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Case Report

Repeated Anastomotic Recurrence After Right Hemicolectomy: A Rare Therapeutic Challenge

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ABSTRACT

Anastomotic recurrence after curative resection of colorectal cancer represents a rare but clinically significant phenomenon, occurring in approximately 2% of operated patients. We present a case report of a 61-year-old male patient who developed two successive anastomotic recurrences after right hemicolectomy with ileocolic anastomosis for mucinous adenocarcinoma. The patient initially underwent right hemicolectomy in 2016 for T4b, N2b, M0 mucinous adenocarcinoma with clear surgical margins. Following completion of adjuvant chemotherapy, the first anastomotic recurrence occurred in January 2019 (36 months postoperatively), treated by ileocolic resection with ileocolic anastomosis. The second recurrence occurred in March 2020 (14 months after the first recurrence), managed by total colectomy with ileorectal anastomosis. Pathological examination confirmed recurrence with characteristics similar to the primary tumor in both instances. At 3 months follow-up after the final intervention, no additional recurrence was observed. Repeated anastomotic recurrence represents a rare therapeutic challenge requiring intensive surveillance, a multidisciplinary approach, and escalating surgical management. Understanding pathophysiological mechanisms, including the role of the anastomotic microenvironment and tumor biology, is important for developing preventive strategies in high-risk patients.

Key words: Colon neoplasms, colectomy, surgical anastomosis, neoplasm recurrence, local, treatment outcome

INTRODUCTION

Colorectal cancer represents the third leading cause of cancer worldwide, with 1.1 million new cases per year, and constitutes the second leading cause of cancer death. [1] Anastomotic recurrence after curative resection of colorectal cancer is a rare event, occurring in approximately 2% of operated patients, [2] but it represents a significant therapeutic challenge when it recurs repeatedly.

The mechanisms of anastomotic recurrence involve several factors: inadequate surgical margins, tumor implantation by exfoliated cells, the anastomotic microenvironment, including local inflammation and immune responses, alterations in the intestinal microbiome, and unrecognized synchronous lesions. [2,3] Recent research has highlighted

the importance of the anastomotic healing process, surgical technique (hand-sewn vs. stapled anastomosis), and tumor-specific biological characteristics, particularly in mucinous tumors. [4,5] Some tumors present unique characteristics with repeated recurrences after multiple resections. [6]

The objective of this report is to present a rare case of two successive anastomotic recurrences after right hemicolectomy and discuss the pathophysiological mechanisms and therapeutic strategies involved. We present a retrospective case report of a patient treated at the Military Hospital of Instruction of Tunis between 2016 and 2020. Clinical data, imaging studies, pathological reports, surgical interventions, and oncological treatments were reviewed.

CASE REPORT

This is a 61-year-old male patient with no significant medical history. In 2016, he presented with bowel obstruction due to a right colon tumor. Following a staging workup that confirmed no distant metastases, he underwent right hemicolectomy with extended lymph node dissection. A manual ileocolic anastomosis was performed.

Pathological examination revealed a mucinous colorectal adenocarcinoma (60% mucinous component), poorly differentiated, with the presence of vascular emboli, perineural invasion, and 10 out of 25 lymph nodes with metastases (T4b, N2b, M0–Stage IIIC). Surgical margins were clear (proximal margin: 8 cm, distal margin: 6 cm). Molecular analysis revealed microsatellite stable (MSS) status with Kirsten Rat Sarcoma viral oncogene homolog (KRAS) wild-type and B-Raf Proto-Oncogene, Serine/Threonine Kinase (BRAF) wild-type. The patient received adjuvant chemotherapy with the Folinic acid (leucovorin) + Fluorouracil (5-FU) + Oxaliplatin (FOLFOX) regimen (12 cycles), which was completed without major complications.

Three-year follow-up with surveillance colonoscopy and computed tomography (performed every 6 months for the first 2 years, then annually) revealed no signs of recurrence. Tumor markers (Carcinoembryonic Antigen (CEA) and Carbohydrate Antigen 19-9 (CA19-9)) remained within normal limits throughout the surveillance period.

First Anastomotic Recurrence

In January 2019 (36 months after initial surgery), the patient consulted for progressive abdominal pain and changes in bowel habits. Computed tomography showed irregular circumferential thickening at the level of the previous ileocolic anastomosis, measuring 3.5 cm in length, without evidence of distant metastases or lymphadenopathy (**Figure 1A**). Colonoscopy revealed a stenosing mass at the anastomotic site, and biopsy confirmed recurrence of mucinous adenocarcinoma. Tumor markers CEA (2.1 ng/mL) and CA19-9 (18 U/mL) remained within normal limits.

