The Egyptian Journal of Hospital Medicine (January 2024) Vol. 94, Page 669-671

Challenging Case: A Case Report on Crohn's Disease Emerging after The Initiation of Capecitabine for Colorectal Cancer

Anas Zaher[1], Hassan Elsaygh[2]

New York-Presbyterian Brooklyn Methodist Hospital, Internal Medicine Department, Brooklyn, NY,11215, USA 1

University of Debrecen, Internal Medicine Department, Egytem Sugarut 1, Debrecen, Hungary, 2

Corresponding author: Anas Zaher, email:qks9002@nyp.org,mobile:001 646 705 2347, ORCID: 0009-0004-6949-4384

ABSTRACT

Background: Inflammatory bowel disease (IBD) is a chronic inflammatory condition that affects the gastrointestinal tract. This group of disorders includes Crohn's disease and ulcerative colitis. Diagnosis of IBD involves a comprehensive approach that combines medical history, physical examination, laboratory tests, endoscopy, imaging, and occasionally biopsy of intestinal tissue. Patients with IBD have an increased risk of developing colorectal adenocarcinoma, a type of colorectal cancer. However, IBD induced by surgical resections of the intestines or chemotherapy drugs is extremely rare.

Objective: This study aimed to throw the light on the importance of careful evaluation and accurate diagnosis in patients presenting with symptoms suggestive of both types of IBD.

Subject and methods: This abstract presents a challenging case in which a patient was initially suspected to have chemotherapy-induced colitis but was ultimately diagnosed with IBD-associated colorectal cancer.

Results: The case highlighted the importance of careful evaluation and accurate diagnosis in patients presenting with symptoms suggestive of both IBD, as the treatment approaches and prognoses can significantly differ between the two conditions.

Conclusion: Capecitabine, commonly used in cancer treatment, can induce colitis with symptoms that overlap with those of inflammatory bowel disease (IBD). Distinguishing between capecitabine-induced colitis and IBD is challenging due to similar clinical presentations. Discontinuation of capecitabine often leads to symptom improvement, but in IBD cases, additional therapies like steroids and biologics may be necessary. Close monitoring and further evaluation are crucial for accurate diagnosis and appropriate treatment strategies in patients experiencing gastrointestinal toxicity from capecitabine-based chemotherapy.

Keywords: Inflammatory bowel disease, Colorectal cancer, Capecitabine, Chemotherapy-induced colitis.

INTRODUCTION

The intricacies of distinguishing between inflammatory bowel disease (IBD) and chemotherapy-induced colitis are exemplified in a compelling case study. A 61-year-old male, initially suspected of chemotherapy-related colitis, presented with persistent symptoms post-treatment cessation. Meticulous evaluation uncovered the unexpected: Crohn's disease. This underscores the challenges of differentiation, where chemotherapy-induced symptoms often resolve upon cessation, while IBD demands sustained intervention.

Chemotherapy-induced colitis's nebulous pathogenesis contrasts with IBD's complexity, spotlighting the critical need for precise diagnosis. This case also unveils the potential link between surgical interventions, chemotherapy, and the emergence of chronic inflammatory conditions. The narrative emphasizes accurate diagnosis's paramount importance, steering clinicians to tailored treatments through continuous monitoring and multidisciplinary collaboration. In the interplay of chemotherapy and inflammation, this case illuminates the necessity of unraveling underlying conditions to guide effective therapeutic choices.

CASE PRESENTATION

A 61-years-old male with a past medical history of diabetes mellitus type II and hyperlipidemia recently went for his first screening colonoscopy and was found to have sigmoidal adenocarcinoma. The patient was referred by his primary care physician for a colorectal cancer routine screening; at that time, he had no abdominal pain, bloody stool, or further signs of disease. His labs were unremarkable, with no anemia. The patient was compliant with taking his medications, which included metformin, pioglitazone, empagliflozin, sitagliptin, omega 3, and atorvastatin.

He had a mild allergy only to Penicillin. Family history was significant only for diabetes mellitus type II on his father's side and denied any smoking or alcohol intake history in the past. His colonoscopy showed a non-obstructing, 2 cm size mass in the sigmoid with multiple polyps. Biopsy was obtained from different regions, revealing well-differentiated adenocarcinoma with no acute changes on the pathology report. He underwent computed tomography (CT) chest, abdomen, and pelvis with contrast, which revealed no metastatic disease. The surgery team was consulted, and he underwent a laparoscopic left hemicolectomy.

Received: 10/10/2023
Accepted: 10/12/2023

The patient was diagnosed with stage IIIB sigmoid adenocarcinoma. Postoperatively, he was stable and had no complications. He was discharged to follow up with the oncology service for chemotherapy initiation. The patient was started on adjuvant gchemotherapy around two months after his diagnosis, which included oxaliplatin 130 milligrams/square meter and capecitabine 500 mg oral tablet. After two weeks, the patient started to have mouth sores followed by loose stools, which got complicated by abdominal pain and bright red per rectum. He was having more than 10 bowel movements, so he went to the Emergency Department (ED).

