Spontaneous rupture of splenic hilar lymph node metastasis from hepatocellular carcinoma

Fujinaka, Ryosuke ; Urade, Takeshi ; Kido, Masahiro ; Komatsu, Shohei ; Gon, Hidetoshi ; Fukushima, Kenji ; Komatsu, Masato ; Yanagimoto,…

(Citation)
Clinical Journal of Gastroenterology,17(3):557-562

(Issue Date)
2024-06

(Resource Type)
journal article

(Version)
Accepted Manuscript

CASE REPORT

Spontaneous rupture of splenic hilar lymph node metastasis from hepatocellular carcinoma

Ryosuke Fujinaka[1], Takeshi Urade[1*], Masahiro Kido[1], Shohei Komatsu[1], Hidetoshi Gon[1], Kenji Fukushima[1], Masato Komatsu[2], Hiroaki Yanagimoto[1], Hirochika Toyama[1], Takumi Fukumoto[1]

[1]Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

[2]Department of Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

Corresponding author: Takeshi Urade, MD, PhD

Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-Cho, Chuo-ku, Kobe 650-0017, Japan

Tel: (+81) 78-382-6302; Fax: (+81) 78-382-6307; E-mail: uradet1125@gmail.com

Abstract

Spontaneous rupture of a primary hepatocellular carcinoma (HCC) is a frequently observed and fatal complication. However, the rupture of lymph node (LN) metastases from HCC is rare. A 79-year-old man with hepatitis B underwent three liver resections for HCC. Two years and six months after the last liver resection, enhanced computed tomography (CT) revealed a nodule with a diameter of 3 cm in the lower pole of the spleen. Splenic metastasis of HCC was suspected, and splenectomy was scheduled. During our hospital stay for a urinary tract infection before the scheduled operation, he complained of acute left-sided abdominal pain, and CT showed intra-abdominal hemorrhage due to rupture of the splenic tumor. Emergency splenectomy was performed, and the postoperative course was uneventful. Histopathological examination revealed a poorly differentiated HCC in the lower splenic pole lesion, which contained LN structures. The ruptured lesion was diagnosed as splenic hilar LN metastasis of HCC. Although laparoscopic partial liver resection was performed for intrahepatic recurrence, and atezolizumab plus bevacizumab therapy was administered for peritoneal metastases, the patient was alive 25 months after the splenectomy. Our case suggests that emergency surgery for LN metastatic rupture can achieve hemostasis and lead improve survival outcomes.

Keywords: Hepatocellular carcinoma, Lymph node metastasis, Splenectomy, Spontaneous rupture

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignant diseases, and is one of the leading causes cancer-related deaths worldwide [1]. HCC has a unique tendency to spontaneously rupture, which leads to massive intra-abdominal hemorrhage. Although HCC rupture is a fatal complication due to hemodynamic instability, a multimodal approach for the hemorrhage has contributed to improved management of ruptured cases [2, 3].

Although hematogenous dissemination of HCC is relatively common, lymph node (LN) metastasis is uncommon, occurring in only 1.0% of patients who undergo surgery [4]. Moreover, the spontaneous rupture of LN metastases from HCC is extremely rare, and few cases have been reported [5-7]. Thus, the clinical course of ruptured LN metastases remains unknown, and the treatment strategy remains unclear.

Herein we describe a case of intra-abdominal hemorrhage due to spontaneous rupture of a splenic hilar LN metastasis from HCC, which was successfully treated with emergency splenectomy.

Case Report

A 79-year-old man who had undergone liver resection three times for hepatitis B-related HCC at 66, 76, and 77 years of age was followed up at our hospital. He had a medical history of mucosa-associated lymphoid tissue (MALT) lymphoma, which was treated with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone at 73 years of age. The clinical courses and treatment details of HCC and MALT lymphoma are shown in Table 1. Two years and six months after the last liver resection, abdominal ultrasonography (Fig. 1a) and computed tomography (CT) revealed a splenic tumor (Fig. 1b) and a solitary swollen LN (Fig. 1c) at the station of the left greater curvature LNs along the left gastroepiploic artery (No. 4sb). Positron emission tomography-CT showed high-level accumulation of 18F-fluorodeoxyglucose in the splenic tumor, No. 4sb, hypopharyngeal tumor, and multiple lung lesions (Fig. 1d). Hypopharyngeal tumor biopsy revealed MALT lymphoma metastasis. The tumor marker levels were as follows: alpha-fetoprotein (AFP), 3190 ng/mL

