Case Report

Journal Homepage: http://crcp.tums.ac.ir

# Cholangiocellular Cancer Metastasis in the Terminal Ileum: A Case Report

**Elif Didem Terzi***, **Bülent Güleç**

*Sultan Abdülhamid Han Training and Research Hospital, University of Health Sciences, Istanbul, Turkey.*

Use your device to scan and read the article online

**Citation** Didem Terzi E, Güleç B. Cholangiocellular Cancer Metastasis in the Terminal Ileum: A Case Report. Case Reports in Clinical Practice. 2026; 11(1): 31-36. DOI:10.18502/crcp.v11i1.22174

**Running Title** Cholangiocellular Cancer Metastasis in the Terminal Ileum

**Article info:**
**Received:** January 6, 2026
**Revised:** February 4, 2026
**Accepted:** February 16, 2026

**Keywords:**
Cholangiocarcinoma;
Intrahepatic cholangiocarcinoma;
Terminal ileum;
Metastasis;
Case report

## ABSTRACT

Intrahepatic cholangiocarcinoma (ICC) is an uncommon and aggressive hepatobiliary malignancy characterized by high recurrence rates and poor long-term survival. Although ICC frequently metastasizes to the liver, lungs, peritoneum, and lymph nodes, metastasis to the small intestine is extremely rare. The diagnostic challenge is further increased by its often-asymptomatic course and the low specificity of radiological imaging modalities. We present a rare case of terminal ileum metastasis from ICC manifesting as focal subileus, diagnosed during postoperative surveillance. A 44-year-old male underwent left hepatic lobectomy, hepaticojejunostomy, and cholecystectomy for well-differentiated ICC (pT2N1) in July 2023. Despite adjuvant capecitabine therapy, follow-up computed tomography revealed segmental pathological wall thickening of the terminal ileum with luminal narrowing, proximal dilatation, and associated mesenteric lymphadenopathy. Colonoscopic biopsy was not feasible due to the lesion's location. Further evaluation suggested malignancy, raising suspicion of metastatic ICC versus primary small bowel adenocarcinoma. The patient underwent right hemicolectomy with partial small bowel resection. Pathology demonstrated poorly differentiated adenocarcinoma (pT2) with lymphovascular and perineural invasion, and isolated tumor cells in one lymph node. Loss of MLH1 and PMS2 expression indicated MSI-H status. The findings were consistent with metastatic ICC. Postoperative recovery was complicated by intra-abdominal ascites requiring catheter drainage. The patient was referred to medical oncology for further management.

Metastasis of ICC to the terminal ileum is exceptionally rare but should be considered in patients presenting with unexplained small bowel obstruction or mural thickening during postoperative follow-up. Complete surgical resection can be effective when the patient's performance status allows. Multidisciplinary evaluation is essential for accurate diagnosis, differentiation from primary small bowel tumors, and appropriate oncological treatment planning.

*** Corresponding Author:**
***Elif Didem Terzi***
***Address:*** *Sultan Abdülhamid Han Training and Research Hospital, University of Health Sciences, Istanbul, Turkey.*
***E-mail:*** *edidem.terzi@sbu.edu.tr*

## Introduction

Cholangiocarcinoma is the most common primary malignancy of the biliary tract [1]. Cholangiocarcinoma (CCA) is a highly mortal malignancy of epithelial cell origin that can occur at any point in the biliary tract and/or within the liver parenchyma [2]. Cholangiocarcinoma is clinically mostly asymptomatic. Due to the low specificity of most radiological imaging methods and the lack of absolute diagnostic criteria, its diagnosis is difficult. In cholangiocarcinoma, symptoms appear in most patients at advanced stages. The clinical picture depends on the stage of the tumor, its location, and its growth pattern. The diagnosis is made based on clinical suspicion according to patients' symptoms and on laboratory and radiological findings [4]. Extrahepatic cholangiocarcinomas may cause jaundice and therefore may sometimes be detected at resectable stages [4]. In contrast, intrahepatic cholangiocarcinomas can remain asymptomatic for a long time and are therefore diagnosed at advanced stages [5]. With the progression of the disease, advanced-stage intrahepatic cholangiocarcinomas generally tend to metastasize to the liver and to extrahepatic organs such as the lungs, bones, brain, and lymph nodes [3]. Nevertheless, due to the scarcity of data on intrahepatic cholangiocarcinoma (ICC) metastases, there are very few studies that examine in detail the profiles of hepatic and extrahepatic metastases. Therefore, the metastatic patterns of ICC have not yet been fully clarified, and it remains uncertain whether different metastatic sites may lead to different clinical outcomes [6].

