Primary diffuse large B cell lymphoma of the common bile duct causing obstructive jaundice

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Abstract We report a rare case of a diffuse large B-cell lymphoma (DLBCL) arising from the common bile duct (CBD). A 77-year old man presented with general fatigue and obstructive jaundice. Abdominal computed tomography revealed a well-circumscribed enhancing mass in the midportion of the CBD with proximal bile duct dilatation. Endoscopic retrograde cholangiopancreatography (ERCP) also showed a midportion of the CBD stricture. Direct peroral cholangioscopy revealed smooth mass in the midportion of the CBD, and narrow-band imaging (NBI) showed irregular tortuous microvessels. The brushing cytology of the CBD was performed, and it was diagnosed as suspicious for poorly differentiated adenocarcinoma or malignant lymphoma. We performed extrahepatic bile duct resection for accurate diagnosis. Histological and immunohistochemical examination of the resected specimen revealed DLBCL. Although systemic chemotherapy is the mainstay of treatment for DLBCL, he refused scheduled subsequent chemotherapy, and died of multiple liver metastases 6 months after surgery.

Keywords Diffuse large B cell lymphoma · Common bile duct · Obstructive jaundice

Introduction

The gastrointestinal tract is the most common site of extranodal non-Hodgkin lymphoma (NHL), mostly arising in the intestines, especially the small intestine [1]. The extrahepatic bile duct is a rare site of primary extranodal lymphoma. Since Nguyen et al. reported the first case in 1982 [2], only 31 cases of primary NHL arising from the extrahepatic bile duct have been reported in the English literature [2–31]. We herein present another case of primary NHL of the common bile duct (CBD) causing obstructive jaundice.

Case report

A 77-year-old man was referred to our hospital with a complaint of general fatigue and painless obstructive jaundice. He had no history of cholelithiasis or abdominal surgery. Physical examination showed no superficial lymphadenopathy, hepatosplenomegaly, or abdominal mass. Laboratory data were as follows: total bilirubin 6.1 mg/dl (normal 0.2–1.2 mg/dl), direct bilirubin 4.5 mg/dl (normal 0–0.4 mg/dl), alkaline phosphatase 879 U/l (normal 85–300 U/l), aspartate aminotransferase 223 U/l (normal 7–40 U/l), alanine aminotransferase 299 U/l (normal 0–35 U/l), and lactate dehydrogenase 235 U/l (normal 100–225 U/l). The serum level of carcinoembryonic antigen, CA 19-9, DUPAN2, and interleukin-2 receptor were within normal limits. Examination of the bone marrow was not performed. The serologic tests for hepatitis B and C were negative. Abdominal computed tomography (CT) revealed a well-circumscribed, homogeneous enhancing, and circular shape mass measuring 17 × 15 mm in the midportion of the CBD, with proximal bile duct dilatation (Fig. 1a, b).

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Fig. 1 **a, b** Abdominal computed tomography reveals a well-circumscribed, homogeneous enhancing, and circular shape mass measuring 17×15 mm in the midportion of the common bile duct, with proximal bile duct dilatation. (**a** axial, **b** coronal). **c** Magnetic resonance cholangiopancreatography shows stenosis of the midportion of the common bile duct with proximal dilatation of biliary tract. **d** Positron emission tomography/computed tomography (PET/CT) shows abnormal 18-fluorodeoxyglucose (FDG) uptake in the mass

Obvious enlarged lymphnodes were not detected. Magnetic resonance cholangiopancreatography (MRCP) also showed stenosis of the midportion of the CBD, with proximal dilatation of biliary tract (Fig. 1c). A whole-body positron emission tomography/computed tomography (PET/CT) showed abnormal 18-fluorodeoxyglucose (FDG) uptake in the mass of CBD with the rest of the whole-body study appearing unremarkable. The maximum standardized uptake value (SUV max) of the CBD mass was 12.45 (Fig. 1d). An endoscopic retrograde cholangiopancreatography (ERCP) revealed a 15-mm mid-common bile duct stricture with significant dilation of proximal biliary tree (Fig. 2a). Furthermore, direct peroral cholangioscopy revealed smooth mass in the midportion of the CBD (Fig. 2b). Narrow-band imaging (NBI) showed irregular tortuous microvessels (Fig. 2c). These findings were not compatible with cholangiocarcinoma. The brushing cytology of the CBD was done, and it showed large atypical cells with irregular nuclear shape, prominent nucleoli, and scant cytoplasm. In a background, it showed a few epithelial cells without atypia (Fig. 2d). These findings were suspicious for malignant lymphoma or poorly differentiated adenocarcinoma. Although we tried to perform endoscopic ultrasonography -guided fine-needle aspiration biopsy (EUS-FNAB) to obtain definitive diagnosis, a tumor could not be detected clearly.