(reference range: <10 ng/mL); protein induced by vitamin K absence or antagonist-II (PIVKA-II), 3457 mAU/mL (reference range: <40 mAU/mL); and soluble interleukin-2 receptor, 1092 U/mL (reference range: <475 U/mL). After consultation with medical oncologists, the multiple lung lesions were diagnosed as recurrent MALT lymphoma. Therefore, we provisionally diagnosed the splenic tumor as a solitary metastasis of HCC and scheduled splenectomy.

However, the patient was admitted to our hospital for urinary tract infection before the scheduled surgery. On the 12th day after admission, the patient complained of acute left-sided abdominal pain. The patient's blood pressure was 74/65 mmHg, heart rate was 124 bpm with sinus rhythm, respiratory rate was 16 breaths/min, and with percutaneous oxygen saturation was 99% on room air. Laboratory tests showed rapid development of anemia, including a decrease in hemoglobin level from 11.1 g/dL (on admission) to 8.1 g/dL. Abdominal CT revealed intra-abdominal hemorrhage due to rupture of the splenic tumor (Fig. 2). Therefore, ruptured splenic metastasis from HCC was diagnosed. Interventional radiology treatment was not indicated because the patient's vital signs improved with blood transfusion and contrast-enhanced CT showed no evidence of arterial bleeding. For these reasons, emergency open splenectomy was performed. At laparotomy, bloody ascites were found in the abdominal cavity. Since swollen No. 4sb was detected during the operation, and metastasis of HCC was suspected, we resected the spleen and No. 4sb simultaneously. Grossly, the coagula were attached to a milky white solid lesion, which was embedded in the lower pole of the spleen (Fig. 3a). The postoperative course was uneventful, and the patient was discharged. Thereafter, he underwent radiation therapy for hypopharyngeal MALT lymphoma. Histopathological examination revealed a poorly differentiated HCC in the lower splenic pole lesion that contained LN structures. The tumor grew expansively against the splenic parenchyma, and the marginal zone between the tumor and the splenic parenchyma was preserved (Fig. 3b). Retrospective review of an abdominal CT scan taken six months before the diagnosis of the splenic tumor revealed a splenic hilar LN that was not initially identified as a metastatic LN (Fig. 4). We suspect that this LN had grown expansively towards the lower pole of the spleen and became embedded. Therefore, we diagnosed

the ruptured lesion as a splenic hilar LN metastasis of HCC. In addition, the resected No. 4sb specimen showed HCC metastasis. One month later, the AFP and PIVKA-II levels decreased to 79 mAU/mL and 24 mAU/mL, respectively. Intrahepatic recurrence was noted 8 months after splenectomy and was resected via laparoscopic partial liver resection. Six months after the last liver resection, atezolizumab plus bevacizumab were administered to several nodules of peritoneal metastases of HCC under the left diaphragm. After nine cycles of atezolizumab plus bevacizumab, a monitoring CT revealed no change in the number of peritoneal metastases; however, one peritoneal metastasis showed no contrast enhancement and was considered as having necrotized. The patient remained alive 25 months after splenectomy while undergoing chemotherapy.

Discussion

Various benign and malignant splenic lesions may spontaneously rupture. A previous report classified atraumatic splenic ruptures into six etiological groups, and neoplastic disorders were noted in 30.3% of the patients [8]. In the present case, the patient had a history of MALT lymphoma and HCC, which made accurately diagnosing the splenic lesion difficult. Because the concentrations of the tumor markers AFP and PIVKA-II increased gradually and ultrasound and CT scans showed that the tumor was seemingly buried in the spleen, we suspected splenic metastasis of HCC before the operation. However, based on the histopathological findings, the ruptured lesion was diagnosed as a splenic hilar LN metastasis.