The incidence of intrahepatic cholangiocarcinoma (ICC) has been reported to account for approximately 4% to 10% of all primary liver cancers [7]. The significance of ICC arises from its rarity and the poor patient prognosis associated with high recurrence rates despite aggressive surgical treatments. For patients with intrahepatic cholangiocarcinoma (ICC), 5-year survival rates range from 13% to 42% [8,9]. The sites in which intrahepatic cholangiocarcinoma (ICC) typically recurs are the remaining liver tissue, the lungs, and the peritoneum (the abdominal lining). When recurrence develops, many patients are treated with chemotherapy and/or radiotherapy; however, these treatments are often insufficient. Nevertheless, in some cases, it has been reported that surgical removal of the recurrent lesion may be effective. However, the impact of surgical resection of recurrent lesions has not been clearly demonstrated [10]. In this report, we present our experience with a case of intrahepatic cholangiocarcinoma (ICC) in which a recurrent lesion was resected after the diagnosis of small intestine metastasis was made using computed tomography during postoperative follow-up due to elevated tumor markers.

## Case Presentation

A 44-year-old male patient was found to have elevated liver function tests and hyperbilirubinemia. Abdominal ultrasonography revealed diffuse, marked dilatation of the intrahepatic bile ducts and a hypoechoic solid lesion measuring 16 × 12.5 mm at the level of the pancreatic neck–corpus. Magnetic resonance imaging detected an irregularly bordered, hypovascular lesion area measuring 14 mm in diameter, located around the intrahepatic bile ducts in the left hepatic lobe and at the right intrahepatic bile duct–left junction. Laboratory examinations showed a CA 19-9 level of 847 U/mL and a CEA level of 6.83 µg/L, both above the reference range. In July 2023, the patient underwent left hepatic lobectomy, hepaticojejunostomy, and cholecystectomy. In the postoperative period, wound site discharge developed, and the patient was followed with a vacuum-assisted closure system.

Pathological examination revealed findings consistent with well-differentiated adenocarcinoma (cholangiocarcinoma, compatible with intrahepatic NOS). No tumor was observed at the surgical margin; the closest parenchymal surgical margin measured 0.5 cm. No tumor involvement was observed at the visceral peritoneum. Lymphatic invasion, portal vein invasion, and perineural invasion were present. One metastatic lymph node was identified. TNM staging was reported as pT2N1. Immunohistochemical evaluations showed CK7, CK19, EMA, MOC31, and M-CEA positivity; CK20, HEPPAR, CDX2, TTF1, Napsin-A, ER, PR, GATA3, and arginase were negative. In the postoperative period, the patient received seven cycles of adjuvant capecitabine therapy. In the computed tomography (CT) examination performed in April 2025, surgical removal of the left hepatic lobe was observed, with no findings suggestive of recurrence or residual disease in the resection bed. The hepaticojejunostomy anastomosis line was visualized. Mild prominence of the intrahepatic bile ducts in the right lobe was present. Postoperative surgical sutures were identifiable at the level of the hepatic hilum. The gallbladder was not visualized (consistent with surgical history).