Segmental ileocolic resection followed by ileocolic anastomosis using a stapling device was performed. The postoperative course was uneventful with no immediate complications. Histology revealed recurrent mucinous adenocarcinoma with characteristics similar to the primary tumor, invading through the muscularis propria. All 12 retrieved lymph nodes were negative for metastases (pT3, N0). Surgical margins were clear. The patient received adjuvant chemotherapy with the Folinic acid (leucovorin) + Fluorouracil (5-FU) + Irinotecan (FOLFIRI) regimen (8 cycles).

Second Anastomotic Recurrence

In March 2020 (14 months after the first recurrence), during routine surveillance computed tomography, a second anastomotic recurrence was detected. The scan showed irregular thickening at the new ileocolic anastomotic site, similar in appearance to the first recurrence (**Figure 1B**). Colonoscopy and biopsy confirmed the diagnosis of recurrent mucinous adenocarcinoma. Tumor markers remained normal (CEA: 2.8 ng/mL, CA19-9: 22 U/mL). The patient remained asymptomatic at the time of diagnosis.

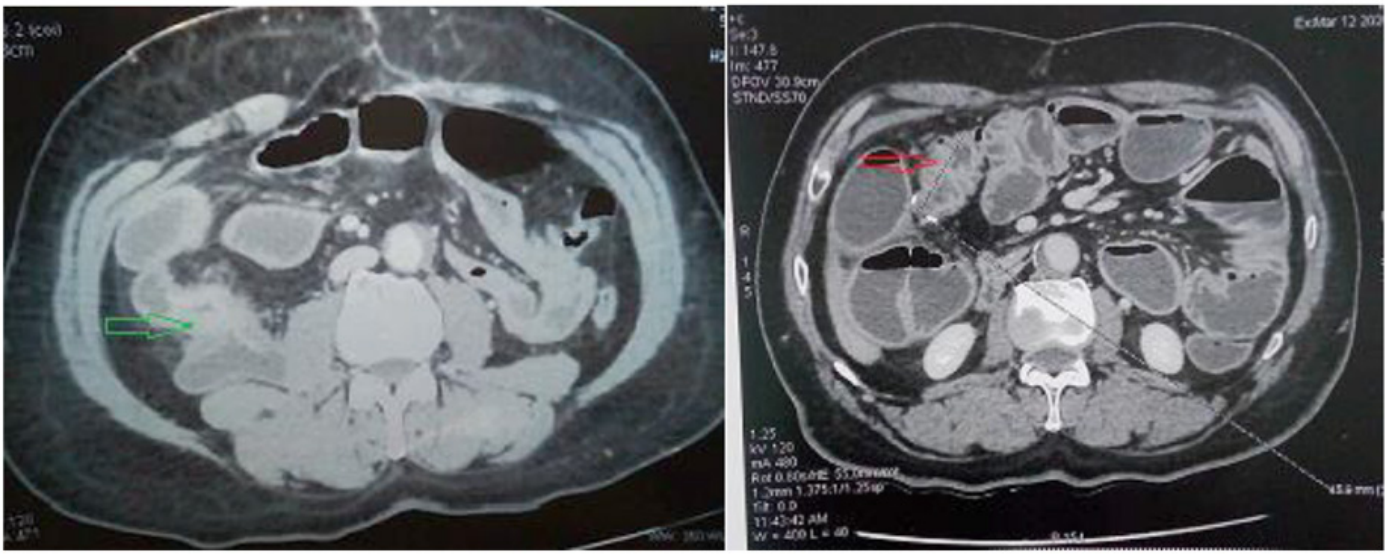

Figure 1: Computed tomography of the abdomen showing (A) the first anastomotic recurrence in January 2019 (green arrow) demonstrating irregular circumferential thickening at the ileocolic anastomosis, and (B) the second anastomotic recurrence in March 2020 (red arrow) showing similar findings at the new anastomotic site.

