Solitary Metastasis to a Distant Lymph Node in the Descending Mesocolon After Primary Resection for Hepatocellular Carcinoma: Is Surgical Resection Valid?

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Conflict of interest: None declared

Patient:	**Female, 65**
Final Diagnosis:	**Mesocolic lymph node metastasis of Hetpatocellular carcinoma**
Symptoms:	**None**
Medication:	**—**
Clinical Procedure:	**Partial resection of descending colon including metastatic lymph node**
Specialty:	**Surgery**

Objective:	Rare disease
Background:	Lymph node metastasis of hepatocellular carcinoma is rare, and lymph nodes located on hepatic hilar and hepato-duodenal ligaments are primary targets. Metastasis to a mesocolic lymph node has not been reported previously.
Case Report:	A 65-year-old woman with liver cirrhosis underwent primary resection of hepatocellular carcinoma. Two and a half years later, tumor marker levels increased remarkably and imaging revealed a mesocolic mass. The tumor measured 27 mm in diameter and showed characteristic findings consistent with hepatocellular carcinoma in dynamic computed tomographic images, although the tumor was negative in fluorine-18-fluorodeoxyglucose positron emission tomographic images. A preoperative diagnosis of solitary metastasis to a mesocolic lymph node was made, and we elected to perform surgical resection, although therapeutic strategies for rare solitary extrahepatic metastasis are controversial. The tumor was located in the mesocolon nearly at the wall of the descending colon. Curative resection was performed and histopathological analysis confirmed metastatic hepatocellular carcinoma to a mesocolic lymph node. Tumor marker levels normalized immediately postoperatively. To date, the patient remains free from recurrence without adjuvant therapy.
Conclusions:	This is the first known case of solitary hepatocellular carcinoma metastasis to a distant mesocolic lymph node, successfully treated. Diagnosing solitary hepatocellular carcinoma metastases to distant lymph nodes can be difficult. Although the ideal therapeutic approach has not be defined, surgical resection of solitary metastatic lymph nodes may be beneficial in carefully selected cases.
MeSH Keywords:	**Carcinoma, Hepatocellular • Lymph Nodes • Lymphatic Metastasis • Mesocolon**
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Background

Extrahepatic metastasis of hepatocellular carcinoma (HCC) occurs in 30%–50% of patients [1], and common metastatic sites are lung, regional lymph nodes (LNs), and bone [1]. The main targets for LN metastasis are regionally located on hepatic hilar and hepatoduodenal ligaments [1]. Regional LN metastasis is relatively rare and is found in only 1.2–7.5% of cases at the time of hepatectomy [2,3]. Among extrahepatic HCC metastases, LN metastasis is especially associated with a poor prognosis [3–5].

Metastatic HCC may also be detected in unexpected locations such as the heart, oral cavity, skin, spleen, and small bowel [1,6–9]. However, metastasis to distant LNs is very rare, and only a small number of cases have been documented, including metastasis to paraaortic, supraclavicular, axillary, or cardiophrenic LNs [10–14]. To the best of our knowledge, no reports of metastasis to a mesocolic LN have been previously documented; therefore, solitary metastasis to a distant LN is exceedingly rare. Primary resection of HCC while carefully considering liver functional reserve has been established as a curative treatment [5,15]. However, the role of resection of extrahepatic metastasis remains controversial [13,15–20] because a variety of interventional-based therapies, chemoembolization, and systemic therapy with sorafenib are currently available to treat unresectable metastases [15,17]. Surgical resection of solitary metastatic LNs may be indicated in highly-selected patients [13,15,16,18–20].

We experienced a rare case of solitary HCC metastasis to a distant mesocolic LN after primary resection. We present our case in detail and discuss our therapeutic strategy.

Case Report

A female outpatient in her 50s had routinely visited our hospital because of liver cirrhosis resulting from hepatitis B virus and biliary duct stones. At 65 years of age, she suffered from HCC with BCLC early stage A. Her liver function was well preserved, and Child-Pugh score was A. She underwent left lateral segmentectomy for HCC, without other preoperative treatments. Histopathological findings revealed bridging fibrosis and pseudolobule formation. Serum levels of alpha-fetoprotein (AFP) and protein induced by vitamin K absence-II normalized after primary resection (Figure 1). In imaging studies, no LN metastasis was detected at the time of primary resection of HCC.