In the right lower quadrant of the abdomen, at the level of the ileocecal valve and in the pelvic small bowel loops, a segmental (approximately 55 mm) mural thickening of the terminal ileum reaching

9 mm in thickness was observed, with concentric pathological mural thickening. In the adjacent mesenteric fat tissue, 7 mm lymph nodes and mild edema were noted. The pathological segment demonstrated marked luminal narrowing, with mild proximal dilatation and intraluminal fluid–food/fecal content accumulation. The appearance was consistent with focal subileus formation secondary to the pathological segment, and malignancy could not be excluded. Small bowel-type adenocarcinoma was considered primarily. Histopathological sampling via colonoscopy was deemed unfeasible as the lesion was located approximately 60 mm proximal to the ileocecal valve. In coronal imaging, the presence of a soft-tissue component extending polypoidly into the lumen in addition to mural thickening strengthened the suspicion of malignancy. Additionally, inferior to the surgical bed, to the right of the midline and anterior to the superior mesenteric vein, a solid nodular lesion measuring 10 mm with homogeneous contrast enhancement was detected. This lesion measured 13 mm and had a more oval shape on CT dated 09.01.2025, whereas the current examination showed regression. Other postoperative changes were stable. The pathological mural thickening in the right lower quadrant, described on CT dated 09.01.2025 as approximately 25 mm in length and 6 mm in thickness, demonstrated significant progression in the current examination(Figures 1&2).

In June 2025, the patient underwent right hemicolectomy, partial small bowel resection, and side-to-side anastomosis. During exploration, no malignant lesions were observed in other solid organs or the peritoneum. Macroscopic examination evaluated a right hemicolectomy specimen consisting of a 13 cm long, 3 cm diameter small bowel segment and an 18 cm long, 4.5 cm diameter colon segment. A 6 cm long and 0.6 cm diameter appendix was present on the specimen. Upon opening, a tumor lesion measuring 3.5 × 3 × 1 cm that circumferentially encircled the lumen was identified, located 12 cm from the proximal surgical margin and 3.5 cm from the ileocecal valve. According to the pathology report, a poorly differentiated adenocarcinoma was identified in the terminal ileum. The tumor had invaded up to the muscularis propria layer (pT2), and lymphovascular as well as perineural invasion were present. The appendix, colon, and surgical margins were free of tumor. No tumor was detected in twelve lymph nodes; however, isolated tumor cells were observed in one lymph node. Microsatellite instability analysis revealed loss of MLH1 and PMS2, consistent with an MSI-H tumor. These findings indicate that the tumor was completely surgically removed but that there is a risk of microscopic spread, and genetic analysis (MLH1 methylation or BRAF testing) and possible immunotherapy evaluation are recommended. These findings were consistent with the clinically known primary cholangiocellular carcinoma metastasis.

Additional immunohistochemical and pathological evaluation of the ileal lesion demonstrated loss of MLH1 and PMS2 nuclear expression, while MSH2 and MSH6 expression were preserved, indicating a high probability of MSI-H/dMMR status. PD-L1 analysis revealed a combined positive

