Case Report

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A case report of rectal adenocarcinoma with intrahepatic cholangiocarcinoma of the liver

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Abstract

Objective: In this case report, we describe our experience with a patient who was treated for rectal adenocarcinoma complicated with primary cholangiocarcinoma of the liver and highlight the problems in the diagnosis and treatment of these potentially fatal lesions.

Methods: In the clinical setting, we often use the concept of "monism" for diagnosis and treatment. In this report, we review the diagnosis and treatment of rectal adenocarcinoma complicated with primary cholangiocarcinoma of the liver.

Results: Four months after surgery, the patient's carbohydrate antigen 19-9 level was elevated, and positron emission tomography/computed tomography showed multiple liver metastases. The patient underwent three rounds of transarterial chemoembolisation and two rounds of radiofrequency ablation at our hospital for recurrent hepatocellular carcinoma. The clinical response was poor and indicative of progression of intrahepatic lesions.

Conclusion: A preoperative multidisciplinary team, rapid intraoperative pathological examination, and active comprehensive postoperative treatment are necessary to improve the prognosis of multiple primary tumours.

Keywords

Multiple primary tumours, rectal adenocarcinoma, intrahepatic cholangiocarcinoma, carbohydrate antigen 19-9, liver metastasis, transarterial chemoembolisation

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Introduction

The liver is one of the most common sites for colorectal cancer metastasis. Up to 25% of patients with colorectal cancer will develop liver metastasis at some point.[1,2] However, the development of multiple liver lesions in patients with rectal adenocarcinoma is rare. The incidence of multiple primary tumours reportedly ranges from 2% to 17%.[3] The digestive system is the most common site of multiple primary tumours. There are some treatment differences between rectal liver metastases and liver tumours. In this case report, we review the diagnosis and treatment of rectal adenocarcinoma complicated with primary cholangiocarcinoma of the liver to provide information that will assist physicians in clinical practice.

Case presentation

The patient and his family provided written informed consent and agreed with publication of this case report. This study was approved by the Ethics Committee of Lishui Hospital.

A 58-year-old man presented with a 1-year history of a space-occupying liver lesion of <2-cm diameter. He had a medical history of hepatitis B virus-related liver cirrhosis (Child–Pugh classification grade A). He had experienced no discomfort for 1 year of regular outpatient follow-up. Abdominal computed tomography (CT) showed a 3.2- × 3.5-cm hepatic lesion in March 2017.

The patient's vital signs on arrival were as follows: blood pressure, 152/93 mmHg; pulse rate, 100 beats/minute; respiratory rate, 20 breaths/minute; and body temperature 36.2°C. Physical examination revealed the absence of yellowish skin, icteric sclera, and abdominal pain. Murphy's sign was negative. The patient's bowel sounds were normal, and his abdomen was soft with no rebound pain. Anal inspection revealed no abnormalities. Laboratory data included a carbohydrate antigen 19-9 (CA199) concentration of >1200.0 U/mL and CA199 (dilution) concentration of 5851.8 U/mL. Liver nuclear magnetic resonance imaging showed a lumpy abnormal signal intensity with a clear boundary (segment 7 of the liver) measuring approximately 4.1 × 3.1 cm. T1-weighted imaging revealed a slightly lower signal, and T2-weighted imaging and fat-suppression imaging revealed a slightly higher signal. We also observed significant edge enhancement in the arterial phase followed by a lesser degree of gradual central enhancement (Figure 1(a)). Electronic enteroscopy showed a wide-based hyperplastic polyp measuring approximately 1.5 × 1.6 cm and exhibiting surface erosion (Figure 1(b)). Pathologic examination of an intestinal biopsy specimen indicated severe heteroplastic hyperplasia of the mucous membranes and canceration. ^{18}F-FDG positron emission tomography (PET)/CT revealed a low-density mass on the right posterior lobe of the liver, indicative of hepatic metastasis of rectal carcinoma or intrahepatic cholangiocarcinoma, and thickening of the local intestinal wall in the upper rectum with increased FDG metabolism. There was no evidence of lymphatic metastasis (Figure 2).