The present case is unique in that spontaneous rupture occurred in a splenic hilar LN metastasis from HCC. Metastasis to a splenic hilar LN is generally uncommon in HCC, although metastasis to a perigastric LN has been previously reported, with an incidence of 10.8% [9]. In the present case, No. 4sb metastasis of HCC was observed. This finding suggests that HCC may have metastasized first to No. 4sb and then to the splenic hilar LN through lymphogenous spread. In addition, the mechanisms underlying LN metastatic rupture in HCC remain poorly understood. In a previous case, which was the first reported case of abdominal LN metastatic rupture from HCC, the HCC tissue in the LN appeared to cause a breakdown of the capsule either by increased

pressure or by direct HCC invasion [7]. In the present case, the metastatic splenic hilar LN enlarged rapidly within 2 months from diagnosis to spontaneous rupture. A few normal LN structures remained in the splenic hilar LN, and the LN was filled with poorly differentiated HCC tissue. Thus, HCC tissue under the LN capsule may have increased intratumoral pressure, leading to spontaneous rupture.

Rupture of LN metastasis in HCC is extremely rare, and to the best of our knowledge, only four cases, including our case, have been reported to date (Table 2) [5-7]. All patients were male and their ages ranged from 55 to 79 years. Notably, our patient was older than any of the previous patients. The location of LN metastasis was the mediastinal LN in two patients, the peripancreatic LN in one, and the splenic hilar LN in our case. Two patients underwent transcatheter arterial embolization (TAE). Our patient is the only reported patient to have undergone surgical resection. The remaining patient received conservative treatment and LN metastasis rupture was revealed by autopsy. Surgical resection and TAE are considered optimal treatments for ruptured HCC. For most patients with ruptured HCC, TAE followed by surgical resection is the preferred first-line treatment option, except for those with poor liver function and advanced tumors [10]. However, the optimal treatment strategy for ruptured LN metastases from HCC remains unclear because little data are available. Based on the findings in Table 2, it is remarkable that our patient survived for at least 25 months after LN metastatic rupture, as the other three reported patients died within 4 months. Thus, our case suggests that surgical resection for LN metastatic rupture may lead to a favorable survival outcome compared to TAE alone, if curative resection is possible.

One possible reason for the relatively long-term survival in this case was the low burden of intrahepatic tumors. Generally, the prognosis of patients with HCC and LN metastasis is poorer than that of patients without LN metastasis [11]. However, previous literature has shown that the intrahepatic tumor status predicts the prognosis of HCC patients with extrahepatic metastasis [12, 13], and it has been reported that optimal management of intrahepatic lesions and complete removal of the LN metastasis may improve the survival outcomes in HCC patients with LN metastasis [14, 15]. Moreover, some researchers have reported that surgical resection of extrahepatic metastases, such as adrenal gland and peritoneal metastases, results in long-term

survival [16, 17]. In the present case, the intrahepatic lesion was well controlled by past liver resection, and the ruptured metastatic splenic hilar LN and swollen No. 4sb LN were the only HCC metastatic lesions and resectable lesions as well. Therefore, a surgical resection was performed. Another possible reason is that the recurrences of HCC after splenectomy were well controlled with liver resection and atezolizumab plus bevacizumab. Our findings suggest that spontaneous rupture may occur in metastatic LN of HCC, and patients with LN metastasis should receive close surveillance and appropriate management to improve survival.

In conclusion, we encountered an extremely rare case of spontaneous rupture of a splenic hilar LN metastasis from HCC that required emergency splenectomy. Although this life-threatening complication may occur in cases of LN metastasis from HCC, emergency surgery is one of the effective treatment options that can lead to hemostasis and favorable survival.

Author contributions

RF collected clinical information and drafted the manuscript. TU reviewed and revised the manuscript. MK, SK, HG, KF, HY, and HT participated in patient treatment. MK made the pathological diagnosis. TF revised the manuscript critically. All authors have read and approved the final version of the manuscript.

Funding None.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Human/animal rights Not applicable.

Informed consent Written informed consent was obtained from the patient for publication of the case report.

