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CASE REPORT | BILIARY

# Isolated Metachronous Intraluminal Colonic Metastasis in Carcinoma Gall Bladder: The Path Less Trodden

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#### **ABSTRACT**

Gallbladder cancer (GBC) is characterized by late presentation, early systemic spread, and poor long-term survival. A 65-year-old woman presented with isolated intraluminal colonic metastasis 46 months after radical surgery for GBC. The patient also underwent subtotal cholecystectomy 12 years before the diagnosis of GBC. In view of gastrointestinal bleeding, the patient underwent laparoscopic transverse colectomy with colocolic anastomosis. Metachronous isolated intraluminal colonic metastasis is being reported for the first time in English literature. The possible routes of colonic metastasis and its optimum management in the metachronous setting are discussed in this report.

KEYWORDS: gall bladder cancer; colonic metastases; colectomy

# **INTRODUCTION**

Gallbladder carcinoma (GBC) is an aggressive malignancy with a dismal 5-year survival rate because of its propensity for early systemic metastasis. Surgery remains the primary therapeutic modality, and systemic chemotherapy is often indicated in locally advanced GBC to reduce systemic recurrence. Liver metastasis, peritoneal recurrence, and metastasis to nonregional lymph nodes are common sites of recurrence after surgical treatment. The present report describes an unusual, isolated intraluminal colonic metastasis 46 months after surgical resection of the primary GBC. The clinical presentation, possible routes of spread, and management of isolated colon metastasis in GBC are discussed in this report.

# CASE REPORT

A 65-year-old woman, diagnosed and treated elsewhere for GBC, presented to our institute with generalized weakness, anorexia, and significant weight loss (10 kg in 3 months). She received blood transfusions for anemia. The patient underwent open subtotal cholecystectomy for cholecystitis in 2007 at a peripheral hospital. The perioperative details and the records of this surgery were not available when she visited our hospital. She remained asymptomatic till 2019 when the patient developed obstructive jaundice, which necessitated further diagnostic workup. Radiological evaluation revealed a mass lesion in the remnant gall bladder (GB) neck extending into the common bile duct (Type II hilar block) with no distant metastasis, suggestive of at least a T3N0M0 clinical stage according to the American Joint Committee on Cancer 8th edition staging. The patient underwent extrahepatic bile duct resection with Roux-en-Y hepaticojejunostomy in October 2019. Intraoperative findings suggest disease in the remnant GB extending into the bile duct. The histopathological evaluation showed a moderately differentiated adenocarcinoma with full-thickness mural extension till the perimuscular adipose tissue grouped under pT3N0/stage 3A as per the American Joint Cancer Committee 8th edition cancer staging. The tumor showed perineural spread, but no lymphatic or vascular emboli were noted. The proximal and distal bile duct margins were free of tumor. She received 8 cycles of adjuvant capecitabine-based chemotherapy and 22 sessions of radiotherapy.

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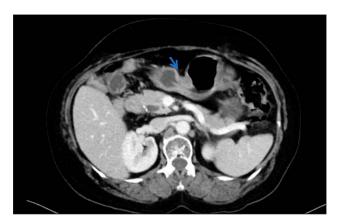
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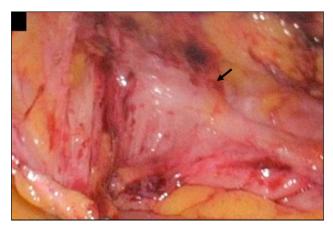
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She had been on regular follow-up every 3 months in the first 2 years after surgery and half-yearly surveillance thereafter for 5 years. At each visit, in addition to a comprehensive clinical examination, we evaluated our patient with serological and radiological investigations including the complete blood count, liver function test, and coagulation profile along with either an ultrasonography of the abdomen and a chest radiograph alternating with an abdominal and pelvic contrastenhanced computed tomography at each visit. However, the postoperative radiological investigations showed no locoregional or distant disease till the present admission to our hospital. The patient did not have medical comorbidities or a family history of malignancy. On examination, she was thinly built and moderately nourished. Chest and abdominal examinations were unremarkable except for the previous laparotomy scar. Abdominal contrast-enhanced computed tomography revealed a heterogeneously enhancing mass in the transverse colon with necrotic mesocolic nodes (Figure 1). No other lesions were identified in the rest of the abdomen and the chest. A positron emission tomography-computed tomography also revealed a solitary metabolically active lesion (SUVmax—3.56) within the midtransverse colon.

Colonoscopy showed an ulceroproliferative growth with luminal narrowing in the midtransverse colon, and the biopsy was suggestive of well-differentiated adenocarcinoma. The unremarkable family history with no suspicion of any luminal growth on the imaging in the previous visits did not warrant an earlier colonoscopy. The diagnostic possibilities at this stage were metachronous colic metastasis from GBC or a second colonic primary. Surgical resection was planned in either scenario as the patient was symptomatic, and the colon was the solitary site of the disease. She underwent a laparoscopic transverse colectomy with colocolic anastomosis (Figure 2). There was no peritoneal disease intraoperatively, and growth was noted in the midtransverse colon with intact serosa. The patient had an uneventful postoperative course and was discharged on the fourth postoperative day.