Two and a half years postoperatively, the patient's AFP level increased dramatically to 780.2 ng/ml. A lobular lesion with fine enhancement was detected by contrast-enhanced magnetic resonance imaging. The tumor measured 27 mm in diameter and
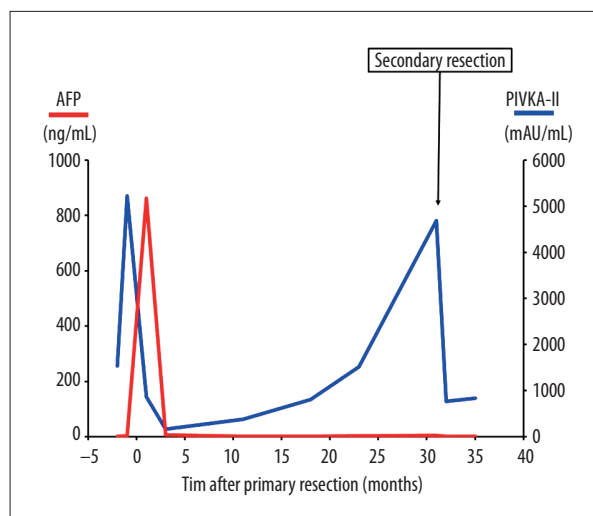
Figure 1. Serum levels of AFP and PIVKA-II. The figure shows the actual changes in AFP and PIVKA-II levels. AFP – alpha-fetoprotein; PIVKA-II – protein induced by vitamin K absence-II.

was located caudally on the left kidney. In contrast-enhanced computed tomography, the tumor showed strong enhancement in the arterial phase (Figure 2A, 2B) and a relatively low density in the portal phase (Figure 2C, 2D). These enhancement findings appeared consistent with a typical HCC pattern. Detailed imaging studies of both magnetic resonance imaging and computed tomography were performed in this case because a very rare metastatic LN initially seemed to be debatable and we needed to rule out exclusion diagnoses. Three-dimensional imaging proved that the tumor was fed by a main vessel from the inferior mesenteric artery (red arrow) and by an accessory feeder from the superior mesenteric artery (Figure 3). Fluorine-18-fluorodeoxyglucose positron emission tomography (FDG-PET) and positron emission tomography-computed tomography did not detect the tumor (Figure 4), although we thought positron emission tomography-computed tomography was helpful to identify other metastatic tumors. Further imaging findings revealed no other intrahepatic or extrahepatic metastasis. Based on the tumor location, the clinical diagnosis was solitary metastasis to a mesocolic LN or HCC dissemination.