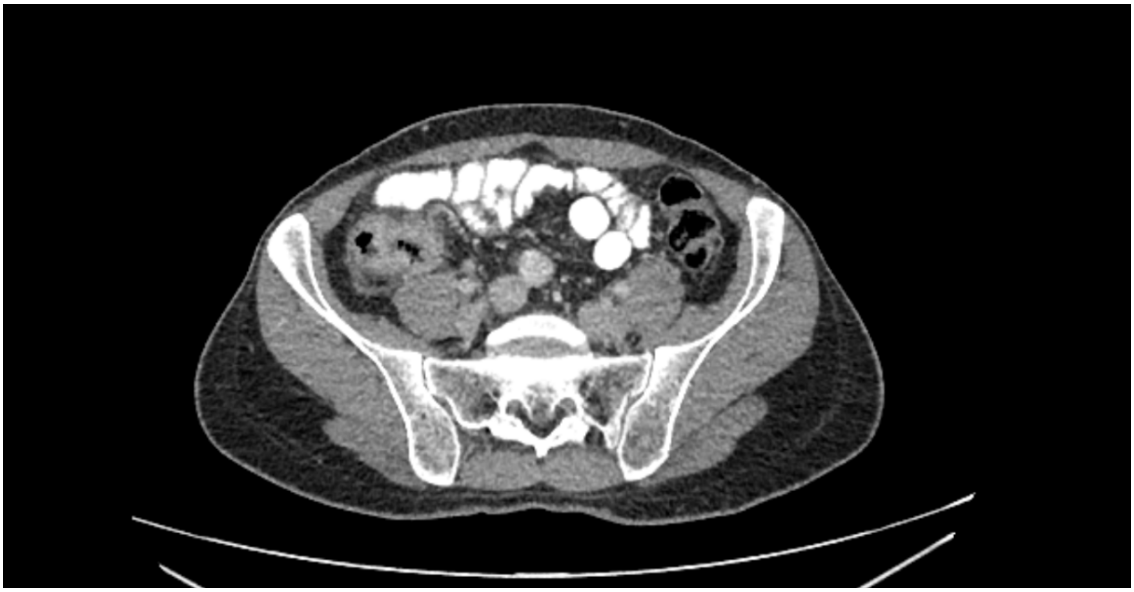

**Fig. 1.** Pathological wall thickening at the level of the terminal ileum in April 2025

score (CPS) of <1%, interpreted as negative. Extended molecular profiling and broader IHC comparison could not be performed because of technical limitations. Furthermore, histomorphological findings were evaluated in correlation with the patient's known history of intrahepatic cholangiocarcinoma, and the lesion was considered compatible with metastatic cholangiocarcinoma rather than primary small bowel adenocarcinoma by the pathology consultation report. On postoperative day 12, due to the development of widespread intra-abdominal ascites, a drainage catheter was placed by interventional radiology. The catheter was removed eight days later. The patient was referred to the medical oncology department for oncological treatment planning. Following multidisciplinary tumor board evaluation, the patient received seven cycles of pembrolizumab therapy because of the MSI-H/dMMR profile demonstrated by loss of MLH1 and PMS2 expression.

## Discussion

ICC is one of the primary liver malignancies associated with poor prognosis despite aggressive surgical treatment. In the vast majority of patients with ICC, recurrence develops within two years after surgery. Due to the high recurrence rate, five-year survival rates have been reported to range between 13% and 42% [8,9]. Postoperative recurrences frequently occur in the residual liver tissue, while extrahepatic recurrences typically appear in the lungs, peritoneum, and lymph nodes [11,12]. Failure to detect metastases in uncommon locations may lead to a rapid deterioration in the patient's overall condition and inadequacy of the treatment administered.

Metastasis of malignant solid tumors to the small intestine is quite rare, with an incidence reported between 1.1% and 8.5% even in autopsy series [13,14]. Possible routes of spread in ICC metastasis to the small intestine include peritoneal dissemination, hematogenous spread, and lymphatic spread [15]. Gastrointestinal metastases from intrahepatic cholangiocarcinoma are extremely rare. Only a limited number of case reports describing small bowel involvement have been published in the literature. Hayashi et al. reported jejunal metastasis occurring after resection of primary ICC, while Akiyama et al. described small bowel obstruction caused by ileal metastasis of ICC. These reports support the rarity of intestinal dissemination in ICC and emphasize the diagnostic difficulty of such unusual metastatic presentations [19]. In the present case, metastasis is thought to have most likely occurred via the hematogenous route. It has been reported that hematogenous spread is the preferred route in metastases located in unusual sites in ICC. Particularly in tumors originating from the right lobe of the liver, tumor cells may reach the small intestine via the hepatic vein → inferior vena cava → systemic circulation → mesenteric vessels pathway. The terminal ileum localization anatomically supports this possibility.

