prescribed by her primary care physician. The patient reported significant improvement in her diarrhea with the antibiotics; however, her symptoms worsened approximately 5 days after completion of the course, this time experiencing 15 - 20 loose, watery bowel movements per day, with associated mucous but no frank blood, chills, or abdominal pain, and cramping rated 8/10, associated with bowel movements, and resolving post-defecation.

She had a family history of Crohn's disease in her first cousin and had never gotten a colonoscopy. Her daily medicines included escitalopram, cholestyramine, and as-needed acetaminophen, other than the recent antibiotics.

She was hemodynamically stable with tenderness; no guarding or rebound tenderness was noted. She had leukocytosis, and stool studies, including *C. difficile* toxin, fecal elastase, osmotic gap, and culture, were negative. Celiac serology with IgA levels and breath tests for lactose intolerance and SIBO were ordered and were negative. Due to high clinical suspicion, a PCR for *C. difficile* was ordered, which turned out to be positive. The patient was then started on oral vancomycin 125 mg 4 times a day for 2 weeks, and a gastroenterology appointment was made given

the chronicity of diarrhea.

The patient had improvement on oral vancomycin with a resolution of cramping in the next 3 - 4 days, and frequency went down from 15 - 20 times to 3 - 4 times, which was her baseline. She then followed up with a colonoscopy, which demonstrated normal mucosa, but random biopsies were taken, all of which demonstrated lymphocytic colitis.

The patient had no history of chronic PPI or NSAID use; however, she had been on SSRIs for years. A follow-up with psychiatry was given to taper it off in favor of a different class of anxiety medicine. The patient was further offered 9 mg of budesonide daily with a taper moving forward. This patient developed complete resolution of the above symptoms (Table 1).

Table 1. Case timeline.

Time period	Intervention/Event
Initial presentation	Sinusitis
Day 0 - 5	Augmentin 5-day course
Day 6 - 12	Second Augmentin 7-day course
During the Augmentin course	Diarrhea onset
Post Augmentin course	CT shows pancolitis, negative stool culture
Outpatient visit	Empirical therapy (ciprofloxacin + metronidazole) for suspected bacterial infection
5 days post empirical therapy	Symptoms worsening (15 -20 bowel movements/day)
Hospital admission	Hemodynamically stable, abdomen tenderness
In patient day 1 - 2	Initial *C. difficile* toxin negative but high clinical suspicion present
In patient day 3 - 4	PCR positive for *C. difficile* → Vancomycin started
Week 2	Improvement of symptoms (bowel movement 3 - 4 times/day)
Follow up colonoscopy	Colonoscopy: Normal mucosa Biopsy: Lymphocytic colitis confirmed
Budesonide given	Bowel movements became normal

3. Discussion

The above patient developed multiple episodes of diarrhea following the ingestion of Augmentin, and moreover, the patient is on an SSRI for her anxiety. There could be multiple causes of diarrhea in this patient, which include microscopic colitis and/or Clostridium difficile-associated diarrhea [8].

Owing to the diarrhea, the patient was prescribed ciprofloxacin and metronidazole following negative initial stool studies, which reflects standard practice for suspected bacterial gastroenteritis, and metronidazole is known to have *C. difficile* coverage too [8]. While fluoroquinolone exposure is a known risk factor for *C.*

difficile infection, the initial improvement followed by a severe symptom recurrence suggests partial suppression of the bacterial overgrowth rather than treatment of the underlying pathophysiology [10]. Thus, this clinical course raises the suspicion of Clostridium difficile infection, which was proved to be positive using PCR [8].

Chronic microscopic colon inflammation, which also manifests as persistent watery diarrhea, is the hallmark of microscopic colitis (MC) [6]. Collagenous colitis (CC) and lymphocytic colitis (LC) are the two subtypes of MC that exist [11]. Proton-pump inhibitors (PPIs), selective serotonin reuptake inhibitors (SSRIs), and non-steroidal anti-inflammatory medicines (NSAIDs) have all been connected to MC [6]. Our patient had chronically been on SSRIs. Common presenting symptoms may include watery, non-bloody diarrhea, fecal urgency, abdominal pain, and weight loss [6].

After other causes of chronic diarrhea have been ruled out, based on medication history, microscopic colitis should be considered and evaluated with a colonoscopy [11]. On macroscopic appearance, the colon looks unremarkable, and this can tempt a gastroenterologist to not take biopsies unless the diagnosis is considered. Like our case, when more than 20 intraepithelial lymphocytes per 100 epithelial cells are seen, lymphocytic colitis is diagnosed [11]. The use of a budesonide taper starting from 9 mg for six to eight weeks is recommended for treatment, which the above patient received [11].

In patients with non-resolving diarrhea (3 - 4 bowel movements/day) and/or a history of unresolved *C. difficile* infections, it is crucial to do a colonoscopy with random biopsies [8]. The direct inspection of the colonic mucosa using colonoscopy showed normal findings, while the biopsy showed lymphocytic colitis [11]. The clinical picture of this patient may have been caused by a connection between *C. difficile* infection and microscopic colitis.

A *C. difficile* infection or its treatment may precipitate microscopic colitis as a side effect. On the other end, individuals who have microscopic colitis may have an increased susceptibility to *C. difficile* infections [9]. There are several proposed mechanisms that could have caused it. Firstly, microbiome changes in the gut create an environment conducive to the chronic inflammatory responses characteristic of microscopic colitis [12]. Secondly, it could be due to direct epithelial damage and active inflammatory cascades involving neutrophil chemotaxis and cytokine release leading to aberrant immune response in a genetically susceptible individual [13]. Thirdly, the toxins disrupt intracellular junctions, causing epithelial barrier dysfunction and increasing intestinal permeability [14].

We think that this patient's presentation indicates that she had lymphocytic colitis at the time of her *C. difficile* infection, which is corroborated by recent case reports [9]. NSAIDs and PPIs were linked to an increased risk of developing MC, according to a study by Masclee *et al.*; however, other medications, such as SSRIs, probably raised the risk of diarrhea in the setting of MC but did not contribute to the disease's development [6]. Older age, female sex, and smoking are further

known risk factors for MC [11].

According to Khalili *et al.*, patients with MC had a higher prevalence of prior gastrointestinal infections than controls did, 7.5% versus 3.0%, respectively [9]. As previously mentioned, they found that *C. difficile* was among the gastrointestinal infections associated with a higher risk of acquiring MC and a higher correlation with the CC than the LC [9].

4. Conclusions

In conclusion, chronic diarrhea should be adequately worked up. A chronic diarrhea panel should include celiac serology, tests for SIBO, lactose intolerance, fecal elastase, and calprotectin along with a good history, including family and surgical history. A colonoscopy should have a low threshold if testing is negative, and a normal macroscopic picture should not discourage random biopsies. Medications associated with microscopic colitis should be evaluated and discontinued if diagnosed. A low threshold for *C. difficile* diarrhea should be kept in patients with chronic diarrhea and recent antibiotic use. Any recurrent *C. difficile* should also prompt a colonoscopy.

The limitations to this study include the inability to establish causality, limited generalizability, and a lot of confounding factors such as prior history of cholecystectomy, chronic antibiotic use, and use of SSRIs. Further studies should focus on examining the temporal relationship between *C. difficile* infection and microscopic colitis and trials involving SSRI discontinuation strategies and budesonide maintenance protocols.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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