Determining the ideal therapeutic strategy for solitary but extrahepatic rare metastasis was difficult. Although rapid growth was a critical concern in this case, the tumor was solitary and not accompanied by other metastases. Considering both diagnostic and therapeutic viewpoints, we finally chose surgical resection in this case. No disseminative nodules, lymphadenopathy, or ascites was observed during surgery. The tumor was located in the mesocolon nearly at the wall of the descending colon, and partial resection of the descending colon with regional mesocolon was performed. The patient's postoperative course was uneventful, and she was discharged on
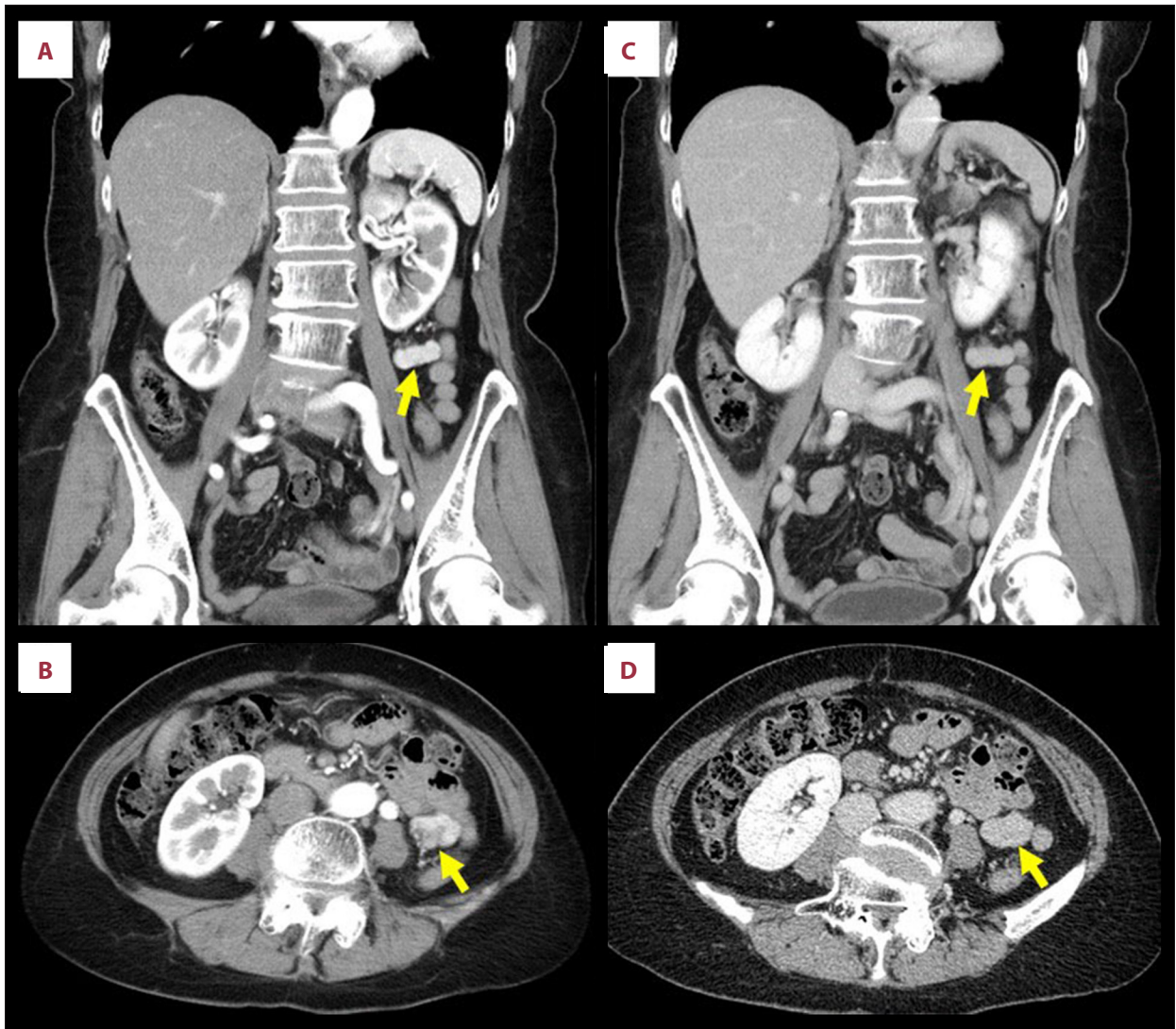
Figure 2. Contrast-enhanced computed tomography. The tumor (arrows) showed strong enhancement in the arterial phase (**A, B**) and a relatively low density in the portal phase (**C, D**).

postoperative day 8. Serum levels of tumor marker decreased immediately after surgery (Figure 1).
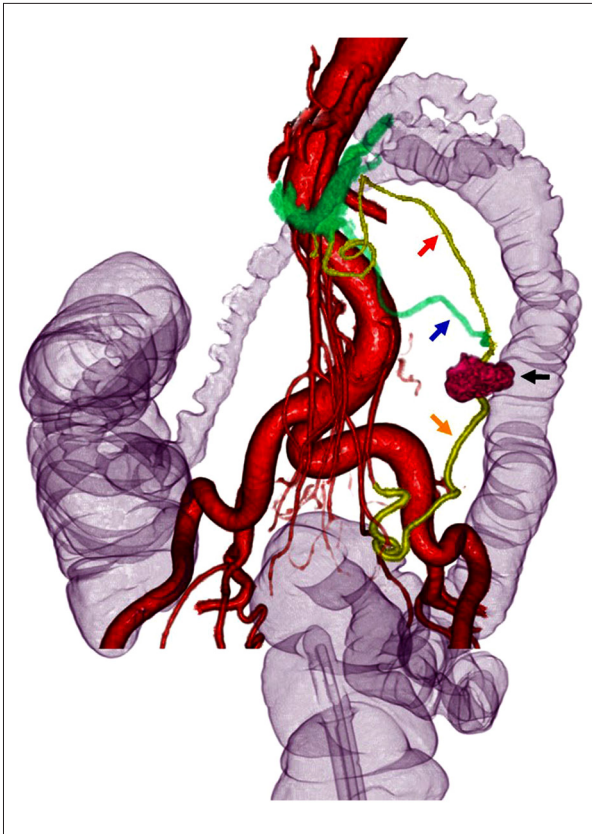
Macroscopically, the mesocolic tumor was a solid and elastic mass with a smooth surface (Figure 5A). A yellowish nodule was encapsulated in the cut surface (Figure 5B). The enlarged LN contained metastatic HCC with a ductal structure (Figure 6A), and immunohistochemically, the tumor was positive for AFP and negative for CK-20, which was consistent with the pattern of primary HCC (Figure 6B). The histopathological diagnosis was metastatic HCC to a mesocolic LN.

