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Colon cancer metastasis mimicking intraductal papillary neoplasm of the extra-hepatic bile duct

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ABSTRACT

INTRODUCTION: An accurate diagnosis of the primary cancer in cases with metastatic lesions is quite important because misdiagnosis may lead to the selection of incorrect adjuvant therapy and worse long-term outcomes after surgery. The metastatic sites associated with the dissemination of colon cancer are well known and normally predictable, which includes the lymphatic, haematogenous, or peritoneal regions, while other locations are quite rare.
PRESENTATION OF CASE: In this report, we present a case of colon cancer with an unusual metastatic pattern mimicking an intraductal papillary neoplasm of the bile duct (IPNB) present in the extra-hepatic bile duct with a cytokeratin (CK)-7–negative and CK-20–positive profile (intestinal type).
DISCUSSION: In the case of this patient who had a history of colon cancer, immunohistochemical staining for the CKs was useful for distinguishing between primary IPNB and colon cancer metastases. We suspect that the metastatic pattern of this case of colon cancer that mimicked IPNB at the extra-hepatic bile duct developed incidentally via the bile stream.
CONCLUSION: This is a rare case of colon cancer metastasis mimicking IPNB at the extra-hepatic bile duct. Our findings also suggest that there may be an incidental 4th metastatic route via the bile stream.

1. Introduction

An accurate diagnosis of the primary cancer in cases with metastatic lesions is quite important because misdiagnosis may lead to the selection of incorrect adjuvant therapy and worse long-term outcomes after surgery. The metastatic sites associated with the dissemination of colon cancer are well known and normally predictable, which includes the lymphatic, haematogenous, or peritoneal regions, while other locations are quite rare. Here, we present a case of colon cancer with an unusual metastatic pattern mimicking an intraductal papillary neoplasm of the bile duct (IPNB) present in the extra-hepatic bile duct.

2. Presentation of case

A 65-year-old woman underwent right transverse colectomy for the treatment of moderately differentiated colon cancer (stage II) with no lymphatic or vascular infiltration or lymph node metastasis. After 7 years, enhanced computed tomography (CT) revealed a large (7–8 cm in diameter) metachronous liver metastasis in the right lobe. The serum carcinoembryonic antigen level was high (11 ng/mL) compared to the normal level of <5.0 ng/mL; whereas, the levels of carbohydrate antigen 19–9 and α-fetoprotein were within the normal range. As analysis of the primary colonic lesion revealed the presence of the wild-type K-ras, four courses of systemic chemotherapy consisting of S-1 and oxaliplatin plus cetuximab were introduced as part of a clinical trial; thereafter, a right lobectomy was performed as a curative measure.

The serum carcinoembryonic antigen level decreased postoperatively, and no apparent recurrence was observed. After 10 months, the patient was detected with jaundice and elevated levels of alkaline phosphatase (408 IU/mL) and γ-glutamyl transpeptidase (1361 IU/mL); enhanced CT revealed soft tissue in the extra-hepatic bile duct with biliary dilatation (Fig. 1a and b). Magnetic resonance cholangiography and endoscopic retrograde cholangiography displayed a papillary tumour in the middle to distal portion of the bile duct (Fig. 1c and d). A blush appearance indicated a class V tumour.

Based on the preoperative diagnosis of intraductal papillary neoplasm of the bile duct (IPNB), subtotal stomach-preserving pancreaticoduodenectomy with lymph node dissection of the hepatoduodenal ligament surrounding the common hepatic artery was performed. Macroscopic examination of the resected specimen revealed a soft papillary tumour at the middle to distal

Abbreviations: IPNB, intraductal papillary neoplasm of the bile duct; CT, computed tomography; CK, cytokeratin.

