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Case and Review

Hepatic Pseudolymphoma with Fluorodeoxyglucose Uptake on Positron Emission Tomography

Kazuhiro Suzumura^a Etsuro Hatano^a Toshihiro Okada^a
Yasukane Asano^a Naoki Uyama^a Seikan Hai^a Ami Kurimoto^a
Kentaro Nonaka^b Tohru Tsujimura^c Jiro Fujimoto^a

^aDepartment of Surgery, Hyogo College of Medicine, Nishinomiya, Japan; ^bDepartment of Surgery, Higashinari Hospital, Osaka, Japan; ^cDepartment of Pathology, Hyogo College of Medicine, Nishinomiya, Japan

Keywords

Pseudolymphoma · Fluorodeoxyglucose positron emission tomography · Liver · Hepatectomy · Reactive lymphoid hyperplasia

Abstract

A 69-year-old woman with chronic hepatitis B was admitted to our hospital with a hepatic tumor. The levels of 2 tumor markers, carcinoembryonic antigen and carbohydrate antigen 19-9, were slightly elevated; however, the α -fetoprotein and protein levels induced by vitamin K antagonist II were within the normal limits. Abdominal ultrasonography showed a well-defined peripheral hypoechoic mass that was isoechoic and homogeneous on the inside. Computed tomography showed a poorly enhanced tumor of 13 mm in diameter in the 5th segment of the liver. Fluorodeoxyglucose positron emission tomography showed a slight uptake (maximum standard uptake value 3.4) by the hepatic tumor. These findings suggested cholangiocellular carcinoma, and we performed anterior segmentectomy of the liver. A histopathological examination showed a hepatic pseudolymphoma. The patient's postoperative

course was uneventful, and she remains alive without recurrence 5 months after undergoing surgery. In most cases, hepatic pseudolymphoma is preoperatively diagnosed as a malignant tumor and a definite diagnosis is made after resection. It is therefore necessary to consider hepatic pseudolymphoma as a differential diagnosis in patients with hepatic tumors.

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Background

Pseudolymphoma is a benign nodular lesion that is histopathologically characterized by marked proliferation of nonneoplastic, polyclonal lymphocytes which form follicles with an active germinal center [1]. Pseudolymphoma can occur in various organs such as the skin [2], orbit [3], lung [4], and gastrointestinal tract [5], but it is rare in the liver. The preoperative diagnosis of hepatic pseudolymphoma is difficult because noninvasive radiological examinations such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging are usually equivocal. Recently, some reports have examined the use of fluorodeoxyglucose positron emission tomography (FDG-PET) in the diagnosis of hepatic pseudolymphoma [6–12]. We herein report a case of hepatic pseudolymphoma with FDG uptake on PET and examine the literature.

Case Presentation

A 69-year-old woman with chronic hepatitis B was admitted to our hospital for the further evaluation of a hepatic lesion that was identified by abdominal US during a health examination. She was asymptomatic and a physical examination revealed no remarkable abnormalities. A laboratory examination showed normal findings (including normal liver enzyme levels): white blood cell count 4,550/ μ L, hemoglobin 13.5 g/dL, aspartate aminotransferase 25 U/L, alanine aminotransferase 21 U/L, alkaline phosphatase 262 U/L, γ -glutamyltranspeptidase 16 U/L, and C-reactive protein 0.0 mg/dL. The patient was hepatitis B virus surface antigen-positive, but hepatitis C virus antibody-negative. The levels of the tumor markers carcinoembryonic antigen and carbohydrate antigen 19-9 (CA19-9) were elevated to 5.3 ng/mL (normal range: <5 ng/mL) and 39.2 U/mL (normal range: <37 U/mL), respectively. The α -fetoprotein and protein induced by vitamin K antagonist II (PIVKA-II) were within normal limits. Abdominal US showed a well-defined peripheral hypoechoic mass that was isoechoic and homogeneous on the inside (Fig. 1a). CT showed a poorly enhanced tumor of 13 mm in diameter in the 5th segment of the liver (Fig. 1b). FDG-PET showed a slight uptake by the hepatic tumor (maximum standard uptake value [SUV max] 3.4) (Fig. 1c). No other sites showed FDG uptake. Upper gastrointestinal endoscopy and colonoscopy did not reveal any pathological findings. Since these findings were suggestive of cholangiocellular carcinoma (CCC), the patient underwent laparotomy. No peritoneal dissemination was found during exploratory laparotomy. We therefore performed anterior segmentectomy of the liver. The resected specimen measured 13 \times 12 mm in size and showed a well-defined, nonencapsulated and yellowish-white tumor (Fig. 2). Microscopy

