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Diagnostic Value of Open Biopsy for Malignant T-Cell Lymphoma of the Liver

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A 62-year-old man was referred to our hospital because of pain in the right upper quadrant. Laboratory tests revealed normal levels of tumor markers. Abdominal ultrasonography showed a hypoechoic mass of approximately 9 cm in diameter in the right lobe of the liver. Computed tomography revealed a low-density mass with peripheral enhancement in the posterior segment of the right lobe. Magnetic resonance imaging showed a low-intensity mass on T_1-weighted images and a high-intensity mass on T_2-weighted images. Abdominal angiography showed enhanced staining only at the periphery of the tumor. An open biopsy was performed and intraoperative examination of frozen sections indicated malignant lymphoma. The histopathologic diagnosis was malignant T-cell lymphoma. After combined chemotherapy, the tumor shrank to 4 cm in diameter. To our knowledge, only 15 cases of malignant T-cell lymphoma have been reported previously. Diagnosis is particularly challenging because this type of tumor has no distinctive imaging characteristics or signs or symptoms. This case emphasizes the need to include malignant T-cell lymphoma in the differential diagnosis and demonstrates the importance of open biopsy in patients with a suspected liver tumor.

Key words: Malignant T-cell lymphoma – Liver tumor – Open biopsy

Primary hepatic lymphoma shows a wide range of imaging findings, which can make diagnosis difficult.[1] Secondary liver involvement is common in patients with non-Hodgkin lymphoma and is detected in up to 50% of patients who undergo pathologic staging.[1] In contrast, non-Hodgkin lymphoma arising in the liver is uncommon, and most cases are diffuse large B-cell lymphomas that manifest as space-occupying lesions. Low-grade B-cell lymphomas of mucosa-associated lymphoid

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tissue can also arise in the liver and transform into diffuse large B-cell lymphomas. Malignant T-cell lymphoma of the liver is rare and may not be considered in the differential diagnosis of these tumors.[2] To our knowledge, only 15 cases of primary hepatic peripheral T-cell lymphoma (PTCL) have been reported previously.[2] Here, we describe a case of PTCL of the liver associated with unusual imaging findings.

Case Report

A 62-year-old man was admitted to our hospital to undergo evaluation and treatment of a liver tumor. Two months earlier he had visited our outpatient clinic because of right flank pain. His personal and family histories were unremarkable. At presentation, there was no anemia or icterus. An abdominal examination showed no evidence of ascites. Laboratory tests on admission revealed increased concentrations of lactate dehydrogenase (619 U/L), alkaline phosphatase (750 U/L), and soluble interleukin-2 receptor (1350 U/mL). Hepatitis B antigen and hepatitis C antibody were negative. There was no evidence of Epstein-Barr virus or cytomegalovirus. Tumor markers (carcinoembryonic antigen, carbohydrate antigen 19–9, alpha-fetoprotein, protein induced by vitamin K absence or antagonist) were negative.

Ultrasonography (US) revealed a tumor in the right lobe of the liver. Computed tomography (CT) showed a low-density mass of 9 cm in diameter in the posterior segment of the right lobe. The border of the mass was poorly demarcated (Fig. 1). Only the periphery of the tumor was enhanced. Part of the tumor appeared to extend beyond the liver capsule and infiltrate the abdominal wall. Magnetic resonance imaging (MRI) showed a low-intensity mass on T_1-weighted images and a high-intensity mass on T_2-weighted images. Contrast MRI showed gradual enhancement from the periphery to the center of the mass. On abdominal angiography, only peripheral staining of the tumor was enhanced. Positron emission tomography with ^{18}F-fluorodeoxyglucose showed a lesion with increased uptake of tracer only in the right lobe of the liver; no other area of increased tracer uptake was evident. A definitive diagnosis could not be reached on the basis of these findings, but a malignant tumor (*i.e.*, a hepatocellular carcinoma, cholangiocellular carcinoma, metastatic liver tumor, or malignant lymphoma) was suspected. Pathologic diagnosis was needed to in order to arrive at a definite diagnosis. There are two ways to do a biopsy, CT/US guided biopsy and open biopsy. Because of potential fatal complications of the CT/US guided biopsy, such as rupture or bleeding of tumor, were reported,[3,4] we considered open surgery to be safer than CT/US guided liver biopsy.

