# Ileocolic Anastomotic Site Recurrence

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## Abstract

Colorectal cancer is associated with high mortality. 50% of the patients tend to develop recurrence even after curative treatment. Most of the recurrences are found in the first three years and a few in five years. Early detection of recurrence is important to improve a patient's survival. Many follow-up plans have been devised for surveillance. Very scant evidence is available in the literature for palliative treatment by chemotherapy of recurrent bowel adenocarcinoma. In advanced cases of recurrence at Ileocolic anastomosis in which medical treatment has failed ileocolic resection is indicated. There is 70% anastomotic recurrence after ileocolic resection.

We are reporting a case of a 47-year-old Asian female who had recurrent colorectal anastomotic site adenocarcinoma and developed peritoneal metastasis. She underwent palliative surgery followed by chemotherapy and will be under observation.

**Keywords:** *Adenocarcinoma, recurrent, palliative surgery, chemotherapy.*

## INTRODUCTION

Recurrence of adenocarcinoma of the colon and rectum at the anastomotic site is a specific pattern of local failure. The most common malignancy of the Colon is Adenocarcinoma [1]. The most important prognostic factor is curative resection, 67% of patients with adenocarcinoma receive curative resection. 39% develop recurrence even after curative resection [2]. There is no randomized control trial available for the benefit of adjuvant chemotherapy after curative resection or palliative chemotherapy for recurrent small bowel adenocarcinoma. In a few cases of advanced or recurrent small bowel adenocarcinoma, surgical intervention is useful [3].

## CASE PRESENTATION

47 Years Old female known case of Adenocarcinoma Colon presented in the outpatient surgical department with 6 months of abdominal pain. On examination, the abdomen was mildly distended and per rectal examination was unremarkable. She was diagnosed with small bowel obstruction due to recurrence at anastomotic site and metastatic lymphadenopathy and underwent palliative resection followed by chemotherapy.

## PAST HISTORY

Her Subtotal Colectomy and Liver nodule resection was done in 2018 in a periphery hospital. Histopathology included a specimen of the colon which showed differentiated infiltrating adenocarcinoma and all resection margins were tumor-free. Eight out of thirty-seven lymph nodes showed tumor metastasis with perinodal extension. However, liver and diaphragmatic nodules were positive for tumor metastasis. She received 7 cycles of Xeloda and had yearly surveillance colonoscopy and dilatation of anastomotic site. Colonoscopy done later showed tight stricture at the anastomotic site with ulcerated mucosa, CRE dilatation was performed. Biopsy taken from the stricture site showed intact colonic mucosa with rare atypical cells seen.

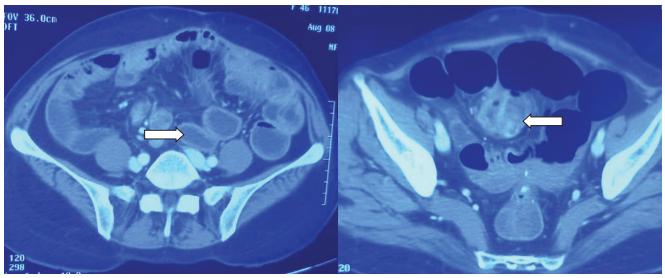

**Fig. (1a&1b):** CT scan abdomen axial view showing dilated small bowel loops likely ileal loops with circumferential thickening of ileal loops.

