

Paralytic Ileus- A Rare but Serious Side-effect of Oral Capecitabine

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ABSTRACT

Paralytic ileus is a condition where the intestine becomes paralysed in the absence of any mechanical obstruction. The common causes are intra-abdominal surgery, severe metabolic problems and drugs. Many anticancer drugs and targeted therapy drugs are important causes of this toxicity. Early diagnosis and appropriate management are essential because if prolonged and untreated it can lead to death in the same way as in acute mechanical obstruction. Capecitabine is an orally administered prodrug of 5-Fluorouracil (5-FU) routinely used in breast and colorectal cancer. Paralytic ileus is a rare but recognised serious side-effect of oral capecitabine. Hereby, authors present a case of 53-year-old male patient, who was a postoperative case of colon cancer and was treated by adjuvant capecitabine based chemotherapy and subsequently, developed capecitabine induced paralytic ileus. He was managed successfully by standard conservative measures, avoiding unnecessary laparotomy.

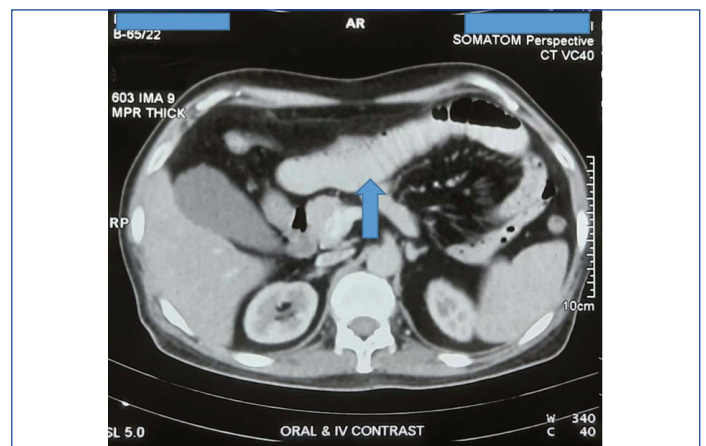
Keywords: Colon cancer, Fluorouracil, Intestinal obstruction, Laparotomy

CASE REPORT

A 53-year-old male patient who was a known case of type 2 diabetes mellitus on oral metformin 500 mg and glimepiride 1 mg twice a day for last two years presented with acute onset vomiting, central colicky abdominal pain and abdominal distension since two days in September 2021. He was diagnosed with acute intestinal obstruction and emergency exploratory laparotomy was planned. During laparotomy, caecal growth was found and he underwent right hemicolectomy with end ileostomy and distal mucus fistula of transverse colon. Biopsy showed moderate to poorly differentiated adenocarcinoma with signet ring cell component. Treatment planned for him was oxaliplatin and capecitabine based adjuvant chemotherapy but it was postponed due to deranged renal function. In January 2022, intravenous (i.v.) oxaliplatin (165 mg every two weeks) followed by oral capecitabine (1.5 gm in morning and 1 gm in evening for 14 days in two weeks cycle) was started after improvement in renal function.

On day 10 of cycle 1 (C1D10), the patient presented with a two-day history of colicky central abdominal pain, bilious vomiting and abdominal distension. His vitals were stable but bowel sound was sluggish. His total leucocyte count was 14,800/cumm, serum creatinine was 1.5 mg/dL and urea was 28 mg/dL. His haemoglobin, platelet count and liver function test were within normal limits. An erect abdominal x-ray showed multiple air fluid levels and a supine film showed multiple dilated jejunal loops [Table/Fig-1]. A Computed

Tomography (CT) scan with i.v. and oral contrast showed contrast filled prominent jejunal loops of 25-28 mm without any transition point or free fluid or free air suggestive of paralytic ileus [Table/Fig-2].

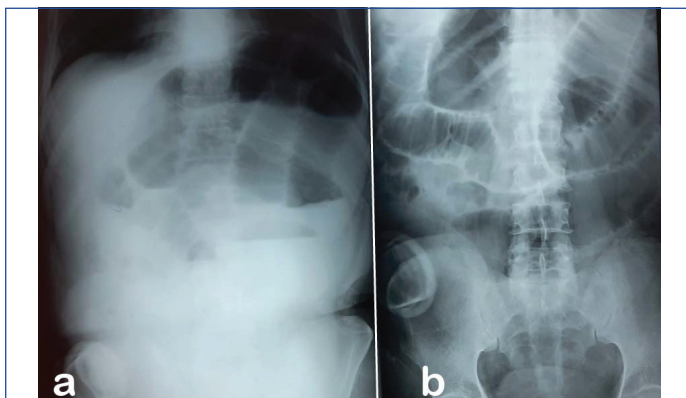


[Table/Fig-2]: Axial image of contrast CT of abdomen showing dilated jejunal loops (arrow).

Nasogastric tube was inserted for gastric decompression and transurethral Foley catheterisation was done for urine output monitoring. Capecitabine was discontinued, i.v. fluid, i.v. analgesics and i.v. antibiotics were started. By day 5 of conservative management, ileus was resolved and stoma became functional. He was discharged on day 7 of admission and was referred to medical oncologist for modification in next cycle of chemotherapy.

DISCUSSION

Paralytic ileus is a rare but recognised side-effect of oral capecitabine with reported incidence of 4-6% [1,2]. The first published case report in 2008 described two cases of capecitabine induced paralytic ileus in patients of breast cancer [3]. A phase III study comparing capecitabine with lapatinib and capecitabine alone reported one case of small bowel obstruction related to capecitabine [4]. A similar report from Netherlands in 2011, also recognised similar toxicity seen on small bowel following use of oxaliplatin, bevacizumab and capecitabine [5]. In 2012, a case report from UK showed a case of ileitis secondary to capecitabine in a patient who was on adjuvant chemotherapy for colon cancer and the patient developed ileitis on day 16 of second cycle of chemotherapy [6].



[Table/Fig-1]: Abdominal x-ray. a) Erect film showing multiple air fluid levels; b) Supine film showing multiple dilated jejunal loops.

The pathophysiology of capecitabine induced paralytic ileus is not clear. There may be an association between 5-FU metabolites and peripheral neuropathy. Another possible reason may be reduction in gastric mucosal blood flow by 5-FU [7,8].

Similar to the present case, in all the reported cases [Table/Fig-3] [3-6,9], this condition was managed successfully by conservative management except one reported case in Australia in 2013, where paralytic ileus was not resolved by conservative management and after giving i.v. neostigmine, it was resolved within 48 hours [9].

Authors	Year	Place	Aetiology	Treatment	Outcome	Additional treatment
Laudadio L et al., [3]	2008	Italy	Breast cancer	Conservative	Resolved	Nil
Cameron D et al., [4]	2008	UK	Breast cancer	Conservative	Resolved	Nil
Bouma G and Imholz ALT, [5]	2011	Netherlands	Colon cancer	Conservative	Resolved	Nil
Radwan R et al., [6]	2012	UK	Colon cancer	Conservative	Resolved	Nil
Mak G et al., [9]	2013	Australia	Colon cancer	Conservative	Not resolved	i.v. Neostigmine
Present case	2022	India	Colon cancer	Conservative	Resolved	Nil

[Table/Fig-3]: Summary of few published cases in literature [3-6,9].

CONCLUSION(S)

The present case is the first reported case of capecitabine induced paralytic ileus from India. The present case highlights the potential serious side-effect related to use of capecitabine and also emphasises on timely diagnosis and appropriate conservative management of this condition to avoid unnecessary laparotomy. The factors which make a patient susceptible to capecitabine induced paralytic ileus, should be investigated further.

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