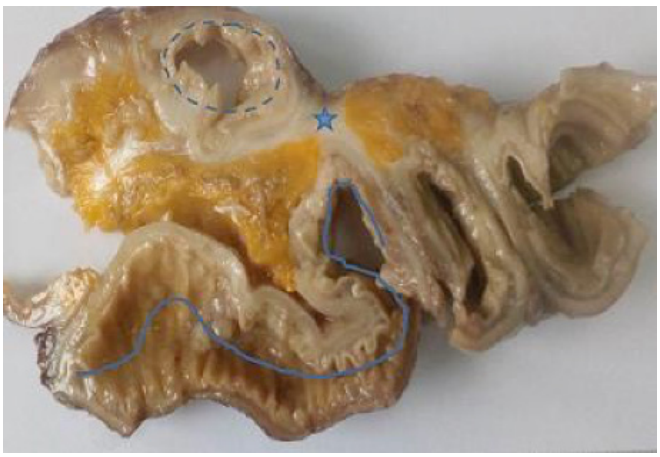

Figure 2: Gross pathology specimen showing anastomotic recurrence (star) at the junction between the ileal segment (cut longitudinally, indicated by solid line) and the colonic segment (cut transversely, indicated by dashed line). The tumor forms a circumferential mass at the anastomotic site.

Total colectomy with ileorectal anastomosis was performed (**Figure 2**). The patient experienced postoperative ileus that resolved with conservative management by day 7. He was discharged on day 10. Pathological examination revealed the second recurrence of mucinous adenocarcinoma confined to the anastomotic site, without lymph node metastases (0/18 nodes positive). Further adjuvant chemotherapy was administered (FOLFOX regimen, 6 cycles).

At 3 months after the last intervention, clinical examination, computed tomography, and endoscopy showed no signs of additional recurrence. The patient reported satisfactory quality of life despite having 3 to 4 bowel movements daily, which were managed with dietary modifications and loperamide as needed.

DISCUSSION

Anastomotic recurrence after curative resection of colorectal cancer is uncommon compared to other types of recurrence, such as hepatic or pulmonary metastases. [7] The incidence varies between 1% and 2% of operated patients but can reach higher rates in selected series with high-risk features. [2] The occurrence of two successive anastomotic recurrences, as observed in our patient, is particularly rare and presents both diagnostic and therapeutic challenges.

Pathophysiological Mechanisms

The pathophysiology of anastomotic recurrence involves multiple complex mechanisms that extend beyond the traditional theory of tumor cell implantation. While exfoliated tumor cells can implant at the anastomotic site, facilitated by local inflammation and the healing process, [2,3] recent research has emphasized the importance of the anastomotic microenvironment in promoting tumor recurrence. [4,8]

The anastomotic site represents a unique biological environment characterized by tissue hypoxia, inflammatory responses, neoangiogenesis, and alterations in the extracellular matrix during healing. [8,9] These factors may create a favorable niche for tumor cell survival and proliferation. Additionally, surgical trauma and the healing process can induce local immunosuppression, potentially allowing residual tumor cells to escape immune surveillance. [10]

In the context of right hemicolectomy, specific anatomical and physiological changes may contribute to recurrence risk. The ileocolic anastomosis creates a new junction between the ileum and colon, leading to alterations in bile acid metabolism and changes in the intestinal microbiome. [11] The microbiome plays an increasingly recognized role in colorectal cancer development and recurrence, with certain bacterial species promoting inflammation and tumor progression. [12] These post-surgical alterations in the gut environment may have contributed to the repeated recurrences observed in our case.

The surgical technique employed may also influence recurrence risk. Our patient initially had a hand-sewn anastomosis, followed by stapled anastomoses for the recurrences. While some studies suggest that stapled anastomoses may have lower recurrence rates due to less tissue manipulation and contamination, [5] the evidence remains inconclusive, and both techniques are considered acceptable.

Tumor-Specific Factors

The mucinous histological type observed in our patient, combined with advanced staging (T4b, N2b) and the presence of vascular emboli and perineural invasion, represents well-established risk factors for recurrence. [2,13] Mucinous adenocarcinomas constitute approximately 10% to 15% of colorectal cancers and are associated with distinct biological behavior, including higher rates of peritoneal dissemination and potentially increased risk of local recurrence. [14]

The MSS status in our patient is relevant, as MSS tumors generally have a poorer prognosis compared to microsatellite instability-high (MSI-H) tumors. [15] Despite wild-type KRAS and BRAF status, which are generally favorable prognostic markers, the combination of mucinous histology, advanced stage, and MSS status likely contributed to the aggressive behavior and repeated recurrences.

Interestingly, the fact that recurrent tumors maintained similar histological characteristics to the primary tumor suggests true recurrence rather than new primary tumors, although molecular comparison between the primary and recurrent lesions would have provided definitive confirmation.

