



Intrabiliary growth of colic cancer metastasis: A case report and literature review

Abstract

Introduction: Biliary metastasis of colorectal cancer is a rare association with metastatic liver carcinoma. Differential diagnosis with cholangiocarcinoma can be difficult but must be established in order to offer the best therapeutic strategy.

Case presentation: We report the case of a 39 years old woman who has undergone subtotal colectomy with ileocolic anastomosis for occluded sigmoid cancer. Histological examination revealed well-differentiated adenocarcinoma pT3N0M0 with perineural and vascular invasion. Adjuvant chemotherapy was undergone. Three years later, a resection of the segment I for liver metastasis was performed. The microscopic examination concluded to adenocarcinoma from a primary colic cancer. Two years later, wedge resection of two liver nodules of segment IV and VIII and a cholecystectomy was performed. Each time surgical margins were negative. In December 2019, follow-up biology revealed elevated carcinoembryonic antigen. A liver metastasis in segment VIII and a suspicious hepatic hilum ganglion were revealed in imaging. Chemotherapy was conducted. Control imaging showed total regression of segment VIII metastasis and a slight increase in the size of the hilum mass. The patient was operated on preoperative examination showed a mass hanging from the right edge of the hepatic pedicle. Its resection resulted in the loss of substance from the left hepatic duct. Macroscopic examination revealed intrabiliary growth. Histological examination revealed carcinomatous metastasis compatible with the first colic cancer. Resection margins were negative.

Conclusion: Intrabiliary growth can have a deceptive presentation. The mechanism and prognosis are not clear. Surgical resection appears to be an acceptable treatment.

Keywords: colic cancer, metastasis, intrabiliary.

Introduction

The liver is a common location of colorectal metastasis [1]. Surgical resection has been accepted as a reasonable treatment for patients with hepatic metastases [2,3]. Intrabiliary growth of liver metastasis originating from colorectal carcinoma is a rare manifestation of metastatic liver carcinoma. This unusual location is thought to be associated with liver metastases in 3% to 10% [3-5]. We report a rare case of intrabiliary carcinoma mimicking a lymph node metastasis.

Case presentation

A 31 years old woman presented with bowel obstruction related to sigmoid cancer. A subtotal colectomy with ileocolic anastomosis. Microscopic examination revealed a well-differentiated adenocarcinoma, pT3 N0 M0, stage IIA according to the Union for International Cancer Control (UICC) 7th edition. The patient received adjuvant chemotherapy based on FOLFOX for 6 months.

Two years later, the follow-up Computed Tomography (CT) revealed liver metastasis in segment I. patient underwent surgical resection of segment I. The histological examination concluded a liver metastasis of colonic adenocarcinoma. The resection margins were negative. The patient received a second course of chemotherapy based on FOLFOX for six weeks.

In 2018, the patient presented with elevated carcinoembryonic antigen. No disturbance in liver function tests was found. CT showed two liver metastasis in segments IV and VIII. She underwent surgical hepatectomy resecting both metastasis and a cholecystectomy. Surgical margins were also negative and microscopic examination concluded the same ascertainment.

In December 2019, biological follow-up showed an increase in the serum carcinoembryonic antigen level from normal at 5 mg/mL to 11 mg/mL. Liver MRI showed an infracentimetric liver nodule and dilation of the left intrahepatic bile duct without a detectable obstacle (**FIGURE 1**).

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A PET imaging was then performed showing abnormal uptake in segment VIII of the liver and the hepatic hilum related to a metastatic lymph node (**FIGURE 2**). Chemotherapy based on 11 courses of Bevacizumab and 13 courses of FOLFIRI was undergone.

In January 2021, reevaluation imaging showed total regression of the liver nodule, an increase

in the size of the metastatic Hilary lymph node from 10 mm to 15 mm, and a discrete increase in the dilation of the left intrahepatic bilbiliaryact (8 mm to 11 mm) (**FIGURE 3**).

The second course of bevacizumab and FOLFIRI was undergone but curtailed due to hematologic intolerance. IMarchsh 2021, an imagery assessment, consisting of a liver MRI,

FIGURE 1. Liver MRI showed an infracentimetric liver nodule and dilation of the left intrahepatic bile duct without a detectable obstacle.