Lymphatic spread may occur to the small intestine

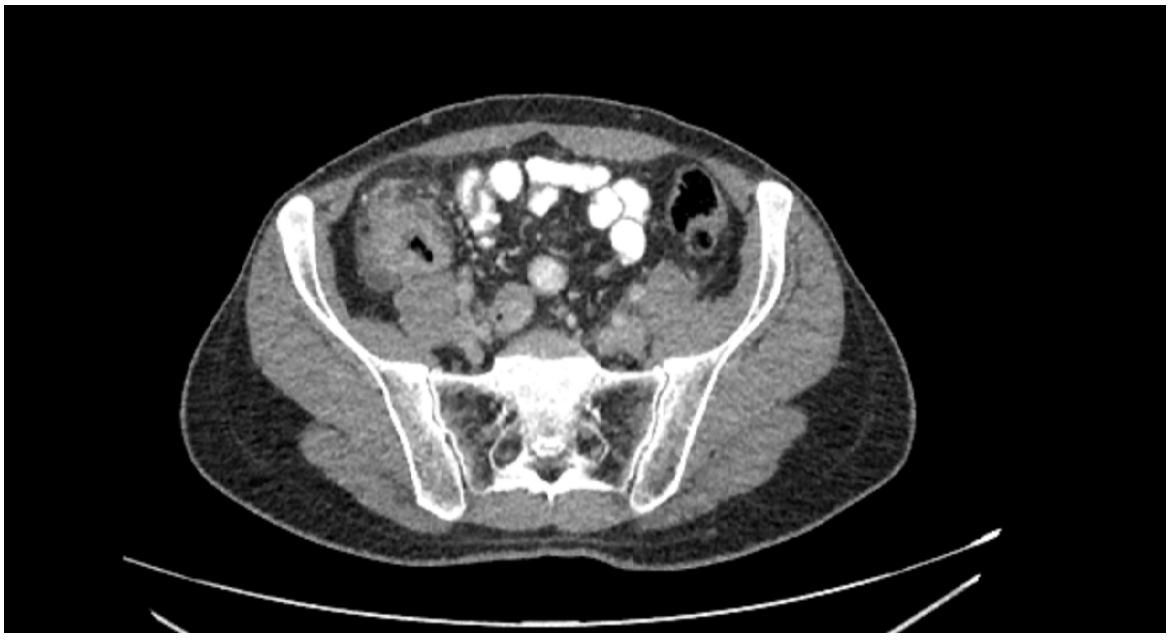

**Fig. 2.** Pathological wall thickening at the level of the terminal ileum in April 2025 at a different angle

through pathways such as the hepatoduodenal ligament, mesenteric lymph nodes, or para-aortic chains. However, this pathway is typically observed in cases with pronounced lymph node metastasis. In this case, the presence of only isolated tumor cells (pN0(i+)) suggests that lymphatic spread was not the dominant route. Peritoneal spread can occur in ICC; however, it usually presents as nodular implants on the peritoneal surface rather than as bowel wall invasion. In this case, the tumor's invasion up to the muscularis propria layer and the absence of tumor in the serosa further strengthen the hematogenous spread theory. The question of whether the detected small bowel lesion represented a primary tumor or an ICC recurrence is controversial. While pathological evaluation provided findings in favor of metastasis consistent with the known primary ICC, the rarity of small bowel metastasis in ICC also raises the possibility of a primary small bowel adenocarcinoma. Additionally, the high likelihood of MSI-H status may also be compatible with a primary small bowel adenocarcinoma. Therefore, differential diagnosis with advanced molecular diagnostic methods is recommended [10]. The differentiation between metastatic cholangiocarcinoma and primary small bowel adenocarcinoma may be particularly difficult because both entities can share overlapping histomorphological and immunohistochemical features. In rare metastatic presentations such as the present case, integration of clinical history, imaging findings, pathological evaluation, and molecular profiling is essential for accurate diagnosis [17]. MSI-H/dMMR status is uncommon in cholangiocarcinoma but has important therapeutic implications. Recent studies have shown that MSI-H biliary tract tumors may respond favorably to immune checkpoint inhibitors such as pembrolizumab. In the present case, loss of MLH1 and PMS2 expression suggested deficient mismatch repair status and supported consideration of immunotherapy in subsequent treatment planning. Although PD-L1 expression was negative (CPS <1%), MSI-H status itself may predict responsiveness to immunotherapy independent of PD-L1 expression. Previous studies, including the KEYNOTE-158 trial, demonstrated that MSI-H/dMMR status may predict response to pembrolizumab across multiple solid tumors regardless of PD-L1 expression status [16]. MSI-H/dMMR status is uncommon in biliary tract cancers; however, its identification has major therapeutic implications. Kai et al. reported that although MSI-H frequency is low in biliary tract tumors, MSI testing may provide critical guidance for immunotherapy-based treatment strategies [18].