References

1. Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55:74-108.
2. Moris D, Chakedis J, Sun SH, et al. Management, outcomes, and prognostic factors of ruptured hepatocellular carcinoma: A systematic review. J Surg Oncol. 2018;117:341-53.
3. Yoshida H, Mamada Y, Taniai N, et al. Spontaneous ruptured hepatocellular carcinoma. Hepatol Res. 2016;46:13-21.
4. Kudo M, Izumi N, Kubo S, et al. Report of the 20th Nationwide follow-up survey of primary liver cancer in Japan. Hepatol Res. 2020;50:15-46.
5. Oh SY, Seo KW, Jegal Y, et al. Hemothorax caused by spontaneous rupture of a metastatic mediastinal lymph node in hepatocellular carcinoma: a case report. Korean J Intern Med. 2013;28:622-5.
6. Seki S, Kitada T, Sakaguchi H, et al. Cardiac tamponade caused by spontaneous rupture of mediastinal lymph node metastasis of hepatocellular carcinoma. J Gastroenterol Hepatol. 2001;16:702-4.
7. Terada T, Takeuchi T, Hirano R, et al. Spontaneous rupture of peripancreatic lymph node with hepatocellular carcinoma metastasis: report of an autopsy case with massive peritoneal bleeding. Hepatol Res. 2003;26:73-6.
8. Renzulli P, Hostettler A, Schoepfer AM, et al. Systematic review of atraumatic splenic rupture. Br J Surg. 2009;96:1114-21.
9. Watanabe J, Nakashima O, Kojiro M. Clinicopathologic study on lymph node metastasis of hepatocellular carcinoma: a retrospective study of 660 consecutive autopsy cases. Jpn J Clin Oncol. 1994;24:37-41.
10. Sahu SK, Chawla YK, Dhiman RK, et al. Rupture of Hepatocellular Carcinoma: A Review of Literature. J Clin Exp Hepatol. 2019;9:245-56.
11. Marsh JW, Dvorchik I, Bonham CA, et al. Is the pathologic TNM staging system for patients with hepatoma predictive of outcome? Cancer. 2000;88:538-43.

12. Jung SM, Jang JW, You CR, et al. Role of intrahepatic tumor control in the prognosis of patients with hepatocellular carcinoma and extrahepatic metastases. J Gastroenterol Hepatol. 2012;27:684-9.

13. Uchino K, Tateishi R, Shiina S, et al. Hepatocellular carcinoma with extrahepatic metastasis: clinical features and prognostic factors. Cancer. 2011;117:4475-83.

14. Lee CW, Chan KM, Lee CF, et al. Hepatic resection for hepatocellular carcinoma with lymph node metastasis: clinicopathological analysis and survival outcome. Asian J Surg. 2011;34:53-62.

15. Tomimaru Y, Wada H, Eguchi H, et al. Clinical significance of surgical resection of metastatic lymph nodes from hepatocellular carcinoma. Surg Today. 2015;45:1112-20.

16. Brochard C, Hamy A, Michalak S, et al. Metastatic hepatocellular carcinoma: when surgery and successive palliative treatments lead to remission. Clin Res Hepatol Gastroenterol. 2014;38:e19-22.

17. Lin CC, Liang HP, Lee HS, et al. Clinical manifestations and survival of hepatocellular carcinoma patients with peritoneal metastasis. J Gastroenterol Hepatol. 2009;24:815-20.