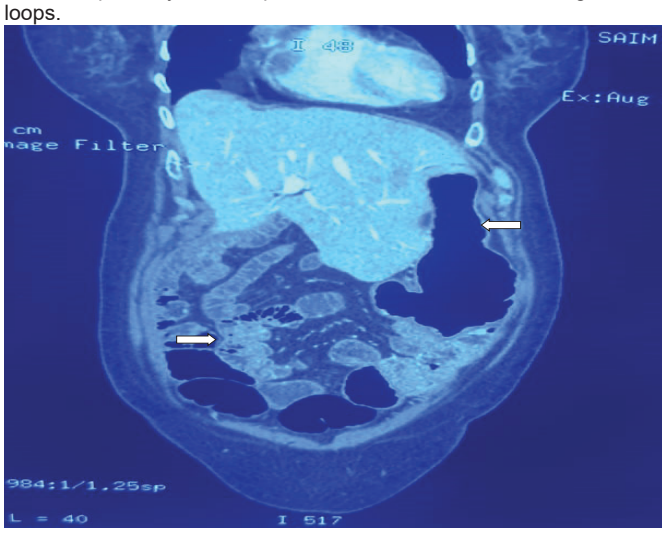


**Fig. (2):** CT scan abdomen coronal image showing dilated stomach and dilated small bowel loops likely ileo-jejunal.

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## RADIOLOGICAL DETAILS

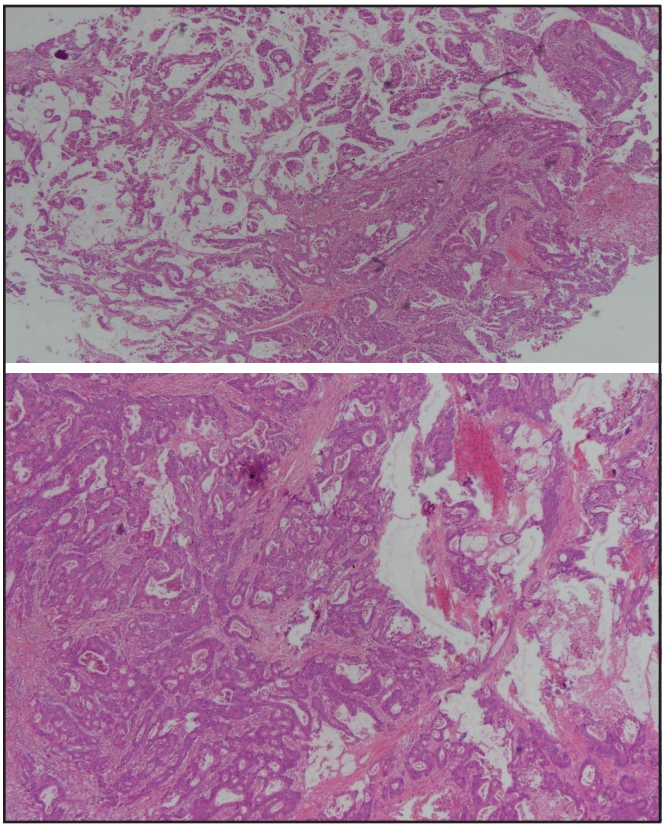
CT scan **(Figs. 1&2)** showed a re-demonstration of enhancing circumferential mural thickening in distal ileal loops showing mild interval increase in thickness measuring 1cm posteriorly resulting in luminal narrowing and mild prominence of proximal ileal and jejunal loops. Redemonstration of enlarged mesenteric lymph nodes in the mid-lower abdomen, appearances were suspicious for recurrence of neoplastic disease with metastatic lymphadenopathy.

## TREATMENT COURSE

Colonoscopy done later showed tight stricture at the anastomotic site with ulcerated mucosa, CRE dilatation was performed. Biopsy taken from the stricture site showed intact colonic mucosa with rare atypical cells seen.

She was planned for exploratory laparotomy for bowel obstruction. There were multiple adhesions for which adhesiolysis was done. There was a 3x3cm mass at the previous ileocolic anastomotic site, resection anastomosis was done and the specimen was sent for histopathology. The post-operative course was unremarkable.

## HISTOPATHOLOGY



**Figs. (3&4):** Sections examined

**Figs. (3&4)** revealed malignant infiltrating neoplasm present in the form of sheets of well to moderately formed glandular architecture. These atypical glands are lined by stratified columnar epithelium with marked atypia, round nuclei, prominent nucleoli and moderate eosinophilic cytoplasm. The background shows extracellular mucin along with mixed inflammatory infiltrates. The tumor is extending through the muscle layer into the surrounding subserosal fat.