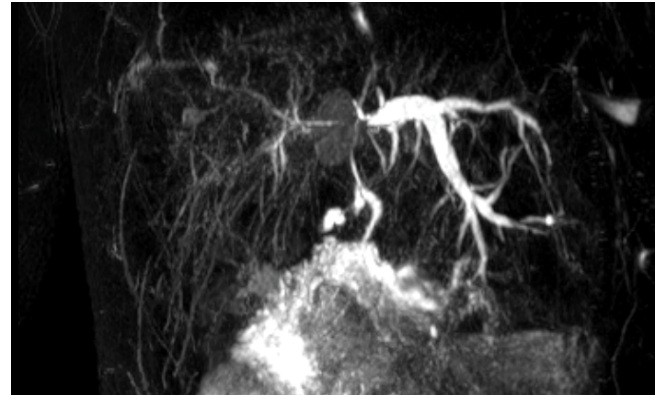
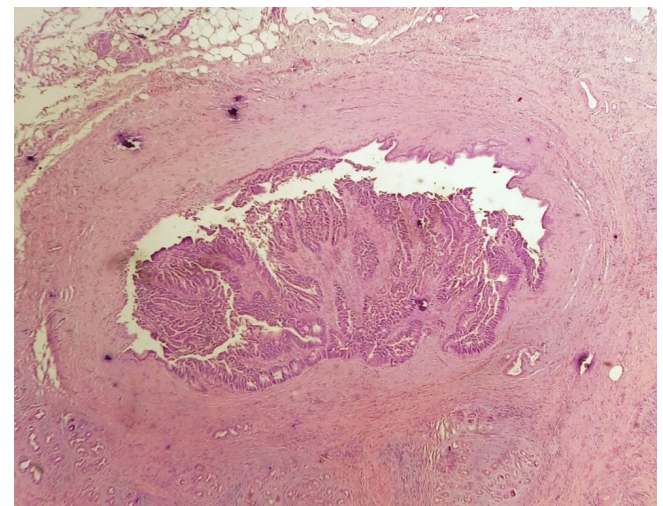


FIGURE 2. Macroscopic examination revealed budding epithelial proliferation in a biliary lumen.



FIGURE 3. Histological examination showed Tubulopapillary carcinomatous proliferation budding in intralumen bordered by a biliary epithelium.



a PET scan, and a thoracic-abdominal-pelvic CT found similar observations compared to those of January the same year. Serum level of carcinoembryonic antigen was 2829 mg/ml. The decision was to operate on the patient. Through a right subcostal incision. Dissection was laborious. Perioperative examinations found a mass hanging from the right edge of the common hepatic duct and invading the left hepatic bile duct. Its resection resulted in the loss of substance from the left hepatic duct. Reparation of the biliary air duct was done using a patch of the falciform ligament. Macroscopic

examination revealed budding epithelial proliferation in a biliary lumen (**FIGURE 4**).

Histological examination showed Tubulopapillary carcinomatous proliferation budding in intra- lumen bordered by a biliary epithelium. This fibrous wall contains also many biliary-type glands. Resection margins were negative. Immunohistochemistry showed strong positivity for CDX2. CK20 positive profile and CK negative, proving the colorectal origin of the metastasis. The postoperative course was complicated by an under hepatic abscess which responded to percutaneous drainage and

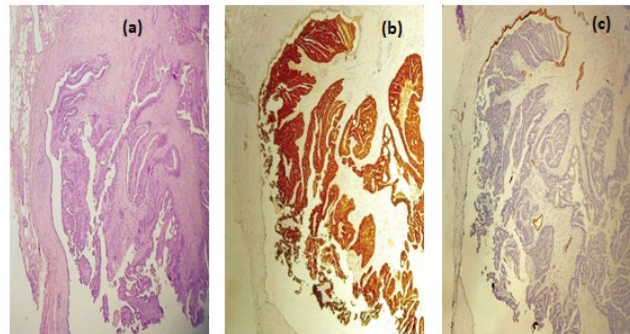


FIGURE 4. (a-c)Immunohistochemistry showed strong positivity for CDX2. CK20 postpositively and CK negative, proving the colorectal origin of the metastasis.m.

TABLE 1. Intrabiliary growth of liver metastasis in colorectal cancer, literature review.