Thus, surgical procedure was attempted, during which the tumor was found to have invaded the abdominal wall and diaphragm. We resected part of the tumor for histopathologic examination. A major hepatectomy was not performed because intraoperative examination of frozen sections indicated a diagnosis of lymphoma. After the operation, a bone marrow biopsy yielded negative results. Histopathologic examination showed diffuse proliferation of atypical cells, with positive immunohistochemical staining for CD3, CD45RO (UCHL-1), and Ki-67, but almost negative staining for CD20. The final histopathologic diagnosis was malignant T-cell lymphoma (Figs. 2 and 3). According to our previous experiences, we considered chemotherapy to be effective for hepatic lymphoma, like this case. And the patient and his family did not want an invasive operation. The patient received 2 cycles of combined chemotherapy with cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone, and the diameter of tumor was decreased to 4 cm after 3 months of chemotherapy (Fig. 4).

Discussion

Primary hepatic lymphoma presents at a mean age of 55 years (range, 5–87 years), with a male-female ratio of 2.3:1. The most common initial symptom is abdominal pain or discomfort, which is experienced by 39% to 79% of patients. Other symptoms include fatigue, jaundice, anorexia, malaise, nausea, and vomiting. The results of liver function tests, including levels of transaminases, alkaline phosphatase, and bilirubin, are abnormal in at least 70% of cases. Radiologically, primary hepatic lymphoma may present as a solitary lesion or multiple lesions of the liver, or as diffuse hepatic infiltration. The most common presentation is a solitary lesion, occurring in 55% to 60% of cases, followed by a multiple lesion in 35% to 40%. Diffuse infiltration is uncommon and portends a poor prognosis.[5]

Only 15 cases of primary hepatic PTCL have been described[2,6–11] prior to the current report (Table 1). Most of these cases have been solitary or multiple mass lesions, rather than a diffusely proliferating lesion in the liver, and have occurred predominantly in men.[6] The results of liver function tests were abnormal in 11 of 13 patients for whom data were available. Coagulopathy was present in 2 of 3