## TUMOR BOARD DISCUSSION

In the multidisciplinary meeting involving general surgery, oncology and radiology, it was discussed that its recurrence of adenocarcinoma at the anastomotic site. It further needs CT scan chest with contrast and palliative chemotherapy. She has received 8 cycles of Folfox till now.

## ONCOLOGIST PERSPECTIVE

Colorectal cancer is the third most commonly occurring cancer in men and the second most commonly occurring cancer in women and stands to be the second most common cause of mortality [4]. Even after receiving adequate treatment for primary colon cancer that is Surgery and/or chemotherapy, still there are 25-40% chances of disease recurrence [5]. According to studies the 5-year overall recurrence rate was 9.3% for Stage I tumors, 27.2% for Stage II and 56.1% for Stage III [6]. The most common sites of recurrence are liver, lung, peritoneal and local recurrence [7]. Local recurrence (LR) is a term used when the tumor is in and around the tumor bed including pericolic fat, adjoining mesentery and lymph nodes (extramural recurrence) or it is in the suture or staple line of the anastomosis (intramural/ anastomotic recurrence) [8]

Anastomotic recurrence of colorectal cancer occurs in approximately 2–15% of cases [9]. Any recurrence at a local site without any systemic disease that occurs within 2 years from previous surgery is deemed as a local recurrence otherwise it is taken as a second primary or metastases [10]. There are various theories postulated to be the cause of anastomotic recurrence. One of them, which was presented by Cole and Goligher in 1956, supported by their paper [11] was that exfoliated cells during surgery, either due to tumor perforation or when it is cut, they implant on the suture line and lead to local recurrence. Another theory is the instability of the mucosa at the site of an anastomosis, or positive distal margin of resection [12] or a margin <2cm can be a reason for anastomotic recurrence.

Experimental studies have been conducted on mice to know the reasons for recurrences. One such study from Spain has shown that the postoperative intra-abdominal infection increases angiogenesis and tumor recurrence after surgical excision of tumor in mice [13]. Despite the hypothetical mechanisms and alleged recurrence factors for AR, relevant clinicopathologic variables are not readily available because of the low incidence of AR.

How shall Anastomotic recurrence be treated, depends upon the magnitude of recurrence. That is in case of

local recurrence only, then surgery with curative intent should be offered. Curative surgery was defined as complete resection of any measurable disease and it should be without the involvement of the resection margin. Depending on tumor location and number, right or left colectomy, anterior resection, low anterior resection, total colectomy were performed. Surgery of local recurrence improves 5-year survival to about 30-35 % [14]. Local recurrences other than anastomotic recurrence, even if they are invading surrounding structures is not a contraindication and should be offered resection [15]. If possible, Anastomotic recurrences should be addressed by re-excision of the anastomosis with 5-cm clear margins.

If there is systemic recurrence with visceral involvement or unresectable disease then the patient should be treated with systemic treatment first and undergo salvage surgery in case of conversion to resectable disease. If anastomotic recurrence is causing symptoms, then symptomatic anastomotic recurrences may be resected with limited mesenteric dissection to offer palliation.

After local treatment, comes the question of giving chemotherapy to such patients. It has been seen that in patients who have hepatic or lung metastases, after curative resection, the course of an active systemic therapy regimen should be given for a total treatment time of 6 months. As isolated anastomotic recurrences are rarely found so no formal guidelines are available but overall there is consensus that chemotherapy should be given to patients [16, 17]. The rationale behind adjuvant chemotherapy after resection of metastases can be extrapolated from a study by Langer *et al.* [18] who studied a group of CRC patients who underwent surgical resection of liver metastases and for the first time, they compared metastasectomy alone vs metastasectomy followed by systemic 5-FU/ LV treatment. DFS and OS were better in the adjuvant chemotherapy arm vs the surgery alone arm (4-year DFS was 45%, vs 35%, and 4-year OS was 57%, vs 47%) but the trial was prematurely closed due to slow accrual and statistical significance was not reached either for OS or PFS (p = 0.35 and p = 0.39, respectively). Then in another trial, Nordlinger *et al.* [19] randomized 364 patients with resectable liver metastases from CRC. Comparing the combination of surgery and perioperative FOLFOX-4 treatment (6 cycles before and 6 cycles after surgery) with liver resection alone, they showed that the 3-year PFS was better in the chemotherapy group compared with controls. However, the gain in PFS did not affect the long-term OS: at a follow-up of 8.5 years, the median 5-year OS was 51.2% in the peri-operative chemotherapy group vs 47.8% in the surgery-only group, without a significant difference between the two. So looking at all these, we extrapolate 6 months of adjuvant treatment for anastomotic recurrence too. Agents to be given can be decided based on prior chemotherapy agents used, safety/toxicity issues associated with the regimens.