We planned to perform extrahepatic biliary tract excision to establish accurate histological diagnosis and to remove the tumor causing obstructive jaundice. The intraoperative pathological diagnosis of the resected

specimen was malignant lymphoma. The biliary tract was reconstructed with a Roux-en-Y hepaticojejunostomy. The gross examination of the resected specimen showed that the lumen of the CBD was stenotic due to the well-defined white and solid polypoid mass, measuring 18×12 mm (Fig. 3a, b). Histologically, beneath the normal biliary epithelium, there were atypical large lymphocytes with irregular nuclear shape and prominent nucleoli in diffuse pattern (Fig. 4a, b). Immunohistochemical stainings were positive for B-cell marker (CD 20) and negative for T-cell marker (CD3) and cytokeratin (Fig. 4c–e). These findings confirmed a primary DLBCL of CBD with clinical Stage I according to UICC classification. In addition, the lymphoma cells expressed BCL6 and MUM1 and did not express CD10 (Fig. 4f–h). These findings confirmed non-germinal center B-cell-like (non-GCB) DLBCL according to Hans' algorithm [32].

Although postoperative chemotherapy was scheduled, the patient refused to receive any chemotherapy. Four months after surgery, CT scan showed multiple liver metastases. No other metastatic or local lesions were observed. This recurrence finally made the patient decide to receive chemotherapy. Although we recommended cyclophosphamide, doxorubicin, vincristine, and prednisolone in conjunction with the anti-CD20 monoclonal antibody rituximab (R-CHOP regimen), he preferred another chemotherapy with less side effect. Then, we chose low-dose VP-16 (etoposide); however, this regimen did not show any effect and the patient died 6 months after surgery.

Fig. 2 **a** Endoscopic retrograde cholangiopancreatography shows a 1.5-cm mid-common bile duct stricture with significantly dilated intrahepatic and common hepatic biliary ducts. **b** Direct peroral cholangioscopy reveals smooth mass in the midportion of the common bile duct. **c** Narrow-band imaging shows irregular tortuous microvessels. **d** The brushing cytology of the common bile duct showed large atypical cells with irregular nuclear shape, prominent nucleoli, and scant cytoplasm

Fig. 3 **a, b** The gross examination of the resected specimen shows that the lumen of the common bile duct is stenotic due to the well-defined solid polypoid mass, measuring 18 × 12 mm

Discussion

Non-Hodgkin lymphoma (NHL) accounts for 1–2 % of all cases of malignant biliary obstruction [33]. Their presentation with obstructive jaundice is mostly secondary to compression of the extrahepatic bile ducts by periportal, perihepatic, or peripancreatic lymphadenopathy [11, 19]. Primary NHL arising from the extrahepatic bile duct is extremely rare, and English literature review between 1982

and 2015 revealed only 32 cases (including our case) (Table 1). The median age was 53 years (range 3–77), and the patients consisted of 21 men and 11 women. All 32 patients presented with obstructive jaundice.

It is difficult to diagnose primary lymphoma of the CBD on the basis of CT scan, MRI, and cholangiography results, because in most cases, these clinical and radiological findings resemble those of bile duct carcinoma. Yoon et al. reported that radiologists should raise the possibility of

Fig. 4 **a, b** Microscopic finding of the common bile duct, beneath the normal biliary epithelium; there are atypical large lymphocytes with irregular nuclear shape and prominent nucleoli in diffuse pattern. (**a** $\times 20$; **b** $\times 200$). Immunohistochemically, the tumor cells are

positive for leukocyte common antigen and B-cell marker (CD 20) (**c** $\times 200$), negative for T-cell marker (CD3) (**d** $\times 200$), and negative for cytokeratin (**e** $\times 100$). The tumor cells express BCL6 (**f** $\times 200$) and MUM1 (**g** $\times 200$), and do not express CD10 (**h** $\times 200$)

primary biliary tree lymphoma when cholangiography shows smooth, mild luminal narrowing of the extrahepatic ducts without mucosal irregularities, in spite of the diffuse thickening of the ductal wall on CT/MRI [28]. However, it is unclear whether such a specific diagnosis of NHL can be made simply based on these findings. In our case, PET/CT showed abnormal FDG uptake in the mass of primary DLBCL of the CBD. It is difficult to diagnose NHL of the CBD on the basis of PET/CT, because FDG uptake is usually detected in cholangiocarcinoma.

Out of previous 32 reports, 22 patients (including ours) were treated by surgery followed by chemotherapy and/or radiotherapy, and 9 patients were treated by only surgery. Only one case reached histopathological diagnosis by an abdominal sonography-guided biopsy without surgery [19]. There have been recent reports of success with EUS-FNAB for a definitive tissue diagnosis [34]. In our case, although EUS-FNAB was tried, a tumor could not be pointed out

clearly. We performed direct peroral cholangioscopy and found that the tumor was not compatible with bile duct carcinoma morphologically. This is the first report that primary NHL of the extrahepatic bile duct is visualized directly by cholangioscopy.

Because of the difference in the prognosis and treatment between cholangiocarcinoma and NHL, accurate histopathologic diagnosis was necessary. Therefore, surgical resection was performed to obtain adequate tissue for diagnosis and remove the tumor causing obstructive jaundice.