revealed that the lymph follicles varied in size and shape with germinal centers that were composed of small or large lymphoid cells and tangible body macrophages (Fig. 3a, b). An immunohistochemical examination revealed that the follicles were CD20-positive and bcl-2-negative (Fig. 3c, d). The interfollicular area was composed of CD3-positive small T cells (Fig. 3e). The lymphoid cells in follicles showed ordinary immunoreactivity, while the cells in the mantle zone were positive for CD5 and the cells in the germinal center were positive for CD10. A final diagnosis of hepatic pseudolymphoma was made on the basis of the histological and immunohistochemical findings.

The patient's postoperative course was uneventful, and he was discharged from the hospital on the 14th day after surgery. She remains alive without recurrence at 5 months after surgery.

Discussion

Pseudolymphoma can occur in various organs such as the skin, orbit, lung, and gastrointestinal tract [2–5]; it rarely occurs in the liver. Pseudolymphoma of the liver was first reported by Snover et al. [13] in 1981. Pseudolymphoma is also referred to as, “reactive lymphoid hyperplasia” or “nodular lymphoid lesion.” Based on a review of the PubMed database from 1981 to 2016 using the keywords “pseudolymphoma,” “reactive lymphoid hyperplasia,” and “nodular lymphoid lesion,” we found 71 cases, including our own case (Table 1). The 71 patients included 7 (10%) males and 64 (90%) females. The female predilection of this disease was obvious. The average age of the patients was 59 years (range: 15–85). Fifty-five (77%) of these cases involved single tumors; 16 (23%) involved multiple tumors. The average tumor size (in greatest dimension) was 18 mm (range: 3–60 mm), and most of the tumors (63 cases: 89%) were ≤ 20 mm in size. The exact etiology of hepatic pseudolymphoma remains unclear. Associations between the development of hepatic pseudolymphoma and some diseases, such as autoimmune disease [1], malignant tumors [6], and chronic liver disease [14] have been suggested in previous reports. Among the 71 reported cases, 16 (23%) had autoimmune disease, 18 (25%) had malignant disease, and 21 (30%) had chronic liver disease. In our case, the patient was hepatitis B virus surface antigen-positive. However, we do not consider this to be a convincing finding. As a result of accumulation of the reported cases, a middle-aged female patient with hepatic tumor (≤ 20 mm) who has autoimmune disease, malignant tumors, or chronic liver disease should be suspected of having pseudolymphoma.

It is extremely difficult to preoperatively diagnose hepatic pseudolymphoma using US, CT, or magnetic resonance imaging. Hepatic pseudolymphoma has been misdiagnosed as hepatocellular carcinoma, CCC, and metastatic liver cancer. Recently, some reports have examined the use of FDG-PET in the diagnosis of hepatic pseudolymphoma. We found 9 cases in which FDG-PET was used to examine patients with hepatic pseudolymphoma, including our own (Table 2) [6–12]. Seven (78%) of 9 cases showed FDG uptake in the tumor, and the median SUV max was 4.3 (range: 3.4–7.2). In a previous report, the median SUV was 2.64 in hepatocellular carcinoma, 5.20 in CCC, and 4.38 in metastatic liver cancer [15]. Therefore, the accumulation of further case information will be needed to determine the utility of FDG-

PET in differentiating between hepatic pseudolymphoma and other malignant hepatic tumors.

