

Small intestinal obstruction due to the metastasis of intrahepatic cholangiocarcinoma

A case report

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Abstract

Rationale: The small intestine (SI) does not commonly harbor cancer but is occasionally involved by metastatic cancer from other organs. To manage SI cancer appropriately, surveillance for primary origin outside the SI is essential.

Patient concerns: This study presents a 54-year-old Thai man diagnosed with SI obstruction which required laparoscopy-assisted partial ileal resection.

Diagnoses: On the basis of the expression pattern of cytokeratins (CKs) and mucins (MUCs) in the resected SI adenocarcinoma, we suspected this was metastasized from the pancreatobiliary tract. Imaging studies revealed a hepatic segmental atrophy with an occlusion of the posterior segmental branch of the portal vein without any contrast-enhanced lesions in the liver. Pathology of the liver biopsy revealed intrahepatic cholangiocarcinoma (ICC) with the same expression pattern of CKs and MUCs as the SI adenocarcinoma.

Interventions: Systemic chemotherapy (gemcitabine and cisplatin) was initiated.

Outcomes: Despite of the chemotherapy for 20 months, he died of ICC.

Lessons: This is the first case of SI obstruction caused by the metastasis of ICC. We demonstrate that immunohistochemical staining of CKs and MUCs discriminate between primary and metastatic SI cancer and predict its primary origin outside the SI. This case also suggests that a hepatic segmental atrophy with portal vein occlusion would be an atypical but important finding to diagnose ICC.

Abbreviations: ¹⁸F-FDG-PET = fluorine-18 fluorodeoxyglucose positron emission tomography, CKs = cytokeratins, CT = computed tomography, GI = gastrointestinal, GIST = gastrointestinal stromal tumor, ICC = intrahepatic cholangiocarcinoma, IHC = immunohistochemical, MUCs = mucins, PB = pancreatobiliary, SBE = single-balloon enteroscopy, SI = small intestine.

Keywords: hepatic portal vein occlusion, immunohistochemical staining, intrahepatic cholangiocarcinoma, small intestinal metastasis, small intestinal obstruction

1. Introduction

In the gastrointestinal (GI) tract, the small intestinal (SI) is a location where cancer development is uncommon. US cancer statistics in 2010 showed the new cases of SI cancer are 6960 (2.5%) among 274,330 estimated new cases of GI tract cancer.^[1]

Several lines of evidence have showed clinicopathological characteristics of SI cancer. Histological studies of SI cancer suggested that the most common type is adenocarcinoma

(35.1%) in the United States, whereas GI stromal tumor (GIST) (30.4%) is the most common in Japan.^[2,3] Another report also suggested that the incidence of GIST in the SI is significantly higher among Asian-Pacific Islanders.^[4] Meanwhile, previous reports showed 49.3% of SI tumors are metastatic cancer; the most prominent primary site is the colon (43.2%) in the United States,^[5] whereas it is the lung (58%) in Japan.^[6] Hence, careful surveillance of primary origin outside the SI is considered to be important for the appropriate management of SI cancer.

Here, we report a rare case of SI obstruction due to the metastasis of intrahepatic cholangiocarcinoma (ICC). In this case, we demonstrated that immunohistochemical (IHC) staining of cytokeratins (CKs) and mucins (MUCs) clearly differentiate the metastatic from primary SI cancer and predict its primary lesion outside the SI. Furthermore, we suggested that a hepatic segmental atrophy with portal vein occlusion is an important finding to diagnose ICC as a primary origin of metastatic SI cancer.

2. Case report

A 54-year-old Thai man was seen by us at the emergency department for postprandial epigastric pain, which developed 1 month prior to examination. He had no notable past medical history except for a traffic injury in his 20s. His family history was significant for his siblings with cancer of the liver.

Editor: N/A.

The authors have no conflicts of interest to disclose.