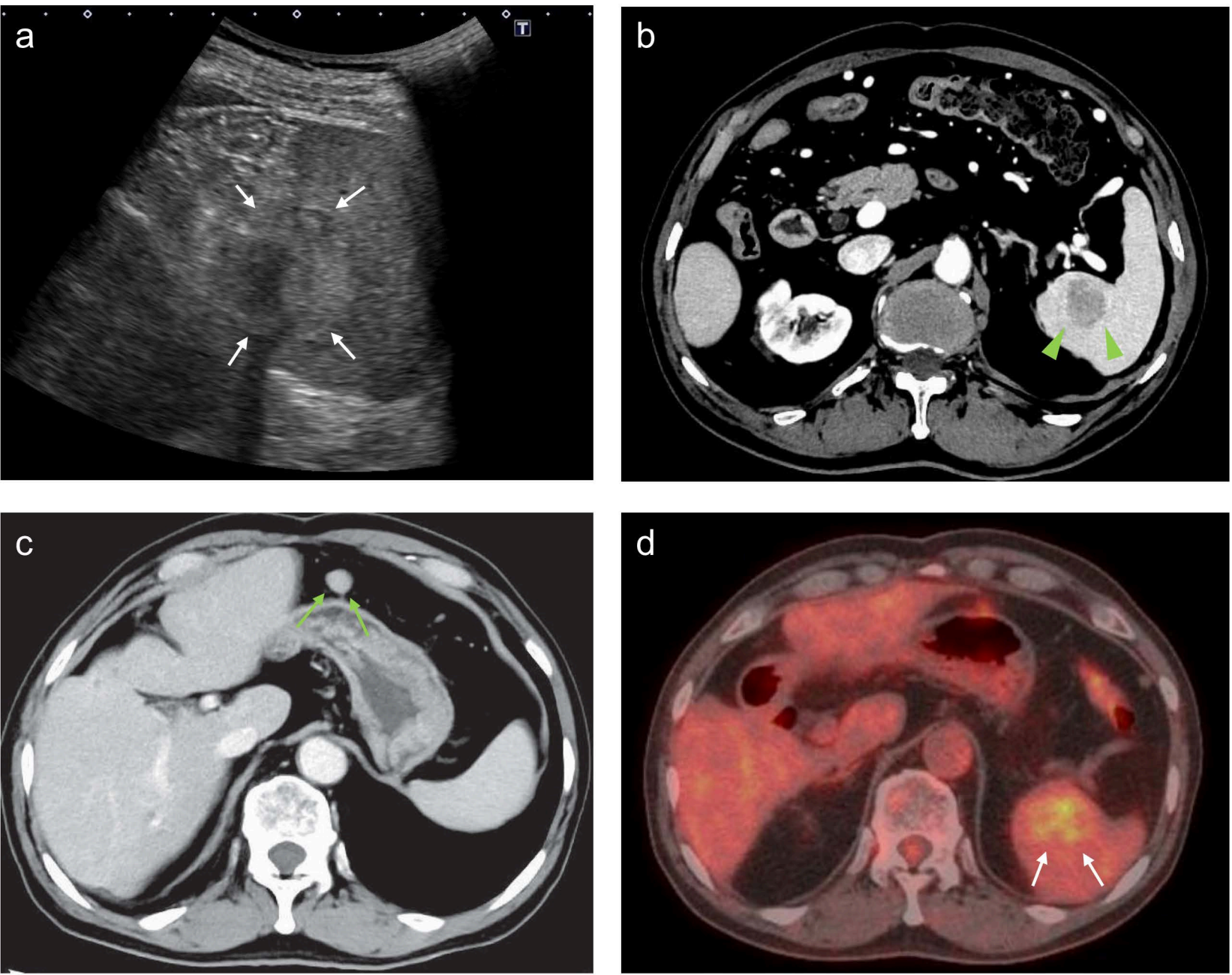
Figure legends

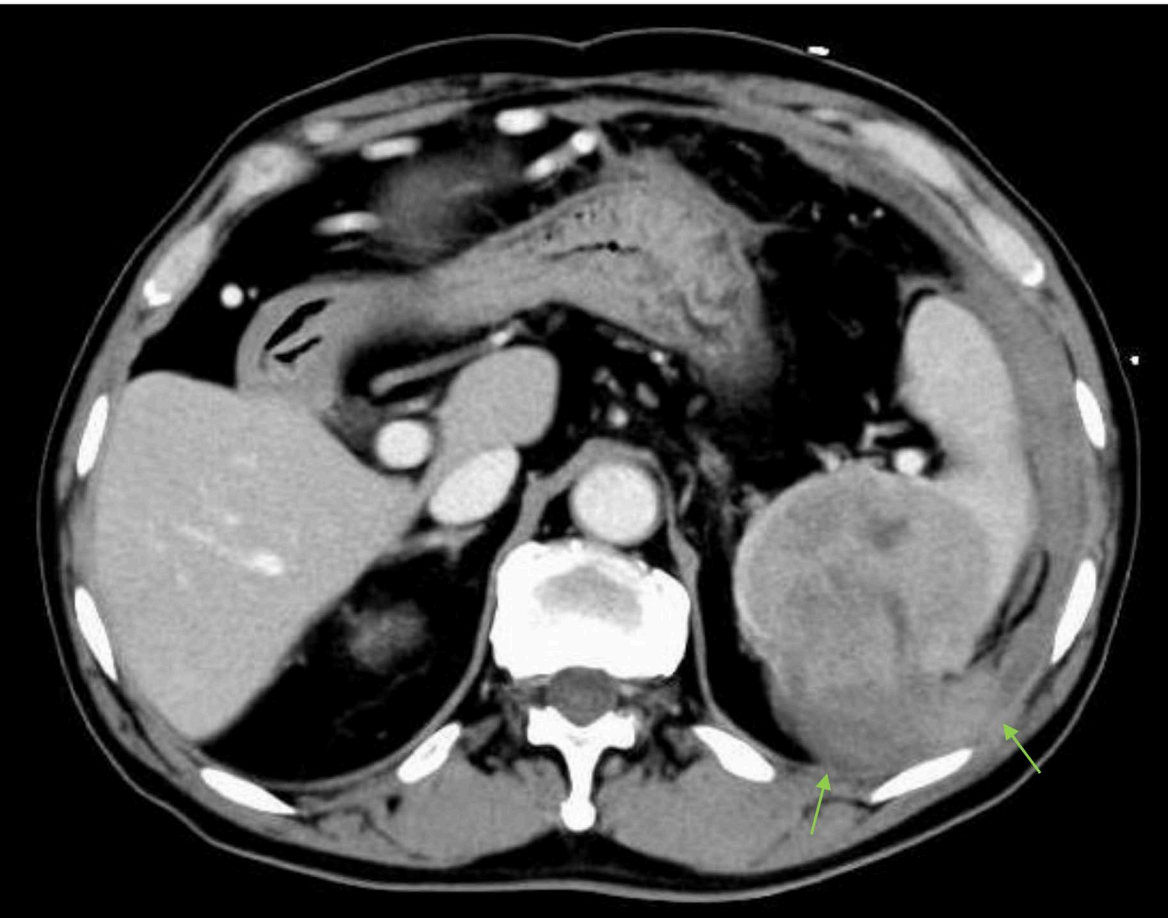
Fig. 1 Image findings two years and six months after the last liver resection. **a** Abdominal ultrasonography shows a lesion measuring 3.8 × 3.5 cm with a mixed-echo pattern with well-defined margins in the spleen (white arrows). **b** Abdominal contrast-enhanced computed tomography shows a low-density tumor measuring 3 cm in the lower pole of the spleen (green arrowheads). **c** Abdominal computed tomography shows a solitary swollen lymph node at the station of the left greater curvature lymph nodes along the left gastroepiploic artery (green arrows). **d** Positron emission tomography-computed tomography shows high-level accumulation of 18F-fluorodeoxyglucose in the splenic tumor (white arrows)