Percutaneous transhepatic needle biopsy is usually avoided in the preoperative period due to the risk of peritoneal dissemination. However, there are some reported cases in which hepatic pseudolymphoma was diagnosed by needle biopsy and followed up without surgical resection [14]. Therefore, needle biopsy may be performed in patients with suspected hepatic pseudolymphoma.

Conclusions

Hepatic pseudolymphoma should be considered in the differential diagnosis of hepatic tumors, especially when a single small (≤ 20 mm) tumor is found in middle-aged female patients. FDG-PET and percutaneous transhepatic needle biopsy may be performed in patients with suspected hepatic pseudolymphoma.

Statement of Ethics

Approval from the Ethics Committee was not required for this case report. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Disclosure Statement

None of the authors has any financial conflicts of interest to declare.

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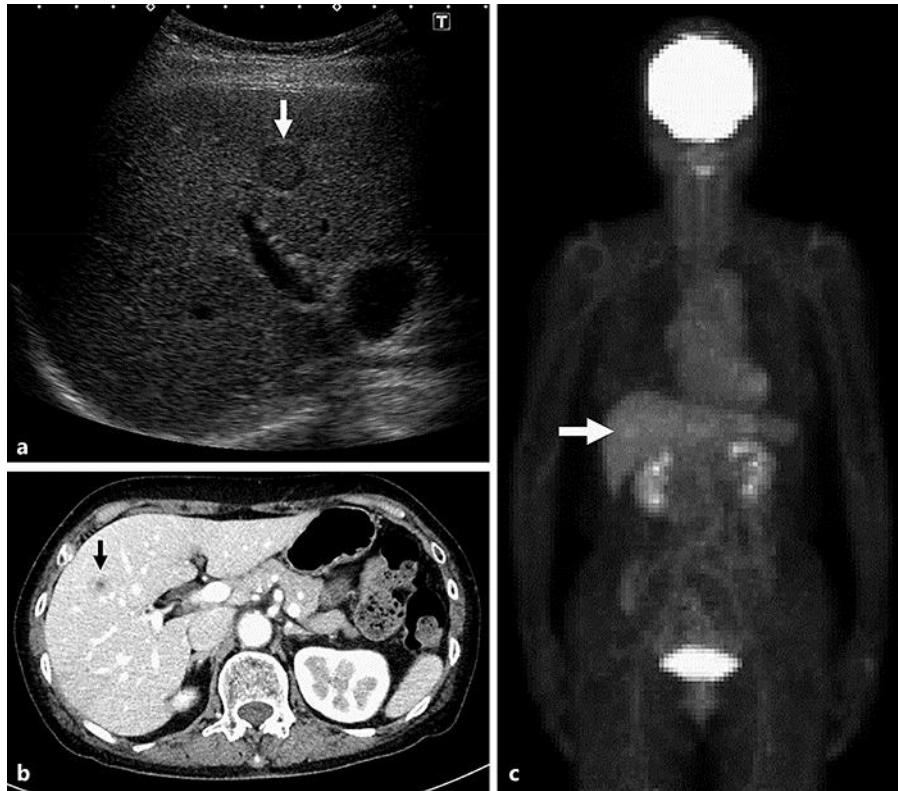


Fig. 1. **a** Abdominal US showed a well-defined peripheral hypoechoic mass that was isoechoic and homogeneous on the inside (arrow). **b** CT showed a poorly enhanced tumor of 13 mm in diameter in the 5th segment of the liver (arrow). **c** FDG-PET showed slight uptake by the hepatic tumor (SUV max 3.4) (arrow).