As of the writing of this report, the patient has remained free of recurrence for 13 months after the second surgery, and has also been carefully followed up. No adjuvant therapies have been performed.

Discussion

Hematogenous spread is the primary pathway in HCC metastasis. The most common sites of metastasis are the liver (86.4%), lung (4.5%), and bone (4.1%), and the rate of LN metastasis is reported at only 2.2% [10]. LN metastasis influences HCC prognosis [3–5,10,21], and the main sites of metastasis are regional LNs located on the hepatic hilar and hepatoduodenal ligaments [1]. Unexpected sites of metastatic HCC have been documented [1,6–9], and rare LN metastases were also reported [10–14]. However, to the best of our knowledge, our case is a rare case of solitary HCC metastasis to a mesocolic LN.
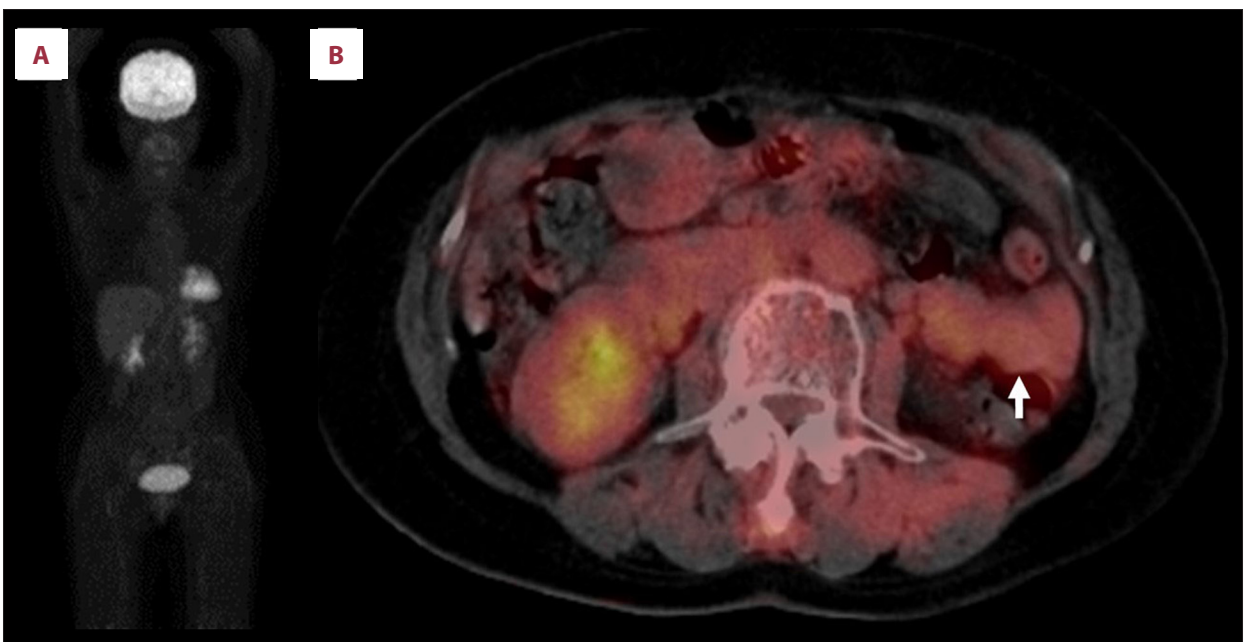
It is interesting that a solitary metastasis to a distant LN in the descending mesocolon after primary resection for HCC developed in the absence of intrahepatic lesion recurrence. It is

Figure 3. Three-dimensional imaging study. The tumor (black arrow) was fed by a main feeder vessel from the inferior mesenteric artery (red arrow) and by an accessory feeder from the superior mesenteric artery (orange arrow). The drainage vein (blue arrow) flowed into the splenic vein.

generally considered that LN metastasis occurs more frequently in larger and/or more poorly-differentiated HCC [22,23]. The LN system in the cirrhotic liver is peculiar [21]; LNs are obstructed and compressed by the hyperplastic fibrous tissue, and this disrupted lymph discharge results in lymph congestion in the liver [21]. Therefore, cancer invasion to lymph ducts is less likely in the cirrhotic liver [21], and the incidence of LN metastasis is commonly higher in non-cirrhotic rather than cirrhotic patients [21]. HCC metastasis can also skip the regional LNs and develop in distant LNs, which is called 'skip metastasis' [24,25]. Collateral pathways of lymphatic drainage are accelerated in the cirrhotic liver, and lymphatic drainage develops beside regional LNs [21]. This may be a why skip metastasis occurs more frequently in cirrhosis patients. Our patient suffered liver cirrhosis and apparent nodal skip metastasis to the descending mesocolon.