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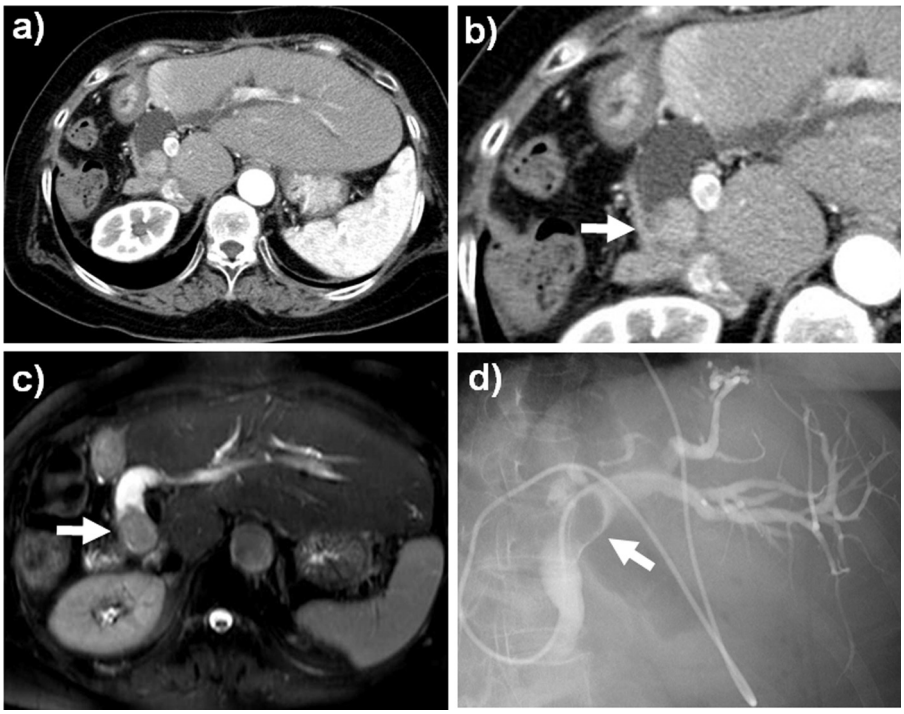

Fig. 1. Radiological findings of colon cancer metastasis mimicking intraductal papillary neoplasm of the extra-hepatic bile duct (IPNB).

portion of the bile duct with intact surrounding epithelial tissue (Fig. 2a). Microscopic findings using haematoxylin-eosin (HE) staining revealed the presence of an intraductal papillary tumour with a fibrovascular core (Fig. 2b). Histological analysis revealed that the IPNB showed moderately differentiated tubular adenocarcinoma; vascular/lymphatic infiltration or lymph node metastasis was not detected. Further examination using immunohistochemical staining uncovered that the IPNB was a metastatic lesion arising from colonic carcinoma (Fig. 3). The neighboring biliary epithelium showed a cytokeratin (CK)-7–positive and CK-20–negative profile (pancreatobiliary type), while the tumour displayed a CK-7–negative and CK-20–positive profile (intestinal type). The expression pattern was similar to those seen in the primary site and liver metastatic site (Supplementary Figs. S1 and S2). The tumour was ultimately diagnosed as a colon cancer metastasis mimicking IPNB, after which adjuvant chemotherapy for colon cancer was initiated.

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3. Discussion

Accurate diagnosis of the primary cancer in cases of colon cancer with metastatic lesions is quite important, as treatment using effective chemotherapy regimens including molecular targets is currently available. Colon cancer-associated metastatic sites are normally predictable because of its three well-known metastatic patterns of dissemination to the lymphatic, haematogenous, and peritoneal regions. Indeed, the most common metastatic sites of colorectal cancer by order of frequency consist of the regional lymph nodes, the liver via the portal circulation, the lungs, the peritoneum, and the ovaries. Although other localizations of colon cancer metastasis occur very rarely, such metastases occasionally mimic the primary cancer.

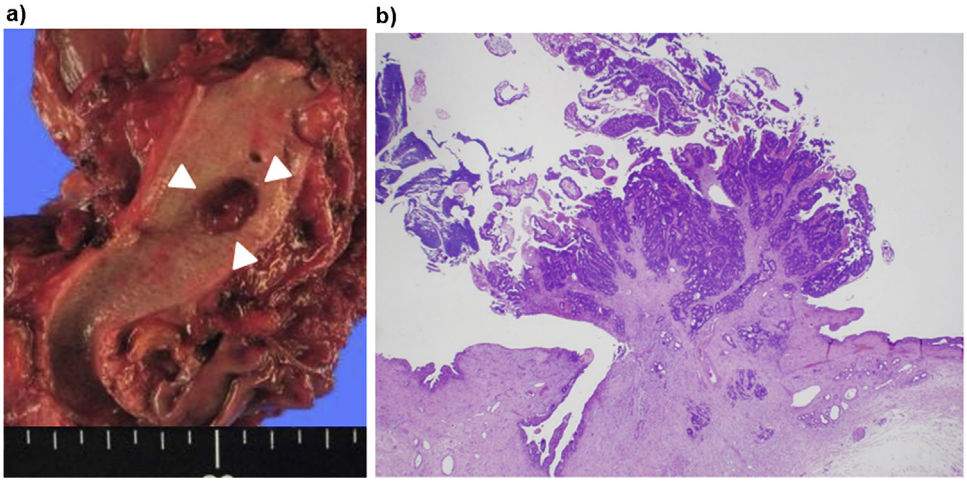

Fig. 2. Macroscopic and microscopic findings of colon cancer metastasis mimicking intraductal papillary neoplasm of the extra-hepatic bile duct (IPNB).