In the ED, the patient's vital signs were afebrile and normotensive. On physical examination, tenderness was found in the right lower quadrant and mouth soreness. Lab tests revealed no neutropenia but a mildly elevated C-reactive protein (CRP). Initial investigations, including blood cultures, gastrointestinal (GI) polymerase chain reaction (PCR) panel, and Clostridium difficile stool antigen tests, which yielded negative results. After one week of hospitalization, he received supportive therapy and Imodium. His symptoms were attributed to possible chemotherapy-induced colitis, and so the decision was made to hold chemotherapy for now. He was discharged to follow up with the gastrointestinal team outpatient.

Due to persistent diarrhea (>16 episodes) and abdominal tenderness, the patient was readmitted again after 1 week of discharge, despite being off chemotherapy during all that time.

This time a CT scan of the abdomen and pelvis was done, showing wall thickening of the cecum and terminal ileum, suggesting possible inflammatory or chemotherapy-related colitis. His fecal calprotectin (FCP) levels were elevated to 580 μg/g (≤ 50 μg/g) and GI PCR panel was negative.

A colonoscopy was scheduled on the 3rd day of readmission showing the terminal ileum contained a few semi-sessile polyps (Figure 1). The colonoscopy revealed granularity and ulceration throughout the examined colon, specifically at the site of the end-to-end colo-colonic anastomosis. Biopsy results confirmed active chronic inflammation involving the ileum, ascending colon, and transverse colon and no dysplasia, consistent with Crohn's disease image.

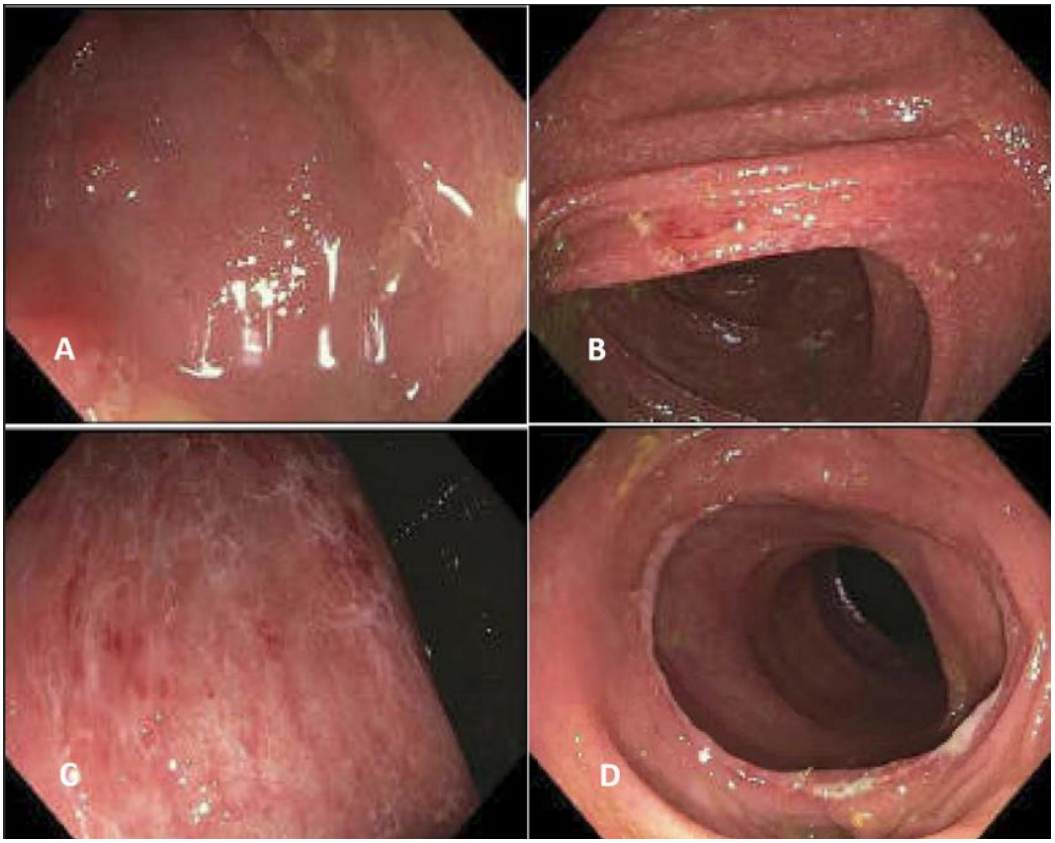

Figure (1): Colonoscopy revealed granularity and ulceration throughout the examined colon, specifically at the site of the end-to-end colo-colonic anastomosis (D). There was no evidence of pseudomembranous colitis. A: represents the terminal ileum, B: represents the ascending colon, C: represents the transverse colon, D: colo-colonic anastomosis.