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Medicine (2018) 97:12(e0190)

Received: 26 December 2017 / Received in final form: 21 February 2018 /

Accepted: 23 February 2018

<http://dx.doi.org/10.1097/MD.00000000000010190>

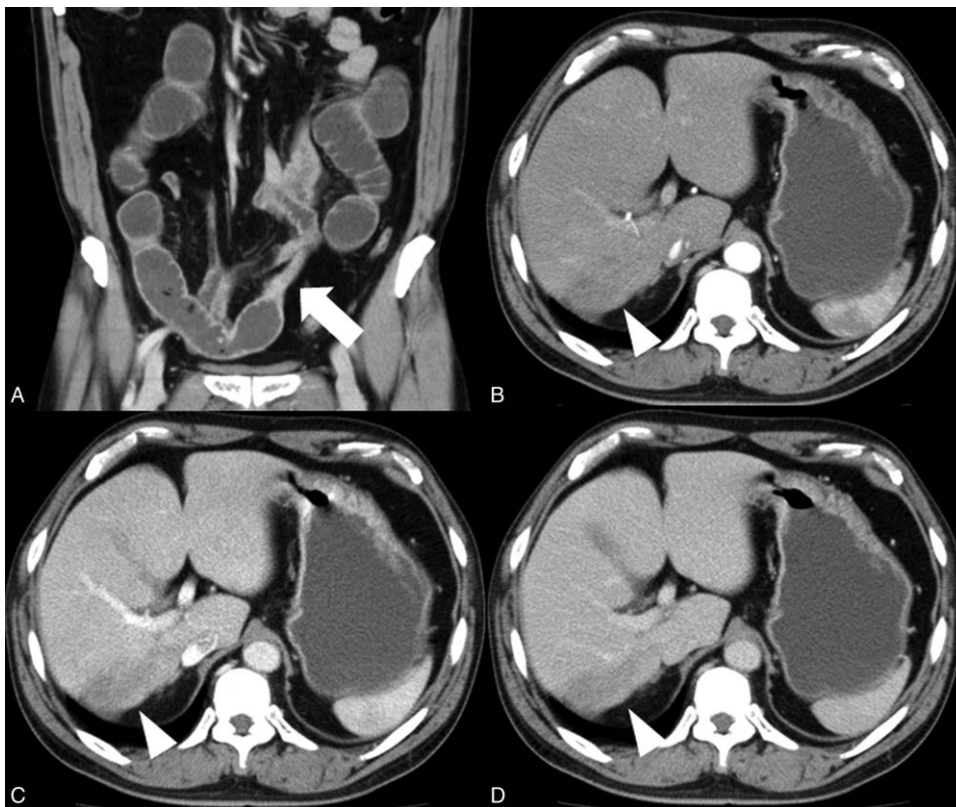


Figure 1. (A) A coronal view of the contrast-enhanced computed tomography (CT) scan reveals a wall thickening of the ileum with a caliber change (white arrow). (B)–(D) Axial views of the arterial (B), portal venous (C) and equilibration venous phase (D) of the contrast-enhanced CT show a hepatic segmental atrophy with an occlusion of the posterior segmental branch of the portal vein without any enhanced lesions in the liver (white arrowheads). CT = computed tomography.

Abdominal x-ray revealed some SI gas with air-fluid levels which indicated SI obstruction. Contrast-enhanced abdominal computed tomography (CT) scan subsequently showed a wall thickening of the SI with a caliber change (Fig. 1A) and an atrophic deformity of the posterior hepatic segment (Fig. 1B–D). Dynamic study also revealed an occlusion of the posterior segmental branch of the portal vein without any contrast-enhanced lesions in the liver (Fig. 1B–D). These findings suggested that his abdominal pain would be caused by SI obstruction, and a hepatic segmental atrophy with portal vein occlusion was presumably associated with a post-traumatic change based on his past history. As a treatment for SI obstruction, we started fluid resuscitation with non per os and a naso-jejunal tube was placed for decompression.