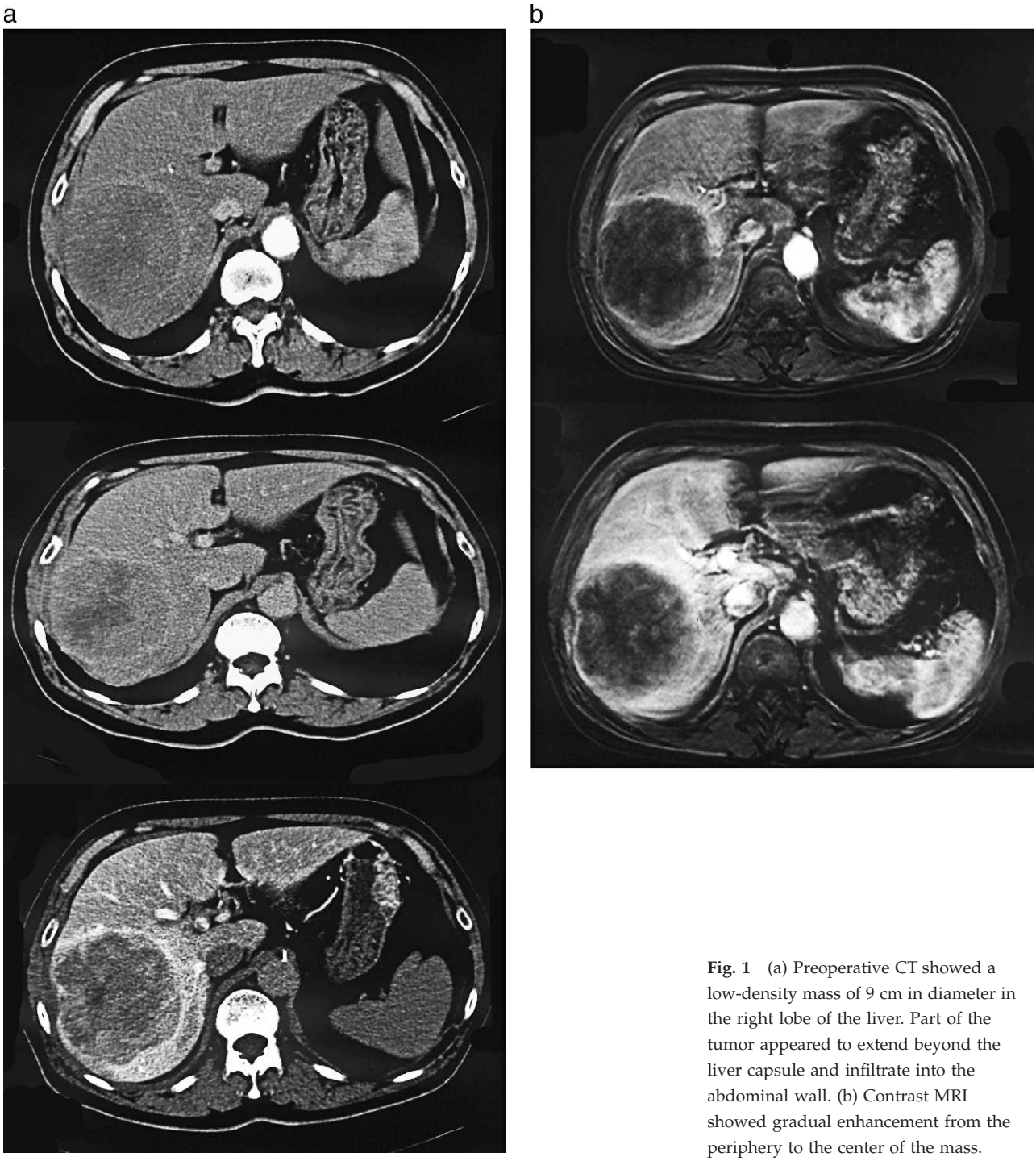

Fig. 1 (a) Preoperative CT showed a low-density mass of 9 cm in diameter in the right lobe of the liver. Part of the tumor appeared to extend beyond the liver capsule and infiltrate into the abdominal wall. (b) Contrast MRI showed gradual enhancement from the periphery to the center of the mass.

patients for whom the results of coagulation tests were reported. Regarding treatment, 9 patients received some form of chemotherapy, 1 underwent surgery alone, 4 received supportive therapy alone, and treatment was not described in 1 patient. Eight patients died (including 7 who died from the tumor) within 27 months after diagnosis. Thus, primary hepatic PTCL appears to have an aggressive course, even in early-stage disease.

Histopathologic diagnosis of primary hepatic PTCL can be challenging. We selected the open biopsy in order to avoid fatal complications.[3,4] On

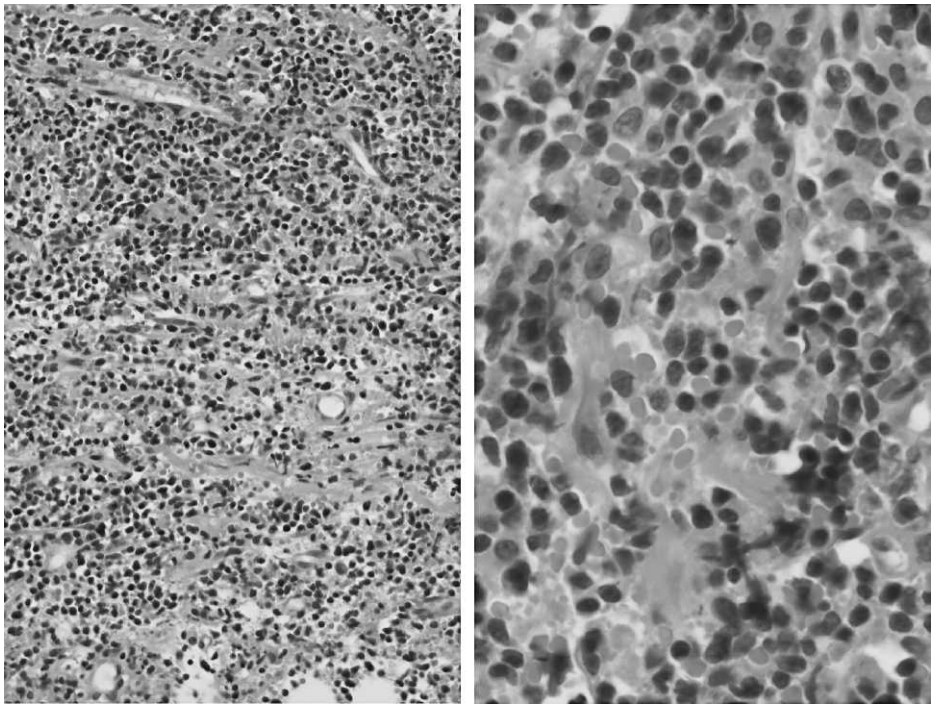

Fig. 2 A histopathologic specimen showing diffuse proliferation of atypical cells [hematoxylin and eosin; ×200 (left) and ×600 (right)].