HCC generally has characteristic findings in imaging studies [26]. However, LN metastasis may not show these characteristics

**Figure 4.** FDG-PET and PET-CT. No hot accumulation into the tumor (arrow) was observed using FDG-PET (**A**) or PET-CT (**B**). FDG-PET – fluorine-18-fluorodeoxyglucose positron emission tomography; PET-CT – positron emission tomography-computed tomography.
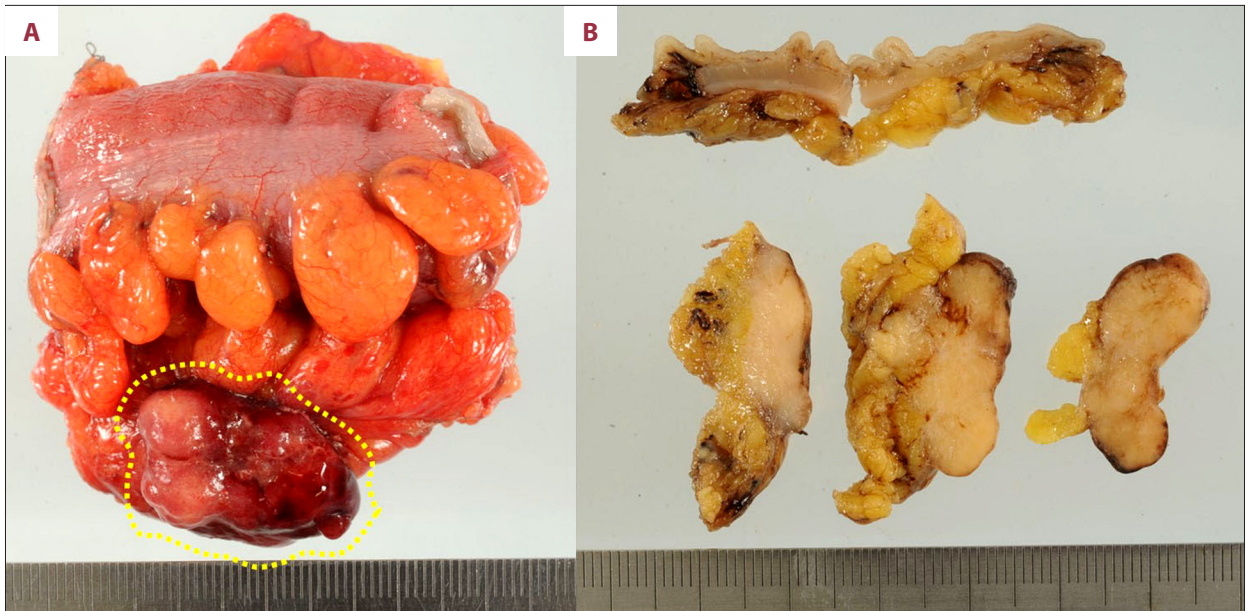
Figure 5. Macroscopic findings. The mesocolic tumor (dotted circle) was a solid and elastic mass with a smooth surface (**A**). A yellowish nodule was encapsulated in the cut surface (**B**). The tumor measured 27 mm in length.
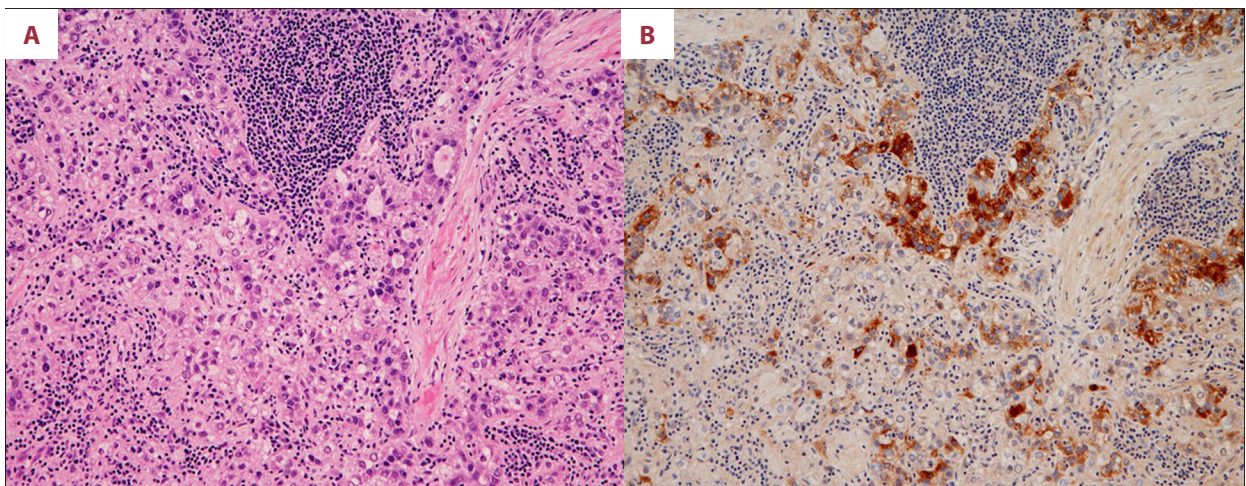
Figure 6. Histopathological diagnosis. Metastatic HCC was confirmed in the enlarged LN (hematoxylin-eosin staining,×100) (**A**). Immunohistochemically, the tumor was positive for AFP (**B**). A histopathological diagnosis of metastatic HCC to the mesenteric LN was made. LN – lymph node; AFP – alpha-fetoprotein; HCC – hepatocellular carcinoma.