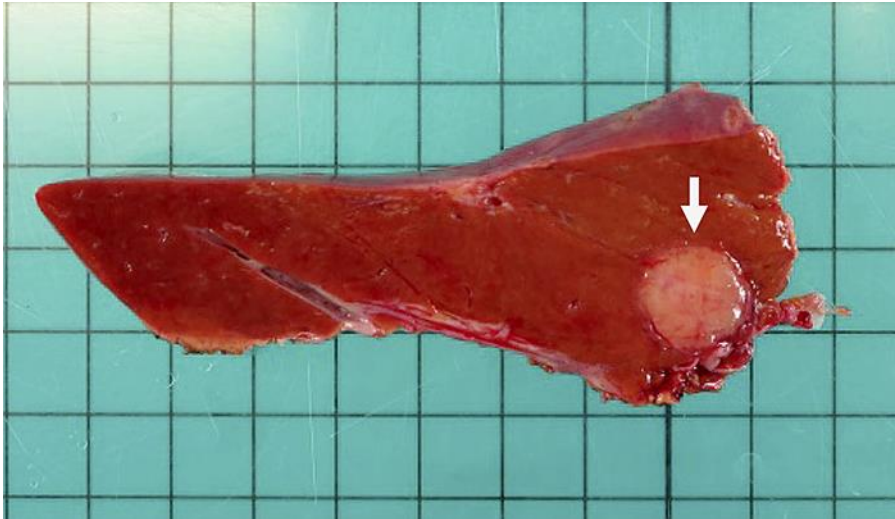


Fig. 2. The resected specimen measured 13 × 12 mm in size and showed a well-defined, nonencapsulated, and yellowish-white tumor (arrow).