Out of 32 cases, the most common immunophenotype was B lineage (21 patients, 66 %), including 8 DLBCL cases. The treatment of DLBCL has been revolutionized in recent years with the addition of rituximab to combination chemotherapy, resulting in an increased proportion of cured patients [34]. However, primary DLBCL of the CBD is a rare primary site, and there is no consensus on the best

Table 1 Summary of literature of primary NHL of the extrahepatic bile duct

	Author	Age /sex	Histopathologic diagnosis	Treatment modality	Follow-up period (month)	Outcome
1	Nguyen [2]	59/M	Lymphohistiocytic lymphoma, diffuse type	Surgery+chemotherapy	8	Died
2	Takehara et al [3]	60/M	Non-Hodgkin's lymphoma	Surgery+chemotherapy	Unknown	Unknown
3	Kaplan et al [4]	42/M	High-grade non-Hodgkin's lymphoma	Surgery+chemotherapy	10	Died
4	Tartar and Balfe [5]	48/M	Bile duct wall lymphoma	Surgery+ chemotherapy	14	Alive
5	Tzanakakis et al [6]	70/M	Mixed small and large cell non-Hodgkin's lymphoma	Surgery+ Chemotherapy	4	Died
6	Kosuge et al [7]	68/F	B cell lymphoma	Surgery+chemotherapy+RT	16	Died
7	Brouland et al [8]	34/F	T cell-rich B cell lymphoma (centroblastic type)	Surgery+chemotherapy	48	Alive
8	Machado et al [9]	43/F	Bile duct lymphoma	Surgery+RT	6	Alive
9	Chiu et al [10]	25/F	Malignant lymphoma	Surgery	12	Died
10	Andre et al [11]	44/F	Non-Hodgkin's lymphoma	Surgery+chemotherapy	48	Alive
11	Maymind et al [12]	39/F	Diffuse large B cell lymphoma	Surgery+chemotherapy+RT	13	Alive
12	Podbielski et al [13]	66/M	Large B cell non-Hodgkin's lymphoma	Surgery	Unknown	Unknown
13	Oda et al [14]	58/M	Non-Hodgkin's lymphoma	Surgery	32 days	Died
14	Corbinais et al [15]	29/M	High-grade T cell non-Hodgkin's lymphoma	Chemotherapy	12	Alive
15	Eliason and Grosso [16]	41/M	Diffuse large B cell lymphoma	Surgery	Unknown	Unknown
16	Gravel et al [17]	4/M	Lymphoblastic lymphoma of the pre-B type	Surgery+chemotherapy	18	Alive
17	Kang et al [18]	73/F	Low-grade B cell lymphoma of MALT type	Surgery	23	Alive
18	Das K et al [19]	36/M	Diffuse large B cell lymphoma	Surgery+chemotherapy	68	Alive
19		51/M	Diffuse large B cell lymphoma	Surgery+chemotherapy	18	Alive
20	Ferluga et al [20]	3/F	Follicular lymphoma	Surgery	36	Alive
21	Suzuki et al [21]	71/F	MALT lymphoma	Surgery	Unknown	Unknown
22	Joo et al [22]	21/F	Diffuse large B cell malignant non-Hodgkin's lymphoma	Surgery+chemotherapy+RT	17	Alive
23	Sugawara et al [23]	33/M	Follicular lymphoma	Surgery	12	Alive
24	Shito et al [24]	71/M	MALT lymphoma	Surgery+chemotherapy	45	Alive
25	Dote et al [25]	63/M	Diffuse large B cell lymphoma	Surgery+chemotherapy	8	Alive
26	Christophides et al[26]	53/F	High-grade follicular lymphoma	Surgery+chemotherapy	48	Alive
27	Kang et al [27]	60/M	Diffuse large B cell non-Hodgkin's lymphoma	Surgery+chemotherapy	Unknown	Unknown
28	Yoon et al [28]	62/M	Marginal zone B cell lymphoma of the MALT type	Surgery	Unknown	Unknown
29	Luigiano et al [29]	30/M	Malignant large B cell-type lymphoma	Surgery+ chemotherapy	6	Alive
30	Khozeimeh et al [30]	32/M	Follicular lymphoma	Surgery+chemotherapy	72	Alive
31	Zakaria et al [31]	57/M	High-grade large B cell non-Hodgkin's lymphoma	Surgery+chemotherapy	41	Alive
32	This study	77/M	Diffuse large B cell non-Hodgkin's lymphoma	Surgery+chemotherapy	6	Died

treatment modality. Joo et al. and Dote et al. suggest that surgery might play an important role in establishing the diagnosis and removing the lymphoma and that subsequent chemotherapy and/or radiotherapy after the initial surgery

might be effective [12, 22, 25]. In our case, however, the patient refused R-CHOP regimen, and multiple liver metastases occurred 4 months after surgery. As a result, surgical resection might not contribute to the improvement

of prognosis, while it was necessary for histological diagnosis and removal of the tumor.

We experienced a rare case of primary NHL of the CBD. Although surgery plays an important role in an accurate histological diagnosis and local tumor control, multidisciplinary therapy including systemic chemotherapy might be necessary to improve prognosis of this disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from a guardian of the patient in this report.

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