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# *Capecitabine Induced Ileocolitis with Acute Colonic Pseudo-Obstruction: A Case Report*

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***Abstract***

*Capecitabine is a commonly used chemotherapeutic drug used in gastrointestinal and non-gastrointestinal malignancy. Mild GI toxicity, like nausea, vomiting, and diarrhea, is common and does not require drug withdrawal. Ileocolitis with pseudo-obstruction is uncommon, with just a few cases described to date. This report describes a case of Capecitabine-induced acute ileocolitis presenting as acute colonic pseudo-obstruction, which was managed conservatively.*

*Keywords: Capecitabine; Ileocolitis; Colonic Pseudo-Obstruction*

## Introduction

Capecitabine is a 5-fluorouracil (5-FU) oral prodrug used in numerous chemotherapy regimens to treat breast, pancreatic biliary, and other gastrointestinal (GI) tract cancers. Mild gastrointestinal toxicity is well known. Severe adverse effects are also noted sporadically, causing serious concerns for chemotherapy withdrawal. Our independent literature research showed only a few Capecitabine-induced ileocolitis cases; however, its complication to acute colonic pseudo-obstruction was not reported. We report a case of Carcinoma Gall bladder who received Capecitabine as part of adjuvant chemotherapy and developed ileocolitis with acute colonic pseudo-obstruction, which was managed conservatively.

## Case Report

A 65 year old gentleman diagnosed with carcinoma gallbladder (stage 1b) underwent open radical cholecystectomy with extended hepatectomy. Post-operatively he received the first cycle of chemotherapy regimen with a single dose of Capecitabine and cisplatin. One week post-chemotherapy, He developed haematochezia and generalized abdominal distension with pain necessitating hospital admission. At admission, He appeared dehydrated, febrile, and had tachycardia. His abdomen was tender, grossly distended, and resonant with hypoactive bowel sounds on percussion. His routine laboratory results showed mild leukopenia (WBC 3600 cc/mm3 with no neutropenia (Absolute neutrophil count -1728), mild hypokalaemia (k+ - 3.4), and a C - reactive protein of 231 mg/L. Stool studies were negative. In the following days, he developed obstipation and distended abdomen with absent bowels sound on examination (Table 1). Abdominal X-rays showed markedly dilated colonic loops (Figure 1). Colonoscopy showed only diffuse erythema and erosions in the entire colon along with terminal ileitis (Figure 2). Biopsy showed chronic moderately active colitis with negative for dysplasia and negative herpes simplex and cytomegalovirus immunohistochemistry. He was treated conservatively with empirical antibiotics, IV hydration, kept on nil per oral, and started on TPN. A colonoscopy-guided flatus tube was inserted, and over the next five days, his abdominal distension was relieved, and he started to have bowel movements. He was started with oral feed and was discharged home. Repeat colonoscopy after

four weeks showed normal colonic mucosa and vascular pattern.