Because carbohydrate antigen 19-9 was remarkably elevated (1151.6IU/mL) in his laboratory finding, we assumed that the cause of his SI obstruction was likely to cancer. To observe the obstructed portion of the SI, we performed retrograde single-balloon enteroscopy (SBE). SBE with a contrast imaging showed an ileal stricture being 2 cm in length at 60 cm from the ileocecal valve (Fig. 2A) and swelling and erythema of intestinal villi in this site (Fig. 2B). Endoscopic biopsy results revealed no remarkable findings. To correct SI obstruction and confirm the diagnosis, laparoscopy-assisted partial ileal resection was quasi-emergently performed. Intraoperative findings showed an ileal stricture with a mesenteric tension and no signs of ascites, lymph node metastasis, and intraperitoneal dissemination except for a resected lesion.

Macroscopic finding of the surgical specimen also showed SI obstruction in the ileum (Fig. 3A). Histopathological evaluations

revealed well- or moderately differentiated tubular adenocarcinoma localized from the mesenteric membrane to the submucosa and the epithelium was mostly intact, suggesting that cancer cells would be disseminated from other organs to SI (Fig. 3B, C, 4A). To determine the cell type of SI adenocarcinoma, we performed IHC staining of CK7 and CK20. SI epithelium was negative for CK7 and positive for CK20 (CK7-CK20+), whereas cancer cells were CK7+ and weakly CK20+ (Fig. 4B and C). IHC staining of MUCs showed SI epithelium was MUC2+MUC5AC- but cancer cells were MUC2-MUC5AC+ (Fig. 4D and E). These observations suggested that cancer cells were not primary SI adenocarcinoma but metastatic cells originated from the pancreatobiliary (PB) tract.

Thus, we next attempted to identify the primary origin by GI endoscopies, an abdominal ultrasonography and fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F -FDG-PET). Both esophagogastroduodenoscopy and colonoscopy were unremarkable. Meanwhile, ^{18}F -FDG-PET scanning detected an ^{18}F -FDG accumulation in the posterior segment of the liver, which was initially presumed as a traumatic change. An abdominal ultrasonography also detected a poorly marginated low-echoic lesion mixed with high-echoic signals being 3.4 cm in diameter at the posterior segment of the liver. Hence, liver biopsy was undertaken and revealed moderately differentiated adenocarcinoma with the same expression pattern of CKs and MUCs as the SI adenocarcinoma (Fig. 4F). We finally confirmed ICC as the primary origin of the SI adenocarcinoma. The final histopathological stage of ICC was a pT4, pN0, pM1 (SI metastasis), corresponding to the Union for International Cancer Control IVB classification. On the basis of the treatment guideline for ICC,

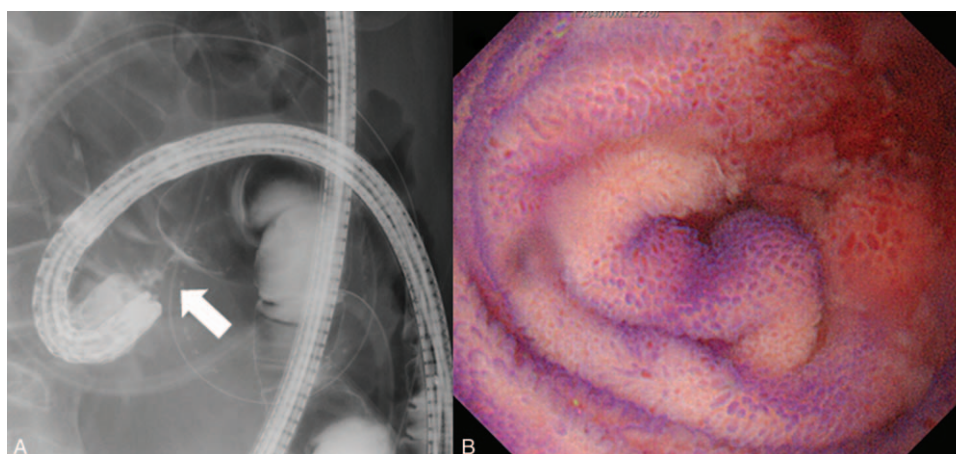


Figure 2. (A) A single balloon enteroscopy (SBE) with a contrast radiography reveals a stricture in the ileum (white arrow). (B) An image of SBE shows an ileal occlusion with swelled and erythematous intestinal villi. SBE=single balloon enteroscopy.