The hepatic lesions and rectal cancer were clearly observed. According to the "monism" concept and clinical anatomy, we first considered hepatic metastasis of rectal carcinoma. However, the imaging findings were consistent with liver tumours. When synchronous liver metastases are present, they are usually small and mostly located in the periphery or limited to half of the liver, and the liver resection volume is typically <50%. Patients who can endure surgical removal of lymph nodes from the abdominal cavity or of other distant metastases of the hepatic portal system may be recommended to undergo phase I synchronous resection. On one hand, the patient's overall condition was not a contraindication

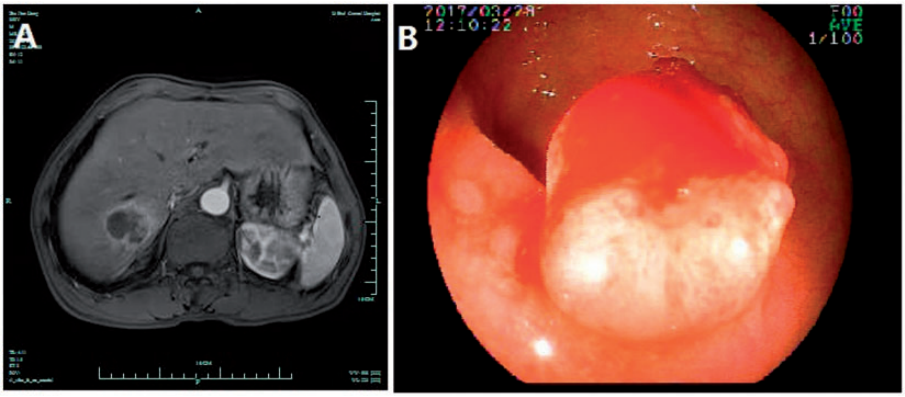

Figure 1. Magnetic resonance imaging and electronic enteroscopy. (a) A liver mass was located in the right lobe and demonstrated significant enhancement in the arterial phase. (b) A wide-based hyperplastic polyp with surface erosion was also observed.

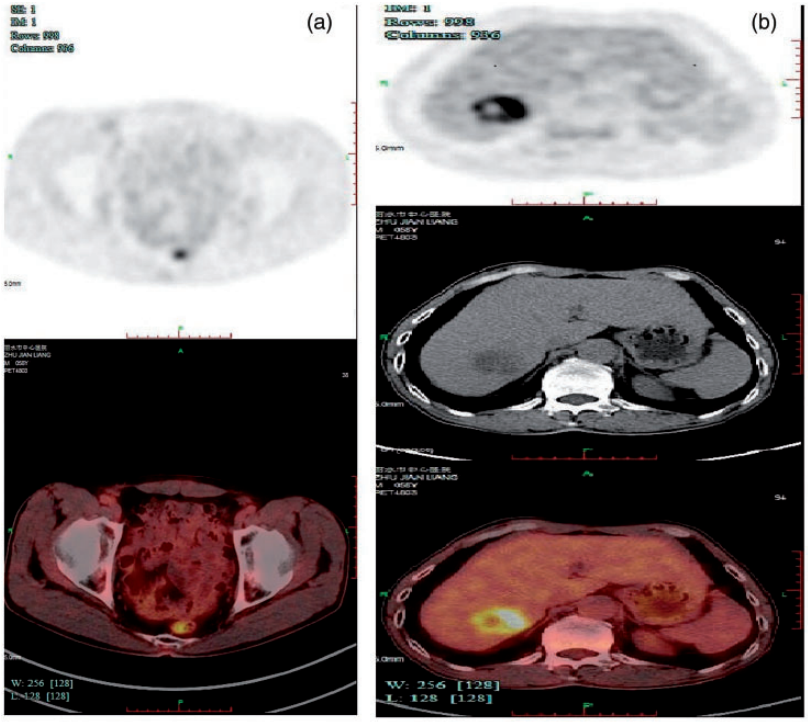

Figure 2. ^{18}F-FDG positron emission tomography. The upper rectum showed local thickening of the intestinal wall and elevated radioactive intake (maximum standardised uptake value, 5.4). Low density was observed in the right posterior lobe of the liver with elevated radioactive intake (maximum standardised uptake value, 9.1).