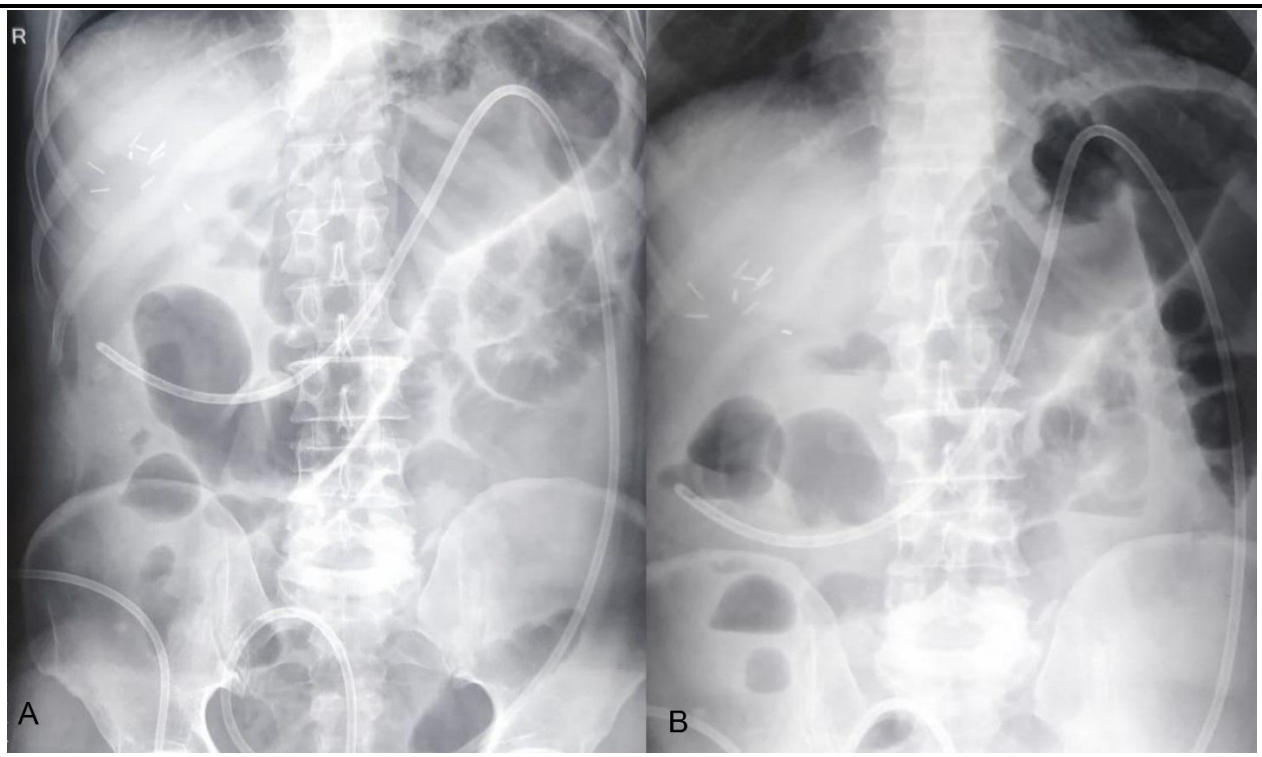


**Figure 1:** Abdominal X-rays showing markedly dilated colonic loops.

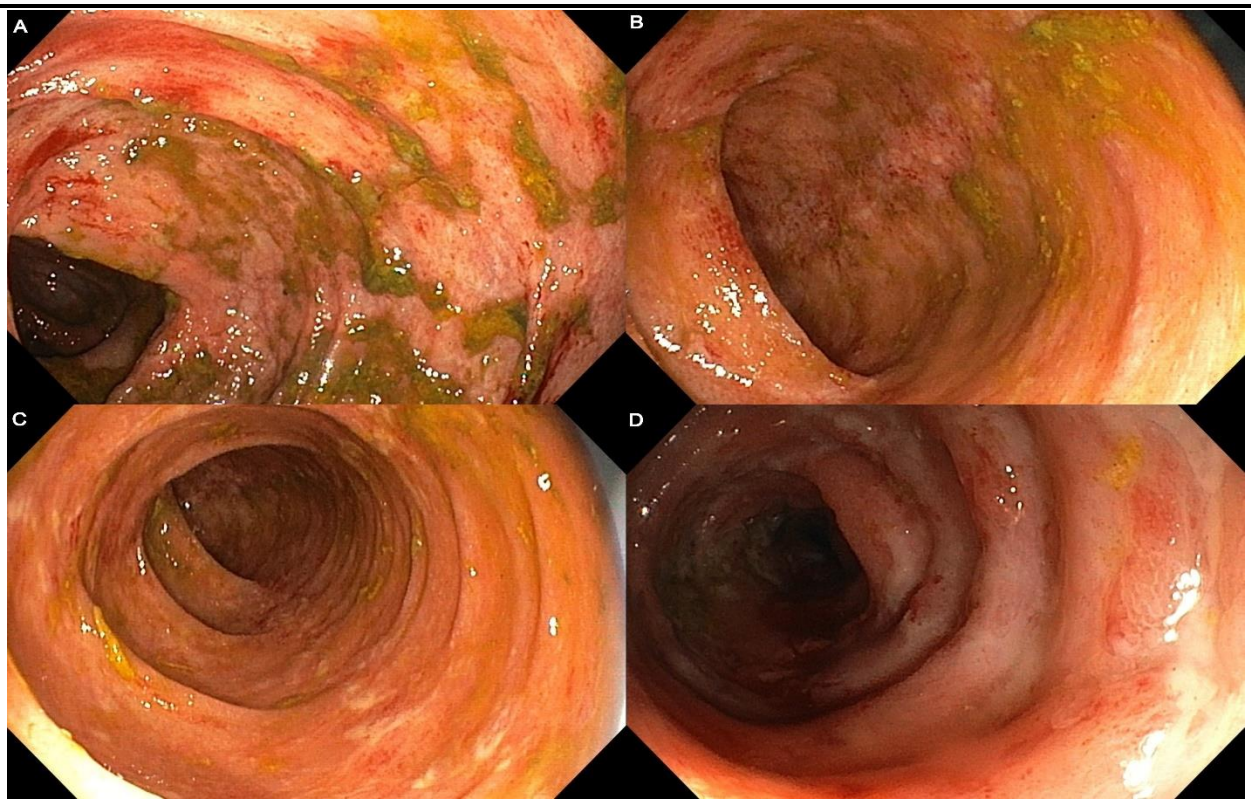


**Figure 2:** Colonoscopy showing only diffuse erythema and erosions in the entire colon along with terminal ileitis.

**Table 1:** Investigations.

| Investigation | Case | Normal range |
|---|---|---|
| Hb | 9.4 mg/dl | 12-14 gm/dl |
| TLC | 3600 $mm^3$ | 4000-11,000/$mm^3$ |
| Platelet | 191000/ $mm^3$ | 1,50,000-4,00,000/$mm^3$ |
| ESR | 42 mm/h | 0-20 mm/h |
| CRP | 33 mg/dl | < 6 mg/dl |
| AST/ALT | 24/33 U/dl | 2-50 U/dl |
| Creatinine/Urea | 0.9/ 22 mg/dl | 0.6-1.0 mg/dL/10-50mg/dL |
| Serum Na+ | 134 mEq/L | 135-145 mEq/L |
| Serum K+ | 3.4 mEq/L | 3.5-5.0 mEq/L |
| Serum Cl- | 99 mEq/L | 95-105 mEq/L |
| Serum Ca++/ Mg | 7.6/1.91 mEq/L | 8.4-10 /1.5-2.5 mEq/L |
| S. protein /albumin | 5.2 / 4 g/dL | 7.5/5.5g/dL |
| HBsAg/ Anti HCV/ HIV | Non-reactive | - |

*Hb: Haemoglobin; TLC: Total leucocyte count; AST: Aspartate transferase; ALT: Alanine transferase; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HCV: Hepatitis C virus; HIV: Human Immunodeficiency virus; HbsAg: Hepatitis B surface antigen*

## Discussion

Capecitabine is a Fluoropyrimidine analogue and thymidylate synthase inhibitor. It is an oral prodrug of 5-fluorouracil (5-FU). It is widely used as monotherapy or in combination with other antineoplastic drugs to treat patients with breast, pancreaticobiliary, and various other gastrointestinal tract malignancies [1]. GI toxicities are well known and a significant cause of chemotherapy withdrawal. Capecitabine prolongs the release of 5-FU, resulting in a greater intratumoral drug concentration. The likely effect of this leads to various GI side effects. The potential impact of this leads to a diverse range of GI side effects [2]. Side effects of Fluoropyrimidine toxicity include mild GI symptoms such as nausea, vomiting, mucositis, and diarrhea requiring frequent dose modifications [3]. In some rare instances, severe adverse events such as GI hemorrhage, paralytic ileus, necrotizing enterocolitis, and colonic perforation were also reported [4]. Chemotherapeutic effects were primarily found in Lieberkühn crypts owing to crypt epithelial cell apoptosis, mucin depletion, and vasculitis [5]. Mucosal necrosis is triggered by the activation of pro-inflammatory cytokines generated by direct mucosal damage caused by free