systemic chemotherapy (gemcitabine 1000 mg/m² and cisplatin 25 mg/m²) was initiated (Table 1). However, renal dysfunction developed at 5 months after chemotherapy and we reduced the dosage of cisplatin. Despite of the chemotherapy for 20 months, peritoneal dissemination had been progressed. Thus, we stopped chemotherapy and continued palliative care for his abdominal pain, back pain, and anorexia. Following his preference, we introduced him to a hospital in the Thailand and he ended in death.

In this study, all patient information was anonymized. This patient had died when we summarized this study, so that we confirmed his daughter's permission to release this case report.

3. Discussion

We reviewed English medical publications in PubMed by using keywords: “intrahepatic cholangiocarcinoma,” “small intestinal metastasis,” “small intestinal obstruction,” or “small bowel obstruction”. Consequently, this search detected only one case report of SI metastasis of ICC^[7] and no reports of SI obstruction due to ICC. Thus, within our extensive literature review, the present case is the first to demonstrate that ICC can be a cause of SI obstruction. A recent review described that 5% or 10% of SI obstructions are caused by neoplasm; colorectal or ovarian cancer.^[8,9] In this case, we initially related a hepatic segmental

atrophy with portal vein occlusion not to SI obstruction but to a post-traumatic change because of 2 reasons; evidence indicating that SI obstruction is rarely caused by liver cancer^[9] and his past medical history including a traffic injury. This case proposed that careful surveillance of any organs with abnormal findings would be essential to diagnose SI cancer appropriately.

There have been few reports to compare primary SI cancer and ICC by using IHC staining of CKs and MUCs. Thus, this case study examined expression patterns of CKs and MUCs to determine the cell type of SI cancer cells. CKs are intracellular intermediate filaments consisting of 20 subtypes.^[10] Different epithelia express a selective combination of CKs and IHC detection of CK7 and CK20 is a useful diagnostic tool to determine the epithelial origin of carcinoma.^[11,12] In this case, cancer cells were CK7+CK20+. A previous study investigating 435 epithelial neoplasms from various organ systems showed the majority of CK7+CK20+ epithelial neoplasms are carcinoma from the PB tract. This demonstrated that 62% of pancreatic cancer and 43% of cholangiocarcinoma were CK7+CK20+.^[12] On the other hand, several reports showed that the percentage of CK7+CK20+ in the primary SI adenocarcinoma is 15.0% or 67.0%, varying by reports.^[11,13] This case study demonstrated that IHC staining of CK7 and CK20 clearly differentiate ICC metastasis from primary SI cancer based on their different expression patterns between SI epithelium and cancer cells (Fig. 4).