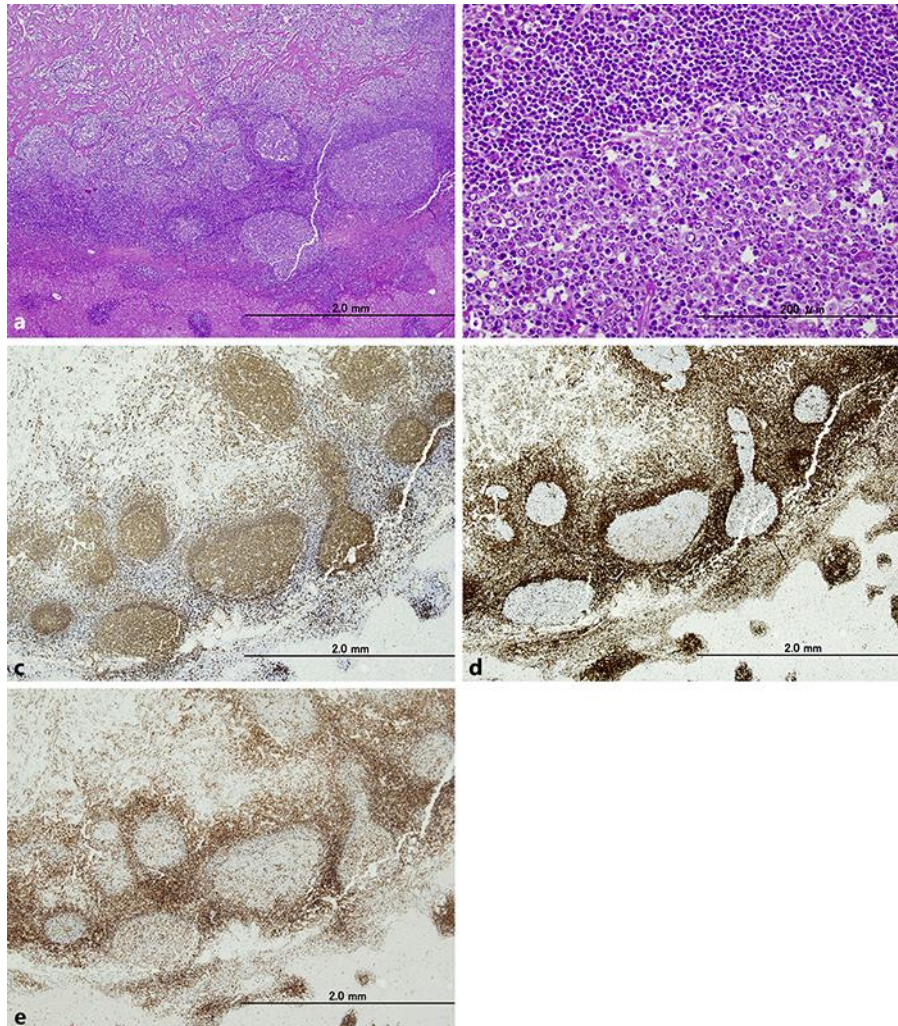


Fig. 3. **a** Microscopically, the lymph follicles varied in size and shape and contained germinal centers. **b** The germinal centers of the lymphoid follicles were composed of small or large lymphoid cells and tangible body macrophages. **c** An immunohistochemical examination revealed that the follicles were CD20-positive. **d** An immunohistochemical examination revealed that the follicles were bcl-2-negative. **e** An immunohistochemical examination revealed that the interfollicular area was composed of CD3-positive small T cells.

Table 1. Clinical presentation of reported cases of hepatic pseudolymphoma (total $n = 71$)

Age, years	59 (range 15–85)
Gender	
Male	7 (10%)
Female	64 (90%)
Associated autoimmune disease	16 (23%)
Sjögren syndrome	4
Autoimmune thyroiditis	4
Autoimmune hepatitis	2
Takayasu disease	2
Antiphospholipid syndrome	1
CREST syndrome	1
Immunodeficiency	2
Associated cancer	18 (25%)
Colon cancer	5
Gastric cancer	4
Renal cell cancer	3
Ovarian cancer	1
Bile duct cancer	1
Pancreatic cancer	1
Cervical cancer	1
Breast cancer	1
HCC	1
Associated liver disease	21 (30%)
PBC	11
Chronic viral hepatitis B	5
Chronic viral hepatitis C	2
Steatohepatitis	3
Preoperative diagnosis	54 (described)
HCC	29
Metastatic tumor	13
CCC	5
Pseudolymphoma	3
Others	4
Tumor number	
Solitary	55
Multiple	16
Tumor size, mm	18 (range 3–60)
Treatment	64 (described)
Resection	54
Biopsy	7
Others	3

HCC, hepatocellular carcinoma; PBC, primary biliary cirrhosis; CCC, cholangiocellular carcinoma.

Table 2. Reported cases of hepatic pseudolymphoma examined by FDG-PET

Case	First author [Ref.]	Year	Age, years	Sex	Preoperative diagnosis	Tumor, n	Tumor size, mm	FDG uptake	Treatment	Associated disease
1	Lin [6]	2008	44	f	Metastasis tumor	1	15	(+) SUV max 4.3	Resection	Colon cancer
2	Marchetti [7]	2011	58	f	Metastasis tumor	1	12	(+) SUV max 7.2	Resection	Ovarian cancer
3	Hayashi [8]	2011	56	f	Metastasis tumor or HCC	1	10	(+) SUV max 3.6	TAE, resection	None
4	Lv [9]	2015	50	f	HCC	1	10	(-)	Resection	None
5	Lv [9]	2015	62	f	HCC	1	9	(-)	Resection	None
6	Calvo [10]	2015	70	f	ND	1	18	(+)	Resection	PBC
7	Kwon [11]	2015	41	f	Hepatic adenoma	1	25	(+)	Resection	Autoimmune hepatitis
8	Taguchi [12]	2015	78	f	Malignant hepatic tumor	4	13	(+) SUV max 4.6	Resection	Tremors
9	Our case	2017	69	f	Cholangiocellular carcinoma	1	13	(+) SUV max 3.4	Resection	Hepatitis B

FDG-PET, fluorodeoxyglucose positron emission tomography; f, female; SUV max, maximum standard uptake value; ND, not described; HCC, hepatocellular carcinoma; TAE, transcatheter arterial embolization; PBC, primary biliary cirrhosis.