A combination of biological targeted agents and chemotherapy improves the outcomes of metastatic CRC, whereas there is no evidence supporting their use in the adjuvant setting after metastasectomy. A phase Ⅲ clinical trial randomized 236 WT-KRAS patients to receive chemotherapy with or without cetuximab before and after liver resection. PFS was 14.1 mo in the chemotherapy plus cetuximab group and 20.5 mo in the chemotherapy alone group, similar to what happens in the adjuvant setting of primary CRC surgery. These results confirm the detrimental effect of cetuximab in the adjuvant post-metastasectomy setting, being associated with a shorter PFS [20]. In Hepatica Study, which was a randomized phase III trial, a total of 79 patients were randomized. At the time of analysis, 23 events were encountered in arm A and 20 in arm B. One-year DFS rate was 79% [95% confidence interval (CI): 68%-93%] and 68% (95% CI: 55%-85%) for arm A and B, respectively (P = .89). Toxicity was evaluated for 75 patients. No significant differences in toxicity between the two arms were found. Because of the premature closure of the study, conclusions about the effect on DFS of additional VEGF inhibition in this setting could not yet be made. So biologics are not recommended in cases where curative resections are done except for cases that are initially unresectable and need conversion to resectability.

Strategies for surveillance of patients with the recurrent disease treated with curative intent, and with no evidence of disease, are similar to those listed for patients with Stage II, III disease except that certain evaluations should be performed more frequently like CT scans every 3 to 6 monthly.

## SURGEON'S PERSPECTIVE

In adenocarcinoma of the bowel, complete tumor resection is the main aim. The first step is to have an early diagnostic approach in patients whose abdominal pain is not clear. The advanced and metastatic tumor presents when there is a delay of diagnosis. The standard treatment is Radical en bloc R0 resection with systemic lymph node dissection. Further investigations are needed to see the progression of the small bowel. [21]

As the patient presented with anastomotic recurrence, it was metastatic and causing obstruction as well so surgery is not curative but palliative and definitive treatment is chemotherapy [22]. Many patients reported chemotherapy in recurrent adenocarcinoma curative [23].

After initial surgery overall recurrence rate from five to ten years is for local recurrence is 2.9% and for distant metastasis is 4.3%. from five to ten years, in men, 1 among 12 had a recurrence and the corresponding cumulative rate was 7.8%. Among women, the recurrence was 1 in 19 and the cumulative rate of 5.2%. In the non-emergency multivariate analysis in females under 75 and low risk of recurrence. The stage at diagnosis was

not a predictor of late recurrence. After colon cancer resection late recurrence can occur. A regular clinical follow-up is necessary to detect early signs of possible recurrence [24]. For stage 1 local recurrence was 4.9%, for stage 2 was 11% and for stage 3 was 23.5%. The risk of local recurrence is associated with tumor location and distant metastasis is associated with age and gross features [25].

## CONCLUSION

In adenocarcinoma of bowel, despite of early diagnosis, on time surgery and completion of therapy, regular follow up and surveillance is necessary.

Despite of all measures, our patient was unfortunate to have recurrence and needs further chemotherapy now.

## CONSENT FOR PUBLICATION

Informed consent was taken from the patient regarding data sharing.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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