Diagnostic Approach and Surveillance

The diagnostic approach in our case highlights important aspects of anastomotic recurrence detection. CEA and CA19-9 remained within normal limits throughout both recurrences, which is particularly noteworthy. While this finding might seem to diminish the utility of tumor markers, it is important to recognize that mucinous adenocarcinomas are known to produce less CEA, [16] making CEA an unreliable marker in this specific tumor type. This case underscores the need for multiple surveillance modalities rather than reliance on tumor markers alone.

The diagnosis relied primarily on imaging studies and endoscopic evaluation. The first recurrence was detected symptomatically at 36 months, while the second was identified during routine surveillance at 14 months after the first recurrence. This temporal pattern is consistent with literature showing that most

recurrences occur within the first 2 years following surgery, with peak incidence between 11 and 24 months. [2,17]

Current surveillance recommendations from European Society for Medical Oncology (ESMO) advocate for thoraco-abdomino-pelvic computed tomography every 6 months for the first 3 years, colonoscopy at 1 year, then every 3 to 5 years, and tumor marker assays (despite their limitations in some cases). [18] Our case reinforces the importance of intensive surveillance, particularly in high-risk patients with mucinous histology, advanced stage, and a history of prior recurrence.

Therapeutic Management

The therapeutic management of repeated anastomotic recurrence, as demonstrated in our case, required an escalating surgical approach. The progression from localized resection to total colectomy with ileorectal anastomosis reflects the principle that management should be tailored to disease extent and recurrence pattern. [7,19]

Total colectomy, while more extensive, was justified by the pattern of repeated recurrences at anastomotic sites. This approach has been shown to provide acceptable long-term outcomes in selected patients with recurrent disease. [19] The absence of distant metastases and limited lymph node involvement in the recurrent tumors supported an aggressive surgical strategy.

The role of adjuvant chemotherapy in anastomotic recurrence deserves discussion. While our patient received chemotherapy after each intervention, the optimal regimen and duration for anastomotic recurrence remain unclear. The use of different regimens (FOLFOX, FOLFIRI) was based on standard practice for recurrent disease, though evidence specifically addressing repeated anastomotic recurrence is limited.

The functional outcome after total colectomy was acceptable in our patient, with manageable bowel frequency and preserved quality of life. This is an important consideration when counseling patients about extensive resections.

Prevention Strategies

Prevention of anastomotic recurrence continues to evolve and includes several approaches, and they are given below. [3,5,20]

Surgical Technique

Rigorous adherence to oncological principles, including adequate resection margins, meticulous handling of tumor tissue to minimize cell spillage, and careful anastomotic technique. The choice between hand-sewn and stapled anastomosis remains debated, though current evidence does not definitively favor one technique over the other for recurrence prevention.

Intraoperative Measures

Intraoperative peritoneal lavage has been proposed to reduce viable tumor cells in the operative field, though its efficacy remains controversial. [21] Some centers advocate for wound protection and instrument changes before creating the anastomosis.

Adjuvant Therapy

Complete adjuvant chemotherapy in high-risk patients is standard, though its specific role in preventing anastomotic recurrence (as opposed to distant recurrence) is uncertain.

Emerging Strategies

Novel approaches, including targeted therapies based on molecular profiling, immunotherapy for MSI-H tumors, and investigation of the microbiome's role in recurrence prevention, represent promising areas of research. [12,22]

The repeated nature of recurrence in our case emphasizes the need for continued research into the biological mechanisms underlying this phenomenon and the development of more effective preventive measures, particularly for high-risk tumor subtypes such as mucinous adenocarcinoma.

CONCLUSIONS

This case illustrates the complexity of managing repeated anastomotic recurrences after curative surgery for colorectal cancer. The rarity of this complication requires prolonged surveillance and a multidisciplinary approach. Understanding pathophysiological mechanisms, including the role of the anastomotic microenvironment, tumor biology, and alterations in the intestinal milieu following right hemicolectomy, is important for developing new preventive and therapeutic strategies.

Post-curative surgery surveillance for colorectal cancer should be maintained for at least 5 years, with particular attention to patients presenting high-risk factors for anastomotic recurrence, including mucinous histology, advanced stage, vascular invasion, and perineural involvement. Future research should focus on identifying molecular markers that predict anastomotic recurrence risk and developing targeted prevention strategies for high-risk patients.

PATIENT CONSENT

Written informed consent was obtained from the patient for publication of this case report.

AUTHORS' CONTRIBUTION

All authors have significantly contributed to the work, whether by following the case at the bedside, conducting literature searches, drafting, revising, or critically reviewing the article. They have given their final approval of the version to be published, have agreed with the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

None.

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