to surgical resection, and the primary rectal cancer could be removed. On the other hand, regardless of whether the liver lesion was metastatic or primary, the patient was amenable to sufficient residual liver volume and function after resection. Therefore, we performed a laparoscopic right liver tumour resection and rectal cancer resection. Microscopic examination revealed intrahepatic cholangiocarcinoma and rectal adenocarcinoma (Figure 3) characterised by nodule-type moderately to poorly differentiated bile duct cell carcinoma with necrosis in the right posterior lobe of the liver (tumour size of approximately $4.0 \times 4.0 \times 3.5$ cm) and a negative liver resection edge. Immunological examination revealed CK19+, CK20+, Hep−, CDX-2−, CD34−, and Ki67+ (approximately 25%) (see Figure 3(a)). Examination of the rectal tissue showed uplifted mucosa with differentiation of adenocarcinoma (tumour size of approximately $0.8 \times 0.7 \times 0.5$ cm) and infiltration to the lower mucosa (peri-intestinal infiltration) and two lymph nodes, but no metastasis. The upper and lower margins were negative. Immunological examination revealed MSH2+, MLH1+, PMS2+, MSH6+ (suggesting microsatellite stability), PD-L1(−), and Ki67+ (approximately 90%) (see Figure 3(b)). The patient refused to undergo chemotherapy. Four months after surgery, his CA199 level was elevated at 213.3 U/mL. PET/CT showed multiple liver metastases (Figure 4). The patient's first radiofrequency ablation was performed for recurrence on 5 February 2018 (power, 40 W; duration, 4 minutes). Forty days later, the patient underwent his first transarterial chemoembolisation (50 mg of lobaplatin, 1 million IU of interleukin-2, and 300- to 500-μm loaded microspheres). The clinical response was poor and indicated progression of the intrahepatic lesions (Figure 5).

Discussion

Multiple primary tumours are defined by the presence of more than one synchronous or metachronous cancer in the same individual. That patients may have multiple primary tumours is not new and was first reported in 1921.[4] Internationally accepted diagnostic standards were developed by Warren and Gates.[5] The pathogenesis of multiple primary tumours remains unclear. Several risk factors of this disease have been identified, including hereditary elements, immune deficiency and immune escape of cancer cells, accumulation of genetic mutations and abnormal gene expression, and

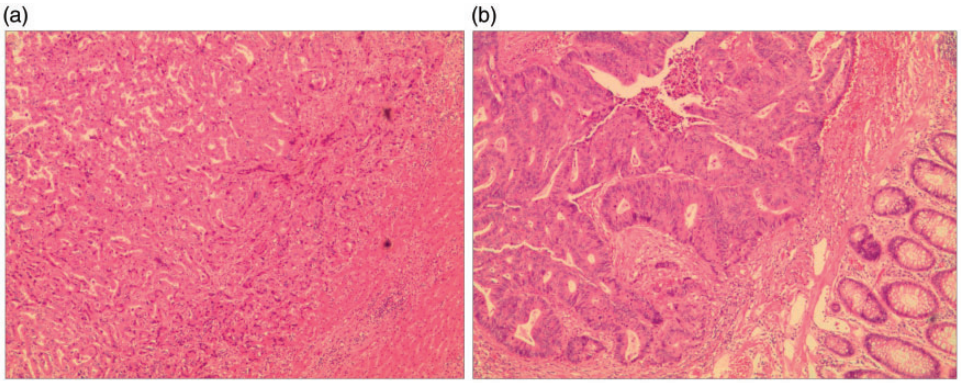

Figure 3. Microscopic findings of the tumour in the present case. (a) Immunophenotypic characteristics of intrahepatic cholangiocarcinoma. (b) Immunophenotypic characteristics of rectal adenocarcinoma.