In our case, although the small intestine metastasis posed a risk of bowel obstruction, the patient's performance status was suitable for surgery. For this reason, resection including the tumor and the relevant lymph nodes was performed. Preoperative diagnosis was made based on laboratory findings and computed tomography results. However, PET-CT was not performed due to the patient's uncontrolled glycemic status. Following surgery, the patient was referred to the medical oncology department for oncological treatment planning.

## Conclusion

Intrahepatic cholangiocarcinoma rarely metastasizes to the small intestine, and terminal ileal involvement is exceptionally uncommon. This case highlights the diagnostic challenge of differentiating metastatic cholangiocarcinoma from primary small bowel adenocarcinoma, particularly in the presence of MSI-H/dMMR features. Surgical resection may provide effective management in selected patients with isolated intestinal metastasis. In addition, comprehensive molecular profiling may contribute to both accurate diagnosis and identification of potential candidates for immunotherapy. Multidisciplinary evaluation remains essential in the management of such rare metastatic presentations.

## Ethical Considerations

### Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

### Funding

No funding was received to assist with the preparation of this manuscript.

### Conflict of Interests

The authors have no conflict of interest to declare.

### Patient perspective

The patient reported that the postoperative period after the second surgery was challenging due to abdominal discomfort and the development of ascites requiring catheter drainage. However, he expressed

relief that the intestinal obstruction was resolved and that the tumor lesion was completely removed. The patient stated that he was satisfied with the multidisciplinary care he received and understood the necessity of further oncological follow-up and treatment. He emphasized the importance of regular follow-up examinations and expressed hope that the ongoing treatment plan would help control the disease.

## Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical images. All patient information has been anonymized to protect confidentiality in accordance with ethical standards.

## Timeline

July 2023 – Left hepatic lobectomy for ICC

Aug 2023 – Adjuvant capecitabine therapy started

April 2025 – CT revealed terminal ileum lesion

June 2025 – Right hemicolectomy performed

Postoperative period – Ascites requiring catheter drainage

## References


[1] Everhart JE, Ruhl CE. Burden of digestive diseases in the United States: Part III - Liver, biliary tract, and pancreas. Gastroenterology. 2009;136(4):1134-44. https://doi.org/10.1053/j.gastro.2009.02.038

[2] Hayran B, Malato Y, Calvisi DF, Naqvi S, Razumilava N, Kaburga S, et al. Cholangiocarcinomas can originate from hepatocytes in mice. J Clin Invest. 2012;122(8):2911-5. https://doi.org/10.1172/JCI63212

[3] Razumilava N, Gores GJ. Cholangiocarcinoma. Lancet. 2014;383(9935):2168-79. https://doi.org/10.1016/S0140-6736(13)61903-0

[4] Blechacz B, Komuta M, Roskams T, Gores GJ. Clinical diagnosis and staging of cholangiocarcinoma. Clin Liver Dis. 2011;15(2):301-15. doi: 10.1016/j.cld.2011.01.002.