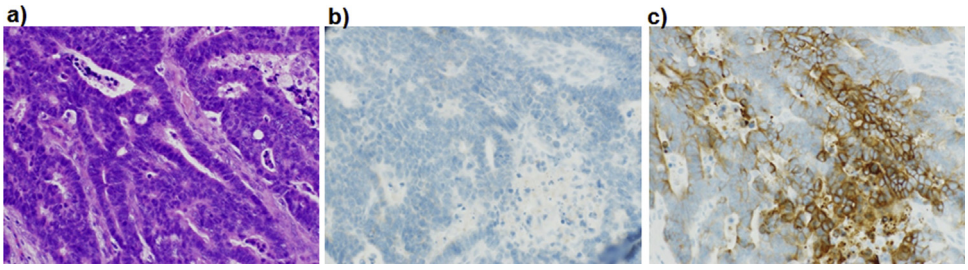

Fig. 3. Microscopic findings of the colon cancer metastasis in the extra-hepatic bile duct (magnification, 20×).

Here, we show a case of colon cancer with an unusual metastatic pattern mimicking IPNB. While there are a few reports of colon cancer metastasis mimicking IPNB at the intra-hepatic bile duct [1–4], this is the first report of colon cancer metastasis mimicking IPNB at the extra-hepatic bile duct. In the present case, it was difficult to distinguish between primary IPNB and colon cancer metastasis using radiological findings and HE staining. Conversely, immunohistochemical staining using CK-7 and CK-20 successfully helped to determine that the ductal tumour was a metastatic lesion arising from a colon carcinoma. Therefore, in patients with a history of colon cancer, careful examinations including immunohistochemical staining are needed to obtain accurate diagnosis of IPNB because misdiagnosis may lead to administration of the incorrect adjuvant therapy and worse long-term outcomes after surgery. In such cases, if the immunohistochemical staining profile (CK-7 and CK-20) of a bile duct tumour can be determined using the biopsy sample, then bile duct resection may be a suitable curative procedure.

The mechanism of extra-hepatic biliary metastasis of colon cancer is not very clear; however, possible mechanisms include vascular invasion via the lymph vessels, blood vessels, or biliary tract, and implantation of malignant cells to the bile duct epithelium via the bile stream. In the case of this patient, there was no clear evidence of vascular invasion of the lymph and blood vessels in the primary or metastatic sites. In addition, direct biliary involvement of colorectal liver metastasis, which frequently shows intraductal growth connected with the primary intraparenchymal tumour, was not detected. Furthermore, the intraductal tumour was limited within the bile duct epithelium of the extra-hepatic bile duct. Therefore, vascular invasion to the lymph vessels, blood vessels, or biliary tract was unlikely in the present case.

To explain the present metastatic pattern to the extra-hepatic bile duct, the other mechanism of metastasis via the bile stream might be possible. Okano et al. [5] reported that bile duct invasion in patients with colorectal liver metastasis was histologically detectable in 62 (42%) of 149 patients. Although there was no clear evidence of microscopic or macroscopic biliary invasions in the metastatic sites in the present case, it is unclear whether biliary invasion was present at the metastatic sites prior to the systemic chemotherapy. Implantation of malignant cells to the bile duct epithelium via the bile stream prior to chemotherapy or during the surgical procedures is possible [4]. Further studies are required to confirm the presence of metastatic patterns via the bile stream.

4. Conclusion

This is a rare case of colon cancer metastasis mimicking IPNB at the extra-hepatic bile duct. Immunohistochemical staining with CK-7 and CK-20 is useful to distinguish between primary IPNB and colon cancer metastasis. Our findings also suggest that there may be an incidental 4th metastatic route via the bile stream.

Conflict of interest

The authors have declared that no competing interests exist.

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None.

Author contribution

Takanobu Yamao and Hiromitsu Hayashi wrote the draft. Takaaki Higashi, Hideaki Takeyama, Takayoshi Kaida, Hidetoshi Nitta, Daisuke Hashimoto, and Akira Chikamoto managed the clinical treatment and collected the data. Toru Beppu critical revisions for this draft. Hideo Baba organized the paper and approved the final version to be published.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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