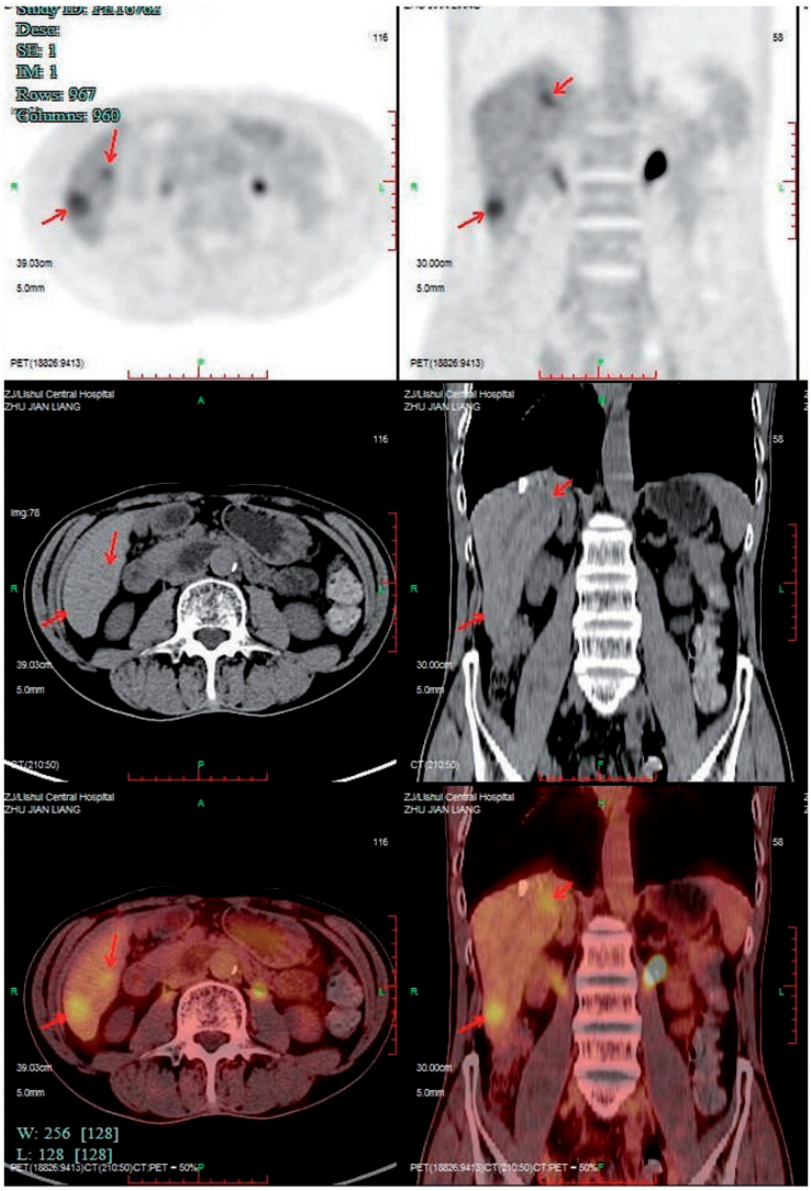

Figure 4. Four-month postoperative ^{18}F-FDG positron emission tomography. Multiple liver masses were present; the largest was located in the right lobe and measured 1.3 × 1.6 cm, with a maximum standardised uptake value of 4.6 (red arrow).

administration of radiotherapy, chemotherapy, and some drugs.[6] The current patient was pathologically diagnosed with rectal adenocarcinoma and primary cholangiocarcinoma, consistent with the presence of multiple primary tumours. Many factors can influence the reported numbers of multiple primary tumours. The frequency of multiple primary tumours is reportedly <50% at any given time.[7] In this case, the