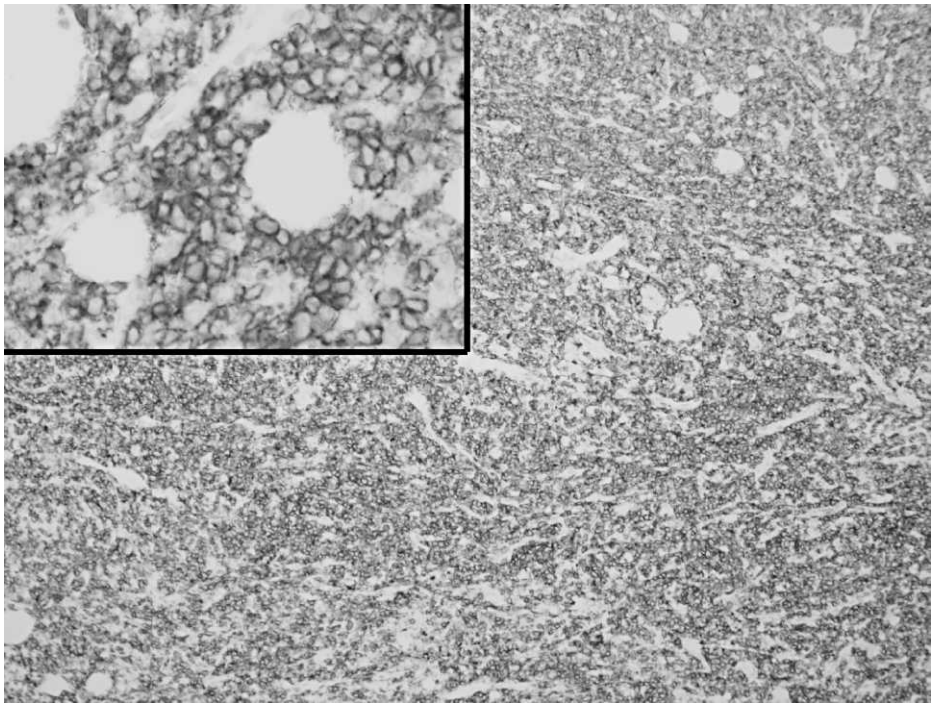

Fig. 3 Immunohistochemical staining was positive for CD3 and Ki-67 in atypical cells of the liver tumor [immunohistochemical staining with hematoxylin counterstain; (×200) and (×600)].

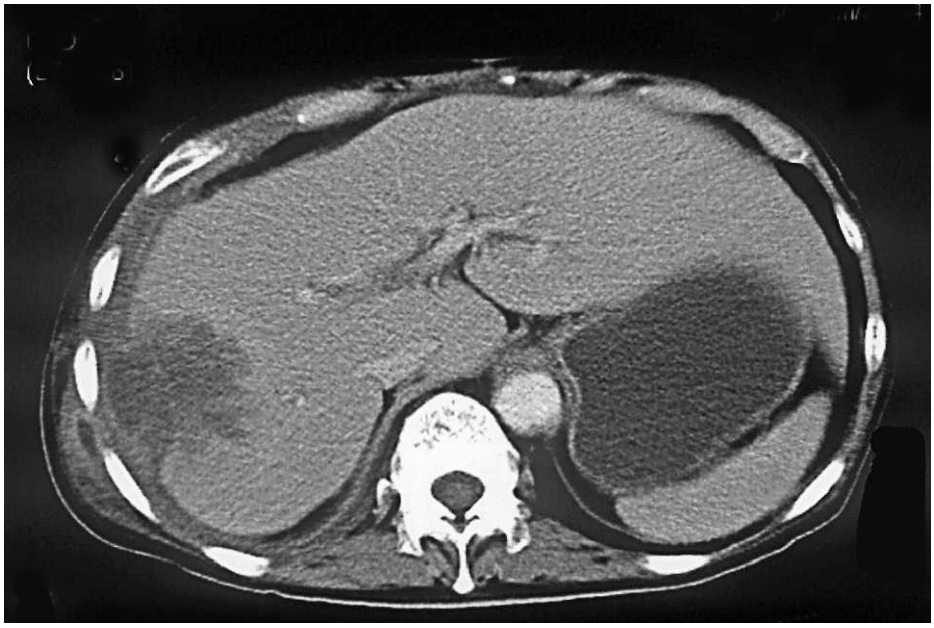

Fig. 4 CT obtained after chemotherapy, showing shrinkage of the tumor diameter to 4 cm.

the other hand, laparoscopic biopsy was not a fit for this case because of tumor location and invasive status. In our case, the tumor was just under the diaphragm dome. And tumor invasion into the diaphragm was suspected by CT. Thus, we thought it was difficult to get a sufficient amount of liver sample with laparoscopy, and it would have been difficult to respond to a rupture or bleeding if we were performing the laparoscopic procedure.