Study	Type of study	Year	Number of cases	Bile duct involvement
Okano et al. [3]	Retrospective	1999	149	Macroscopic: 18 (12%)
				Microscopic: 44 (30%)
Kubo et al. [5]	Retrospective	2002	217	Macroscopic: 23 (10.6%)
				Microscopic: 89 (40.6%)
Estrella et al. [7]	Retrospective/prospective	2013	Retrospective: 1114	Major: 22 (1.9%)
				Minor: 19 (1.7%)
			Prospective: 170	Major: 9 (5.3%)
				Minor: 9 (5.3)
Kawakatsu et al. [8]	Case report	2015	-	-
Yamao et al. [9]	Case report	2015	-	-
Watanabe et al. [6]	Case report	2018	-	-
Sasaki et al. [1]	Case report	2019	-	-
Nakagawa et al. [4]	Case report	2020	-	-

antibiotics. The patient was released on day 11.

Discussion

The liver is the first site of metastasis from colorectal cancer [6]. Intrabiliary growth of liver metastasis is a rare association. Sasaki and all reported an incidence rate of intrabiliary growth raging between 3.6% and 10.6%[1]. This incidence is still disputed. Japanese

studies suggested that the occurrence of intrabiliary microscopic invasion reaches 46% and macroscopic growth reaches 10.6% [5]. However, in 2013, Estrella and all [7] found lower bile duct involvement at a rate of 5.3% prospectively and 3.6% retrospectively. The reason for this discrepancy is unclear and may be related to the different management strategies for colorectal metastases (**TABLE 1**).

This localization may pose the problem of differential diagnosis with intrahepatic cholangiocarcinoma [8]. Some authors recommend the use of immunohistochemistry to establish the diagnosis of colorectal metastasis by determining the expression of CK7 and CK20 [7]. CK7 negative and CK20 positive expression pattern has a 93% predictive value for the diagnosis of colorectal metastases [4]. In our case, the metastasis mimicked a hilum lymph node that was responsible for dilatation of the left intrahepatic bile ducts. This was an exceptional presentation of colorectal liver metastasis. An aggressive therapeutic strategy based on iterative surgery and chemotherapy was conducted to give the patient the best curative chances.

Okano et al. found that macroscopic bile duct invasion of colorectal metastases was paradoxically associated with a better prognosis than liver metastases with no bile duct extension [3]. In 2002 Kubo proceeded with this work and found similar results [5]. The authors found that this group of patients had well-differentiated phenotypes, no venous invasion, and longer intervals between colectomy and hepatectomy [5]. These findings were confirmed by other papers [2,7,10]. However, a more recent study associated intrabiliary metastasis with a poorer prognosis [6]. Furthermore, Estrella et al. did not find a significant difference between patients presenting bile duct invasion with those who have no invasion [7].

Colon cancer is known to disseminate through three patterns, lymphatic, hematogenous, and peritoneal. However, the mechanism of intrabiliary extension remains unclear [5].

Sano et al. suggested that the mechanism of metastasis was through cancer cell implantation [11]. This may be due to spontaneous shedding of cancer cells or may arise from a complication of percutaneous transhepatic biliary drainage. This theory is not applicable in our case because there was no need for transhepatic biliary drainage. Kawakatsu et al. suggested that the mechanism involves cancer cell implantation rather than hematogenous dissemination. This may be explained by the fragile nature of well-differentiated adenocarcinoma [8]. In this mechanism, Nakagawa et al. supposed that implantation occurred in injured bile ducts or at the site of the resection stump [4]. In our case, there was no injury to the left bile duct reported preoperatively and resection margins were negative. The mechanism remains unclear such as in the case reported by Yamao et al. [9].

Furthermore, intrabiliary invasion of liver metastases can be seen in noncolorectal cancer. But this eventuality remains extremely rare and it appears that this localization is more specifically associated with colorectal cancer [7].

Conclusion

Intrabiliary growth of liver metastases from colorectal cancer remains a rare localization. Still, Japanese authors state that this entity may be largely overlooked. Some authors associated this localization with a better prognosis than patients with liver metastases did. Diagnosis may be challenging. In our case, intrabiliary localization mimicked a hilum lymph node. Surgical resection seems to be the most appropriate treatment. Nevertheless, a clear strategy should be established.

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