compared with other extrahepatic metastases [27]. Interestingly, our case showed characteristic findings in both the primary HCC and the metastatic LN, and we speculate that well-developed feeders into the metastatic LN may be explain the similarity. The detection rate of FDG-PET for extrahepatic metastases >1 cm in diameter is documented at 83%. Therefore, FDG-PET is considered useful for detecting extrahepatic metastases, although this modality could not detect the metastatic tumor in our case. The imaging findings in our case support the opinion that making a precise diagnosis of LN skip metastasis in HCC patients is difficult [25].

Primary resection of HCC while carefully considering liver functional reserve has been established as a curative treatment [5,15]. However, the prognosis for HCC patients with LN metastasis is generally poor, even if primary resection with regional LN dissection is performed [22]. Interestingly, an excellent survival (approximately 5 years) after selective lymphadenectomy for solitary LN metastasis has been documented [16], reporting that the survival rate of patients with solitary LN metastasis was higher than that of patients with multiple LN metastases [16]. Better survival rates may be obtained in selected patients with LN metastasis if the metastatic tumor is solitary and surgical resection is curative [16,20,28]. A

simple question arose: Is surgical resection valid? We had difficulty choosing a surgical approach for the LN metastasis in our case, despite the solitary LN metastasis.

The role of resection of extrahepatic metastases remains controversial [13,15–20], and a variety of non-surgical therapies are currently available [15,17]. Therefore, it was difficult to choose a therapeutic strategy for this solitary but rare extrahepatic metastasis. Although rapid growth was a critical concern in this case, the tumor was solitary and not accompanied by other metastases. We speculate that surgical resection for extrahepatic metastasis may be optionally indicated in carefully selected patients with limited metastasis, preserved liver function, and an adequately-controlled primary tumor. Considering both diagnostic and therapeutic viewpoints, we finally chose surgical resection in our case. Surgical resection of solitary metastatic LNs may be beneficial in highly-selected patients [13,15,16,18–20]. Although we agree that long-term survival may be achieved in highly-selected HCC patients with extrahepatic metastasis [13,15,16,18–20], we suggest that surgery should be carefully considered in each case.

Conclusions

We present a very rare case of solitary HCC metastasis in a distant mesocolic LN after primary resection. To the best of our knowledge, this is a rare case of solitary HCC metastasis to a distant mesocolic LN. Although the ideal therapeutic strategy remains controversial, surgical resection of solitary metastatic LNs may be a beneficial option in carefully selected cases.

Conflict of interest

All authors have no conflict of interest.

Ethical approval

This report was approved by the Institutional Review Board at Tenri Hospital, Tenri, Japan. The patient involved in this paper gave written informed consent authorizing the use and disclosure of her protected health information.

Statement

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