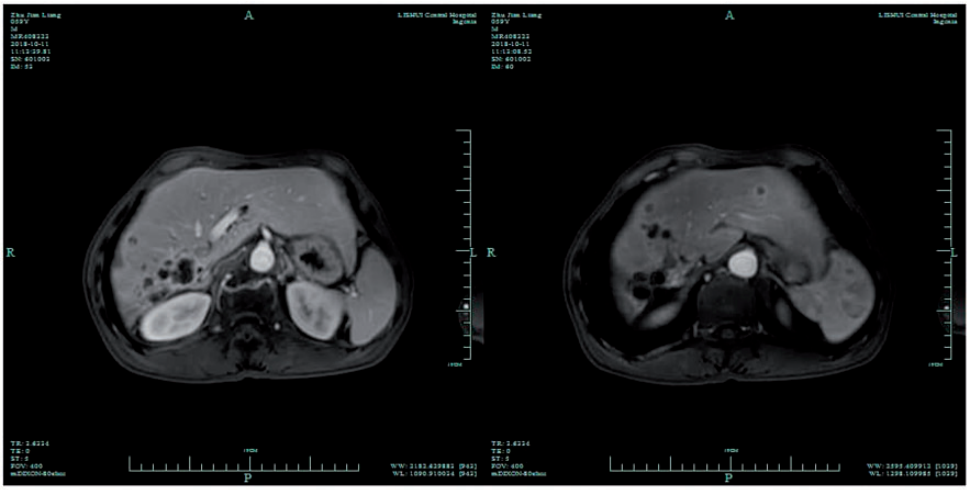

Figure 5. One-year postoperative magnetic resonance imaging. Multiple liver masses were present, and the lesions demonstrated significant enhancement in the arterial phase.

patient presented with rectal adenocarcinoma with multiple liver lesions. A search of the Chinese literature revealed only one previous case report of rectal adenocarcinoma with primary neuroendocrine carcinoma of the liver, indicating the rarity of this phenomenon.[8] A PubMed search revealed no other reports similar to our case.

Hepatitis B virus has a close and consistent causal relationship with primary liver cancer. In geographical areas with a high incidence of liver cancer, the associated incidence is as high as 80% to 90%.[9] The development of liver metastasis is a common phenomenon in the clinical course of colorectal cancer[10] Approximately 40% of patients with colorectal cancer eventually develop liver metastases, and 15% to 20% of patients with colorectal cancer have synchronous colorectal liver metastases at the time of initial diagnosis. The metastases are limited to the liver in 70% to 80% of these patients. Complete radical resection of primary and metastatic lesions is a potential curative treatment strategy for patients with resectable colorectal cancer and synchronous colorectal liver metastases and is directly related to the prognosis of these patients.[11,12] The current patient had a history of hepatitis B infection and concurrent rectal cancer and liver lesions. First, we considered a diagnosis of rectal cancer and isolated colorectal liver metastases. Second, we considered a diagnosis of rectal cancer and hepatocellular carcinoma. The timing of surgery for colorectal liver metastases is divided into simultaneous resection and staged resection. The advantage of simultaneous resection is not only avoidance of the pain and stress caused by the second operation and the delay in surgical treatment of liver metastases, but also the improvement in economic factors (the hospital stay, the total hospitalization cost, and related factors). Some retrospective studies have confirmed that simultaneous resection of colorectal cancer does not increase the incidence or mortality of perioperative complications.[13] In the present case, we performed laparoscopic right liver tumour resection and rectal cancer resection. The current treatment options and prognoses for patients with initially unresectable isolated colorectal liver metastases or hepatocellular carcinoma vary.

When a patient is found to have both colorectal and liver tumours, especially isolated liver tumours, a related auxiliary examination should be performed because it may reveal multiple primary tumours. As with single tumours, multiple primary tumours should be actively treated. In patients with multiple primary tumours, surgical resection is currently the only curative approach for early-stage neoplasia.

The prognosis of intrahepatic cholangiocarcinoma is poor, and the 5-year overall survival rate is <5%. Even if surgery is performed, the median survival duration is only 36 months.[14] The main cause of death in patients with intrahepatic cholangiocarcinoma is postoperative recurrence, with a recurrence rate of 46% to 68%. Studies have shown that adequate incision, lymph node sweeping, and postoperative comprehensive treatment can improve the patients' survival time.[15]

A review of this patient revealed some deficiencies in treatment, and the pathological nature of the liver tumour was unknown before surgery. The related auxiliary examination revealed no obvious lymph node metastasis, and no lymph node dissection was performed during surgery. The postoperative pathologic examination suggested intrahepatic cholangiocarcinoma, and surgery for lymph node sweeping was not recommended. The patient underwent three rounds of transarterial chemoembolization and two rounds of radiofrequency ablation at our hospital. However, the clinical response is not satisfactory. To improve the prognosis, a preoperative multidisciplinary team (tumour multidisciplinary consultation), rapid intraoperative pathological examination, and active postoperative comprehensive treatment are necessary.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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