radical production and a rapid shift in intestinal microflora caused by the cytotoxic action of chemotherapeutic agents. Female sex, Caucasian race, dihydropyrimidine dehydrogenase (DPD) impairment, and Diabetes mellitus are all predictive variables for fluoropyrimidine cytotoxicity [6]. DPD is a primary and rate-limiting enzyme involved in the metabolism of 5-FU. DPD deficiency leads to decreased clearance of 5-FU from the body causing prolonged exposure to the drug, but the prevalence of this enzyme deficiency is usually low (up to 3%). Approximately 10 % of patients may also exhibit secondary lactose intolerance and cause osmotic diarrhea; however, this hypolactasia can be reversible [7,8]. Capecitabine colitis should be diagnosed based on temporal correlations, consistent endoscopic and pathological alterations, and negative stool cultures. Clostridium difficile infection, ischemic, and neutropenic enterocolitis should be ruled out [9]. Management should be conservative, including withholding chemotherapy, Bowel rest (Nil per oral), Adequate hydration, fluid and electrolyte management, IV antibiotics, Total parenteral nutrition, and avoiding antimotility agents [10]. Surgical intervention should be reserved for complicated cases with severe toxic

megacolon and perforation peritonitis. Successful treatment with Uridine triacetate [11], cholestyramine [12], budesonide [13], and octreotide [14] have been reported in a few case reports.

In conclusion, ileocolitis occurs in a small percentage of capecitabine patients, and the development of acute colonic pseudo-obstruction is unusual. It is critical to maintain a high level of suspicion and intervene as soon as possible. The initial treatment strategy is discontinuing chemotherapy, close monitoring, and supportive care. Specific management protocols and histopathology results have yet to be developed.

## Author Contribution

Budumuri Gautam V Kumar conceptualized and wrote the first draft; Purna Ch Sethy edited the manuscript. All authors reviewed and approved the published version of the manuscript.

## Conflicts of interest and Financial Disclosures

None.

## Previous Presentation

This case was presented at Korean Digestive Disease Week (KDDW-2019); 28-30 November 2019, Grand Hilton Seoul Hotel, Seoul, South Korea.

## Informed Consent

Written consent is obtained from the patient

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