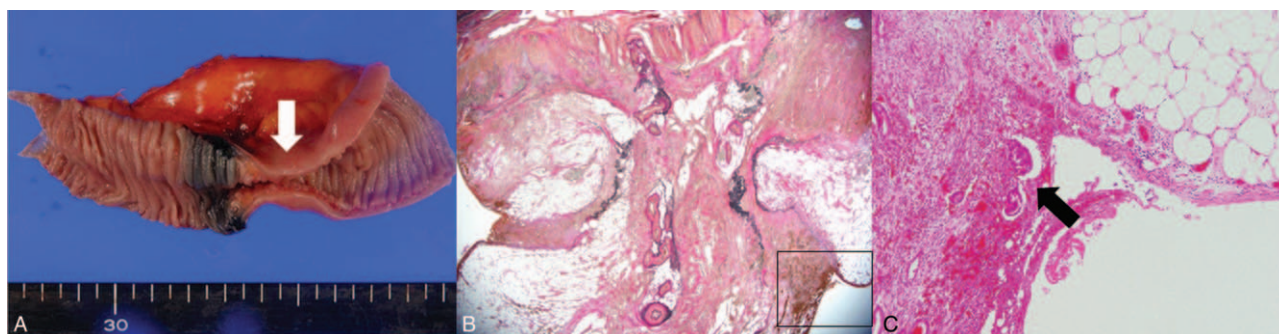


Figure 3. (A) A gross histological image of the resected SI reveals an ileal stricture (white arrow). (B, C) Histopathological examination of the SI tumor shows tubular adenocarcinoma invading the SI mesenteric membrane (black box) (Elastica van Gieson staining $\times 10$). The black box is magnified in the right panel (C) and a black arrow indicates invaded tubular adenocarcinoma (HE staining $\times 200$). SI, small intestine.

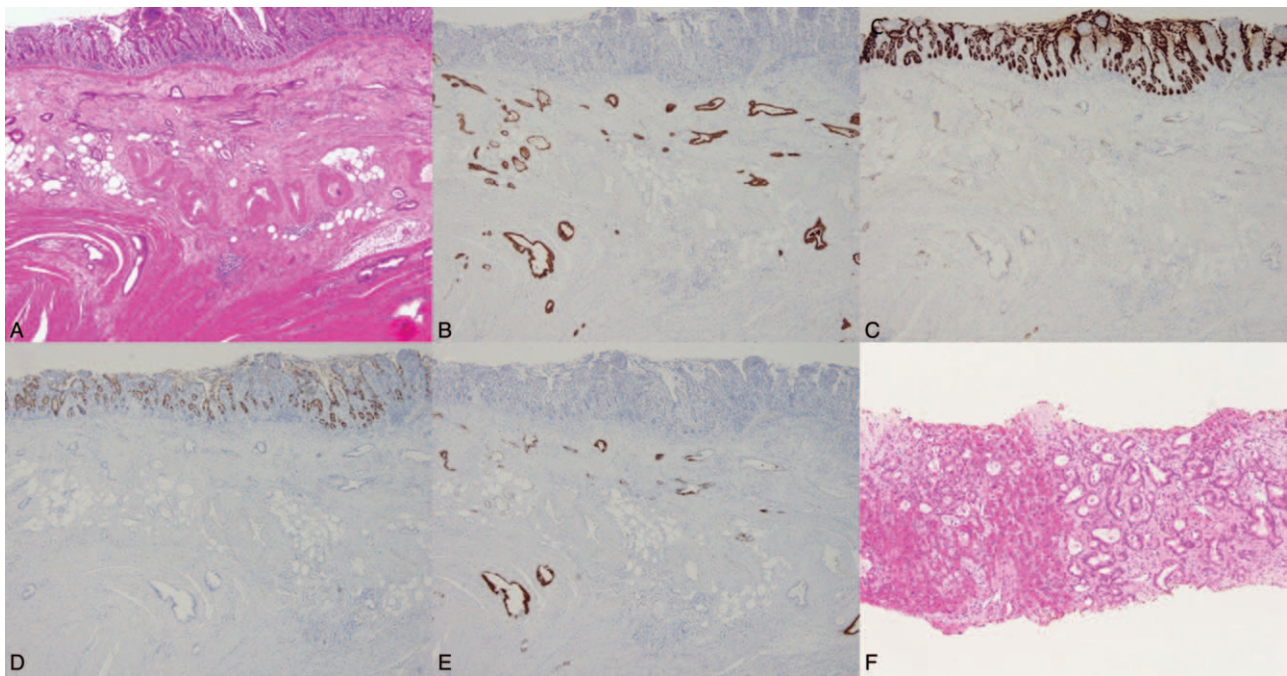


Figure 4. (A) An image of HE staining shows well- or moderately differentiated tubular adenocarcinoma in the SI submucosa ($\times 20$). (B)–(E) Immunohistochemical stainings of CK7 (B), CK20 (C), MUC2 (D), and MUC5AC (E) in the SI adenocarcinoma ($\times 20$). (F) An image of HE staining of the liver biopsy specimen shows moderately differentiated tubular adenocarcinoma ($\times 100$). CK = cytokeratin, MUCs = mucins, SI = small intestine.