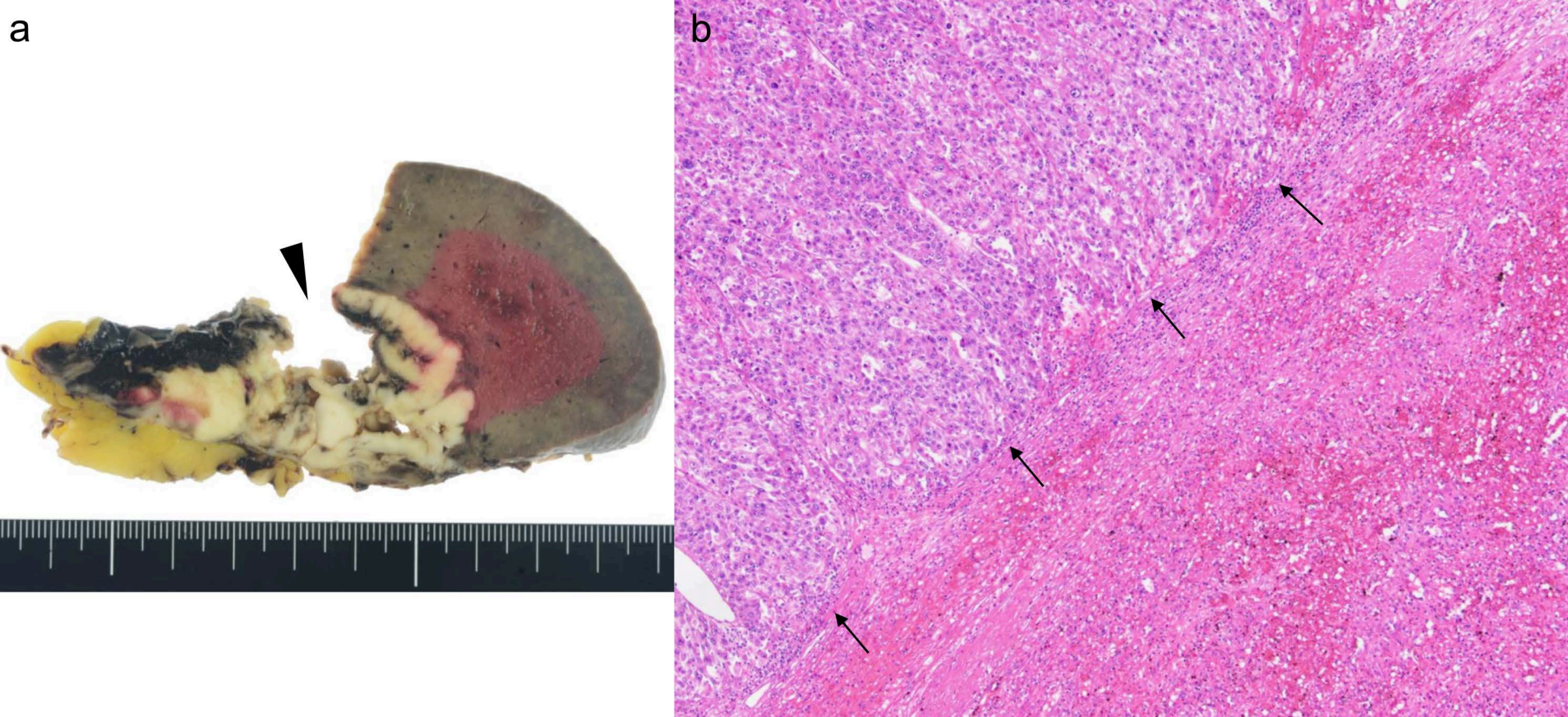
Fig. 2 Abdominal computed tomography (CT) image after the patient's complaint of acute left-sided abdominal pain. CT shows intra-abdominal hemorrhage due to rupture of the tumor (green arrows)

Fig. 3 Pathological findings of the ruptured splenic hilar lymph node. **a** Grossly, the blood coagula were attached to the ruptured splenic hilar lymph node (black arrowhead). **b** Microscopically, poorly differentiated hepatocellular carcinoma is noted in the splenic hilar lymph node. The tumor grew expansively against the splenic parenchyma, and the marginal zone (black arrows) between the tumor (left part) and the splenic parenchyma (right part) is preserved

Fig. 4 Abdominal computed tomography (CT) image taken 6 months before the diagnosis of splenic tumor. CT shows a splenic hilar lymph node (LN) that was not initially identified as a metastatic LN (green arrows). **a** Axial image of dynamic CT. **b** Coronal image of dynamic CT