The most common misdiagnoses are idiopathic granulomatous hepatitis, chronic active hepatitis, granulomatous cholangitis, inflammatory myofibroblastic tumor, and hepatocellular carcinoma. Primary hepatic PTCL may be detected at an early stage

Table 1 Profiles of reported 16 cases of malignant T-cell lymphoma of the liver

No.	Age, y/sex	Initial symptoms	Stage	Diagnosis	Therapy	Outcome (survival)	Author
1	22/F	FU, JD, AP	I E	Diffuse large noncleaved cell (WF)	Surgery	Alive (62 mo)	Andreola[7]
2	60/F	FU, WL, AP, HM	I E	Centrocytic (Kiel)	Chemotherapy	Dead (27 mo)	Anthony[8]
3	53/M	WL, JD, AP, NS	I E	Plemorphic small cell (Kiel)	PNS, chemotherapy	Dead (15 mo)	Anthony[8]
4	76/M	JD, AP, HM	I E	T zone (Kiel)	PNS	Alive (36 mo)	Anthony[8]
5	61/M	FU, WL, M, CD	I E	Pleomorphic small cell (Kiel)	PNS, antibiotics	Dead (18 mo)	Anthony[8]
6	82/F	CHF, WL, JD, HM	I E	T zone (Kiel)	PNS	Dead (1 wk)	Anthony[8]
7	46/M	FU, WL, JD, AP	I E	Pleomorphic small cell (Kiel)	Antibiotics	Dead (3 wk)	Anthony[8]
8	41/M	NS, AP, HM	I E	Pleomorphic small cell (Kiel)	Chemotherapy	Alive (72 mo)	Anthony[8]
9	41/M	FU, WL, JD, HM	I E	Small lymphocytic (WF)	CRB, PNS	Dead (2.4 mo)	Lei[9]
10	50/F	FU	I E	Peripheral T-cell lymphoma (REAL)	NA	Alive (12 mo)	Kim[10]
11	40/M	AP, WL	I E	Diffuse large noncleaved cell (WF)	Chemotherapy	Dead (2 mo)	Scweiger[11]
12	57/M	FU, NS, HM	II E	Peripheral T-cell lymphoma (WHO)	Chemotherapy	Alive (12 mo)	Stancu[2]
13	54/M	WL, AP, HM	II E	Peripheral T-cell lymphoma (WHO)	Chemotherapy	Alive (84 mo)	Stancu[2]
14	50/M	FU, JD, HM	I E	Peripheral T-cell lymphoma (WHO)	Antibiotics	Dead (4 d)	Stancu[2]
15	32/M	LD	I E	Peripheral T-cell lymphoma (WHO)	Chemotherapy	Alive (6 mo)	Leung[6]
16	62/M	AP	I E	Peripheral T-cell lymphoma (WHO)	Chemotherapy	Alive (3 mo)	The present study

Stage, based on AJCC cancer staging[12]. AP, abdominal pain; CD, celiac disease; CHF, congestive heart failure; CRB, chlorambucil; FU, fever up; HM, hepatomegaly; JD, jaundice; Kiel, Kiel classification; LD, liver dysfunction; NA, not available; NS, night sweats; PNS, prednisone; REAL, revised European-American classification of lymphoid neoplasms; WF, Working Formulation; WHO, World Health Organization classification; WL, weight loss.

because the neoplasm impairs hepatic function, causing elevated serum liver enzyme levels and coagulopathy. Although a poor prognosis has been reported, 2 of 3 patients with primary hepatic PTCL who received chemotherapy showed complete responses and were in clinical remission at the last follow-up. Thus, a correct diagnosis is very important. Prevention of misdiagnosis requires awareness that the presence of the tumor can be partly obscured by a necroinflammatory and granulomatous background that may mimic an inflammatory process, particularly in small biopsy specimens. Blood tests should include measurement of the level of soluble interleukin-2 receptor.

In conclusion, primary hepatic PTCL is a rare disease that we suggest should be included in the differential diagnosis of liver tumors. Because some cases of PTCL respond to chemotherapy, an open biopsy may be indicated for patients suspected to have this tumor.

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