Table 1

Timeline of clinical course.

Timeline, months	Clinical course
0	Epigastric pain Abdominal x-ray: SI obstruction CT: a wall thickening of the SI with a caliber change and an atrophic deformity of the posterior hepatic segment with an occlusion of the posterior segmental branch of the portal vein
1	Single-balloon enteroscopy: an ileal stricture being 2 cm in length at 60 cm from the ileocecal valve Endoscopic biopsy result: no remarkable findings
1.5	Laparoscopy-assisted partial ileal resection Pathological finding: well- or moderately differentiated tubular adenocarcinoma
4	^{18}F -FDG-PET scanning: an ^{18}F -FDG accumulation in the posterior segment of the liver
6	Abdominal ultrasonography: a poorly marginated low-echoic lesion mixed with high-echoic signals being 3.4 cm in diameter at the posterior segment of the liver Liver biopsy result: moderately differentiated adenocarcinoma with the same expression pattern of CKs and MUCs as the SI adenocarcinoma Diagnosis: Intrahepatic cholangiocarcinoma with SI metastasis
6.5	Systemic chemotherapy (gemcitabine and cisplatin)
27	Discontinuation of the chemotherapy due to disease progression Palliative care
28	Death

^{18}F -FDG-PET = fluorine-18 fluorodeoxyglucose positron emission tomography, CKs = cytokeratins, CT = computed tomography, MUCs = mucins, SI = small intestine.

MUCs are large, abundant, filamentous glycoproteins composed of 14 subtypes.^[14] In the MUC gene family, MUC1, MUC2, MUC5AC, and MUC6 have been studied in various GI organs.^[15,16] For instance, a previous study of 486 primary GI carcinoma showed MUC2 expressed in the adenocarcinoma of

the pancreas (9.3%), extrahepatic (17.5%), intrahepatic bile duct (8.0%), and SI (43.5%), whereas MUC5AC being positive for the adenocarcinoma of the pancreas (70.4%), extrahepatic (60.0%), intrahepatic bile duct (44.0%), and SI (30.4%).^[16] These data suggest that MUC2 are highly positive for adenocarcinoma of the SI rather than the PB tract, whereas MUC5AC are conversely more positive for the adenocarcinoma of the PB tract than the SI. In the current case, IHC staining showed SI epithelium was MUC2+MUC5AC- but cancer cells were MUC2-MUC5AC+, consistent with this previous report.

In this case, we experienced that a hepatic segmental atrophy with portal vein occlusion was a finding of ICC. Previous reports demonstrated that cholangiocarcinoma can occlude the portal vein by direct or by extrinsic compression.^[17–20] A study investigating 17 cases with hilar cholangiocarcinoma and intrahepatic bile duct dilatation showed all 6 cases with an obstructed or narrowed portal vein had hepatic lobar or segmental atrophy.^[18] A case report of invasive cholangiocarcinoma also suggested that portal vein occlusion is alone sufficient to induce hepatic infarction even if hepatic blood flow is patent.^[17] Hence, we believe that a hepatic segmental atrophy in our case was caused by portal vein occlusion secondary to ICC. Furthermore, our case suggested that even if image studies do not reveal typical findings of ICC including contrast-enhanced lesions or intrahepatic bile duct dilatation, a hepatic atrophy with portal vein occlusion could be a sign of ICC.

Author contributions

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