a
b
c
d




a
b

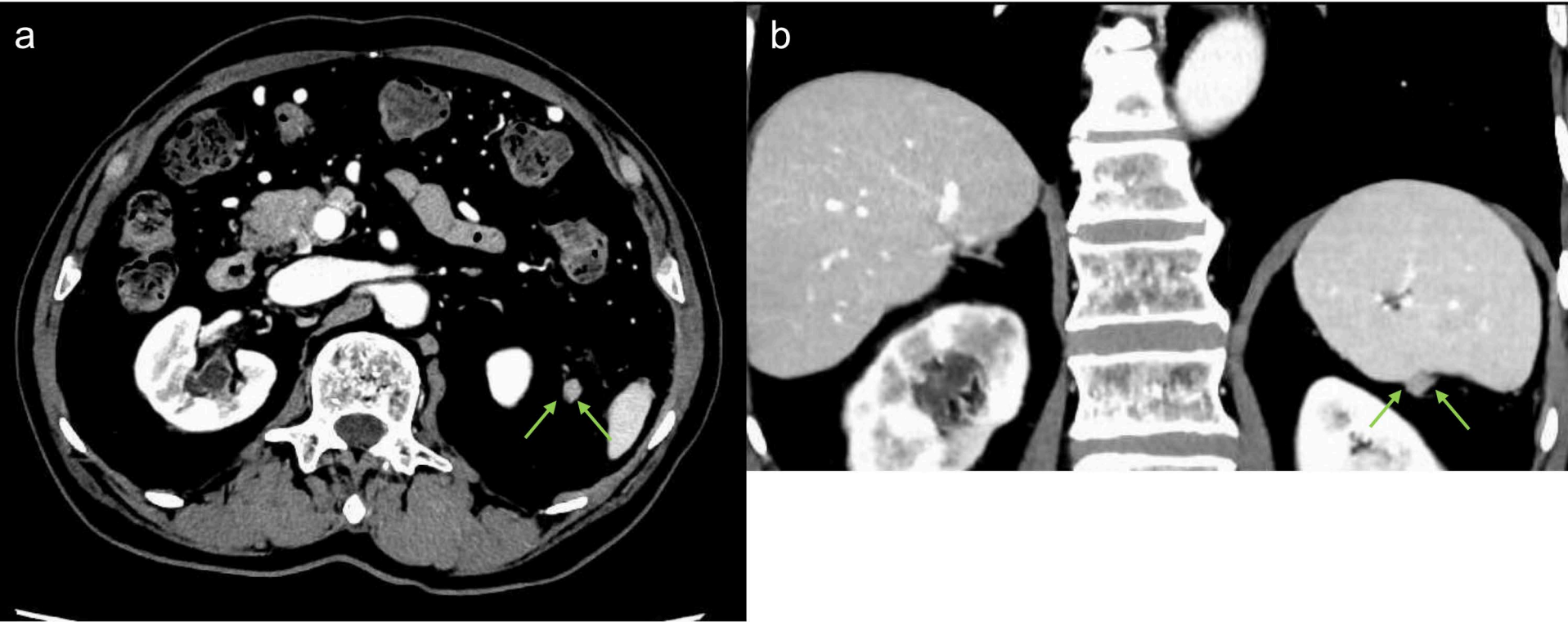

a
b

Table 1 The clinical courses and treatment details of HCC and MALT lymphoma before the splenic hilar lymph node metastasis rupture

Patient's age, y	HCC[a]	MALT lymphoma
66	Segment VIII Right anterior segmentectomy	–
73	–	MALT lymphoma Stage IVA R-CHOP 4 cycles
76	Segment VI Laparoscopic partial liver resection	–
77	Segment II Laparoscopic partial liver resection	–
78	–	Right periureteral recurrence IMRT (30.6 Gy/17 fr)

HCC hepatocellular carcinoma, *MALT* mucosa-associated lymphoid tissue,
R-CHOP rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone,
IMRT intensity modulated radiation therapy, *Gy* gray, *fr* fraction

[a] HCC localization was indicated by Couinaud's segment

Table 2 The reported cases with spontaneous rupture of lymph node metastasis of HCC

No.	Author	Year	Age/Sex	Symptom	Location of ruptured LN	Complication	Type of treatment	Follow-up	Outcome	Cause of death
1	Seki [6]	2001	57/M	Dyspnea, heart palpitations	Mediastinal LN	Cardiac tamponade	TAE	2 months	Dead	Liver failure
2	Terada [7]	2003	55/M	Hemorrhagic tendency	Peripancreatic LN	Intraperitoneal hemorrhage	Conservative treatment	ND	Dead	Liver failure
3	Oh [5]	2013	60/M	Dyspnea, Chest pain	Mediastinal LN	Hemothorax	TAE	4 months	Dead	ND
4	Our case	2023	79/M	Abdominal pain	Splenic hilar LN	Intra-abdominal hemorrhage	Surgical resection	25 months	Alive	–

HCC hepatocellular carcinoma, *M* Male, *LN* lymph node, *TAE* transcatheter arterial embolization, *ND* not described