**Figure 1.** Abdominal contrast-enhanced computed tomography showing heterogeneously enhancing mass in the transverse colon (blue arrow).



**Figure 2.** Intraoperative photograph showing the transverse colon thickening with no involvement of serosa (black arrow).

The gross pathology examination of the resected specimen showed an ulceroproliferative circumferential luminal growth of size  $2 \times 2 \times 0.7$  cm in the transverse colon, reaching the subserosa with intact serosa and tumor deposit in the mesocolon. The histology showed grade 1 adenocarcinoma with pathological staging of pT3N1c. All the resected margins were free of tumor. The tumor cells stained positive for CK7, CK19, and CDX2 and negative for CK20, suggesting metastatic growth from the GB primary tumor (Figure 3).

At 5-month follow-up, the patient was clinically free of recurrence. She had received 3 cycles of chemotherapy with capecitabine and cisplatin. The current plan is 3-monthly surveillance visit for the next 2 years. A serology workup including complete blood count, liver function test, and ultrasonography is planned at each visit. An abdominal contrast-enhanced computed tomography along with colonoscopy is planned to be included in the surveillance workup annually for the next 3 years.

### **DISCUSSION**

GBC is unique for its late presentation with vague symptoms and a high rate of distant metastasis. In a recent report from the Indian Cancer Registry, only 8.8% of patients had an early stage in the initial presentation, 23.6% were already in the locally advanced stage, and the remaining two-thirds had systemic spread.<sup>3</sup> Although primary GBC is common in high-incidence areas, incidental GBC is frequent in regions with a low prevalence of GBC. In the present report, although the patient was diagnosed with GBC after subtotal cholecystectomy, the longer interval (12 years) between index surgery and malignancy suggests de novo development of carcinoma from the remnant GB neck. The common sites of distant metastasis include the liver in 60%-75% of cases, nonregional lymph nodes in 50%-60%, peritoneal metastasis in 25%-30%, and less commonly to other organs such as lungs, bones, and subcutaneous tissues.4-7 Metachronous isolated intraluminal colonic metastasis in GBC is extremely rare.

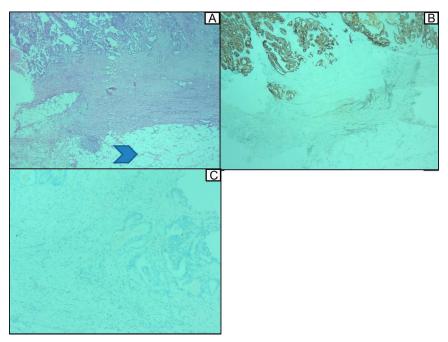


Figure 3. Photomicrographs from the transverse colon show (A) adenocarcinoma infiltrating from mucosa to muscularis propria. Serosa free from tumor (arrowhead) (hematoxylin and eosin,  $\times$ 40); (B) IHC with CK7 and CK19 positive in tumor cells (DAB,  $\times$ 100); and (C) IHC with CK20 negative in tumor cells (DAB,  $\times$ 100). IHC, immunohistochemistry; DAB, 3,3'-diaminobenzidine.

Colon involvement in GBC is often due to direct infiltration. In the present patient, the possibility of implantation metastasis after radical surgery of GBC is less likely as the serosa was free and metastasis was predominantly intraluminal. Hematogenous spread is the most plausible route in this patient. Signorelli et al have previously reported a metachronous colonic metastasis with intraluminal bleeding as the presenting symptom.8 However, the patient also had a synchronous colonic metastasis. Isolated colonic metastasis in a treated GBC is being reported for the first time in English literature. The role of surgery in metastatic GBC is debatable. However, isolated colonic metastasis with gastrointestinal bleeding and a longer recurrencefree interval after radical surgery tilted the balance toward surgical treatment. Surgical treatment of metastatic disease should be combined with systemic chemotherapy to kill occult tumor cells. In view of good performance status, cisplatin-based chemotherapy was given in the postoperative period.

The unique findings in the present report are de novo development of GBC from the remnant GB neck after subtotal cholecystectomy and isolated metachronous colonic metastasis managed surgically.

#### **DISCLOSURES**

Author contributions: R. Kalayarasan/P. Mohan: study concept/design. A. Soori/P. Saikrishna: data collection. A. Soori/BH Srinivas/P. Saikrishna: data analysis. A. Soori/R. Kalayarasan: writing the paper. P. Mohan/R. Kalayarasan/B. Pottakkat: final check and corrections. R. Kalayarasan is the article guarantor.

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