[5] Sempoux C, Balabaud C, Bioulac-Sage P. Intrahepatic cholangiocarcinoma: New insights in pathology. Semin Liver Dis. 2011;31(1):49-60. https://doi.org/10.1055/s-0031-1272839

[6] Yoh T, Hatano E, Yamanaka K, et al. Is surgical resection justified for advanced intrahepatic cholangiocarcinoma? Liver Cancer. 2016;5(4):280-9. https://doi.org/10.1159/000449271

[7] Patel T. Increasing incidence and mortality of primary intrahepatic cholangiocarcinoma in the United States. Hepatology. 2001;33(6):1353-7. https://doi.org/10.1053/jhep.2001.25087

[8] Lieser MJ, Barry MK, Rowland C, Ilstrup DM, Nagorney DM. Surgical management of intrahepatic cholangiocarcinoma: A 31-year experience. J Hepatobiliary Pancreat Surg. 1998;5(1):41-7. https://doi.org/10.1007/s005340050034

[9] Chu KM, Fan ST. Intrahepatic cholangiocarcinoma in Hong Kong. J Hepatobiliary Pancreat Surg. 1999;6(2):149-53. https://doi.org/10.1007/s005340050095

[10] Hayashi H, Tani T, Tajima H, Shoji Y, Terai S, Onishi I, et al. Small intestinal metastasis from intrahepatic cholangiocarcinoma: Report of a case. Surg Today. 2011;41(6):859-64. https://doi.org/10.1007/s00595-010-4358-1

[11] Ikai I, Arii S, Okazaki M, Okita K, Omata M, Kojiro M, et al. Report of the 17th nationwide follow-up survey of primary liver cancer in Japan. Hepatol Res. 2007;37(9):676-91. https://doi.org/10.1111/j.1872-034X.2007.00122.x

[12] Valverde A, Bonhomme N, Farges O, Sauvanet A, Flejou JF, Belghiti J. Resection of intrahepatic cholangiocarcinoma: A Western experience. J Hepatobiliary Pancreat Surg. 1999;6(2):122-7. https://doi.org/10.1007/s005340050093

[13] Good CA. Tumors of the small intestine. Am J Roentgenol Radium Ther Nucl Med. 1963;89(4):685-705.

[14] Fujii K, Nagino M, Kamiya J, Uesaka K, Sano T, Yuasa N, et al. Complete resection of hepatocellular carcinoma with direct invasion to the stomach remnant. J Hepatobiliary Pancreat Surg. 2004;11(6):441-4. https://doi.org/10.1007/s00534-004-0926-3

[15] Gill SS, Heuman DM, Mihas AA. Small intestinal neoplasms. Am J Gastroenterol. 2001;96(10):2992-3. https://doi.org/10.1097/00004836-200110000-00004

[16] Marabelle A, Le DT, Ascierto PA, Di Giacomo AM, De Jesus-Acosta A, Delord JP, et al. Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: Results from the phase II KEYNOTE-158 study. J Clin Oncol. 2020;38(1):1-10. https://doi.org/10.1200/JCO.19.02105

[17] Jiang S, Huang L, Jiang Q. A case report of a rare intrahepatic cholangiocarcinoma with rectal metastasis. Medicine (Baltimore). 2021;100(18):e25703. https://doi.org/10.1097/MD.0000000000025703

[18] Kai Y, Ikezawa K, Takada R, Daiku K, Maeda S, Abe Y, et al. Success rate of microsatellite instability examination and complete response with pembrolizumab in biliary tract cancer. Case Rep Oncol. 2021;14(2):1140-9. https://doi.org/10.1159/000516514

[19] Akiyama S, Eguchi H, Goi T, Nakazawa T, Yamaguchi A. Small intestinal obstruction due to the metastasis of intrahepatic cholangiocarcinoma: A case report. Medicine (Baltimore). 2018;97(13):e9776. https://doi.org/10.1097/MD.0000000000009776