After multidisciplinary discussions with different teams, the patient was diagnosed with Crohn's disease due to persistent inflammation after holding the chemotherapy. Given the findings, the patient was started on intravenous steroids, resulting in symptomatic improvement, and was discharged on the 8th day with prednisone PO 40 mg daily. The patient was evaluated by the GI team in a clinic one week after discharge; the patient had significant improvement in his symptoms overall, repeat FCP down trended to 150 μg/g. He started on slow tapering prednisone followed by prednisone 2.5 mg PO for two weeks.

After completing prednisone by one week, he was reevaluated by oncology service for adjuvant chemotherapy and deemed stable for restarting his oxaliplatin 130 milligrams/square meter and capecitabine 500 mg oral tablet. The patient had so far completed one month of chemotherapy with no recurrence of symptoms. After two months, the patient had a repeat colonoscopy showing chronic inactive colitis changes, suggestive inactive stage of the disease.

DISCUSSION

Capecitabine, a prodrug of the antimetabolite 5-fluorouracil, is commonly used as an adjuvant treatment for colon, breast, and gastric cancers. However, its toxicity profile can cause gastrointestinal symptoms such as diarrhea, nausea, and abdominal pain and in rare cases, it can cause necrotizing enterocolitis and hand-foot syndrome [1].

Differentiating chemotherapy-induced colitis or immunotherapy-induced colitis from inflammatory bowel disease (IBD) poses a significant challenge due to overlapping of clinical symptoms and diagnostics. While several cases of capecitabine-induced colitis have been reported in the literature, only two cases have shown an association between capecitabine and IBD [2]. The precise pathogenesis of chemotherapy-induced colitis remains unclear but could involve mucosal injury caused by direct chemotherapy toxicity, weakened host defense against intestinal microorganisms, or microvascular disruption [3]. Additionally, there have been reports of severe ischemic colitis following chemotherapy with cisplatin and capecitabine, with an association found between arterial thrombosis of mesenteric blood vessels and the development of colitis [4].

Differentiating between capecitabine-induced colitis and IBD is crucial for determining appropriate treatment strategies. Patients with capecitabine-induced colitis typically show improvement after discontinuation of the medication, and, in some cases, with the addition of antidiarrheal medication, symptoms should resolve in a few days. However, in cases of IBD, steroids and additional therapy with biologic agents are often required. An accurate diagnosis is therefore essential, necessitating further evaluation [5]. In our case, the patient's symptoms persisted even after discontinuing capecitabine. The patient was discharged with antidiarrheal medications but was readmitted due to the progression of diarrhea. After performing a colonoscopy and initiating steroid treatment, the patient's symptoms resolved. When patients treated with capecitabine-based chemotherapy present with gastrointestinal toxicity symptoms, it is crucial to consider ischemic colitis as a potential cause. This is particularly true when the patient has a normal white blood cell count and the diagnosis of pseudomembranous colitis has been excluded [4]. On the other hand, chemotherapy-induced IBD is more likely to persist even after discontinuing therapy and often requires immunosuppressive treatment to alleviate symptoms. Close monitoring is essential for understanding the disease course in these patients.

CONCLUSIONS

In conclusion, capecitabine, commonly used in cancer treatment, can induce colitis with symptoms that overlap with those of inflammatory bowel disease (IBD). Distinguishing between capecitabine-induced colitis and IBD is challenging due to similar clinical presentations. Discontinuation of capecitabine often leads to symptom improvement, but in IBD cases, additional therapies like steroids and biologics may be necessary. Close monitoring and further evaluation are crucial for accurate diagnosis and appropriate treatment strategies in patients experiencing gastrointestinal toxicity from capecitabine-based chemotherapy.

Funding: No external funding was received for this research.

Conflict of Interest: The authors declare that they had no conflicts of interest related to this research work. The content of this manuscript was not influenced by any financial or personal relationships with individuals or organizations that could have biased the findings or conclusions.

REFERENCES

1. **Lam S, Guchelaar H, Boven E (2016):** The role of pharmacogenetics in Capecitabine efficacy and toxicity. **doi:10.1016/j.ctrv.2016.08.001.**
2. **Trontzas, I (2022):** Capecitabine-associated enterocolitis: Narrative literature review of a rare adverse event and a case presentation. **doi:10.1080/1120009x.2021.2025316.**
3. **Halen C, Kin N (2012):** Chemotherapy–induced colitis. **doi:10.5772/28125.**
4. **Cetin B (2010):** Ischemic colitis after Capecitabine plus cisplatin treatment in advanced gastric cancer. **doi:10.1007/s11239-010-0525-x.**
5. **Schutte B, Vijayasekar K, Jenkins E (2022**): S271 capecitabine-induced ileitis vs late-onset crohn's disease: A case report. **doi:10.14309/01.ajg.0000867488.18579.d0.**