J Hepatobiliary Pancreat Surg (2008) 15:440–443
DOI 10.1007/s00534-007-1229-2

Journal of HBP Surgery

Primary non-Hodgkin's lymphoma of the main hepatic duct junction

Masaya Shito[1], Toshihiro Kakefuda[1], Tai Omori[1], Seiichiro Ishii[1], and Hitoshi Sugiura[2]

[1] Department of Surgery, Kawasaki Municipal Hospital, 12-1 Shinkawadori, Kawasaki-ku, Kawasaki, Kanagawa 210-0013, Japan
[2] Department of Pathology, Kawasaki Municipal Hospital, Kawasaki, Japan

Abstract
A rare case of primary non-Hodgkin's lymphoma of the main hepatic duct junction is reported. A 71-year-old man was admitted for treatment of obstructive jaundice. Radiological examination revealed stenosis of the main hepatic duct junction. Biliary drainage was not necessary because total bilirubin decreased spontaneously. A left hepatic and caudate lobectomy, combined with resection of bile ducts and lymph node dissection, was performed with the preoperative diagnosis of cholangiocarcinoma of the main hepatic duct junction. Macroscopic examination of the resected specimen revealed tumorous growth in the main hepatic duct junction. Histological and immunochemistry findings disclosed a mucosa-associated lymphoid tissue (MALT) lymphoma. The patient received three courses of combination chemotherapy [cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP)], and there was no evidence of recurrence 45 months after the surgery. Although primary non-Hodgkin's lymphoma of the main hepatic duct junction is extremely rare and difficult to diagnose preoperatively, aggressive surgery followed by chemotherapy, as here, is a possible curative option.

Key words Non-Hodgkin's lymphoma · MALT lymphoma · The main hepatic duct junction · CHOP · Cholangiocarcinoma

Introduction

Although several case reports of non-Hodgkin's lymphoma (NHL) arising from the extrahepatic bile duct have been published,[1–4] primary NHL of the main hepatic duct junction is extremely rare. We report a case of mucosa-associated lymphoid tissue (MALT) lymphoma of the main hepatic duct junction. The patient had a rare type of primary NHL of the bile duct, which was identified only after examination of the surgical specimen.

Offprint requests to: M. Shito
Received: October 24, 2006 / Accepted: March 17, 2007

Case report

A 71-year-old man presented to our hospital for investigation of obstructive jaundice. At the time of admission, he appeared well nourished, and no erythema or superficial lymphadenopathy was detected. His head and neck findings were normal and there was no evidence of parotid enlargement. The lungs were clear, the heart was normal, and there was no fever or abdominal pain. Laboratory evaluation revealed white blood cell count, 5470/mm^3; hemoglobin, 14.6 g/dl; platelet count, $15.0 \times 10^{4/}$mm^3; total protein, 7.0 g/dl; aspartate aminotransferase, 513 IU/l; alanine aminotransferase, 748 IU/l; alkaline phosphatase, 1113 IU/l; and gamma-glutamyl transpeptidase, 596 IU/l. Total bilirubin was 8.8 mg/dl with 5.9 mg/dl direct fraction. Coagulation profiles were within normal limits. Serologically, hepatitis B surface antigen and anti-hepatitis C virus antibody were negative. The tumor marker, carbohydrate antigen (CA)-19-9 was slightly elevated (56 U/ml), while carcinoembryonic antigen (CEA) was within normal limits (1.2 ng/ml).

Abdominal ultrasonography (US) showed dilatation of the intrahepatic bile ducts, but no dilatation of the common bile duct was found. Abdominal computed tomography (CT) showed a circumscribed heterogeneous mass in the main hepatic duct junction, with dilatation of intrahepatic bile ducts. There was no evidence of lymph node swelling or hepatosplenomegaly. Endoscopic retrograde cholangiography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) showed stenosis of the main hepatic duct junction (Fig. 1). Cytological examination of the bile duct was not performed. Biliary drainage was not necessary because total bilirubin decreased spontaneously and

the intrahepatic bile duct dilatation also reduced spontaneously.

The patient underwent a laparotomy, with a diagnosis of cholangiocarcinoma of the main hepatic duct junction. On the opening of the abdomen, there was no ascites, lymphadenopathy, or dissemination of malignancy. A hard mass was palpated on the main hepatic duct junction. A left hepatic and caudate lobectomy, combined with resection of bile ducts and lymph node dissection, was performed following the operative diagnosis of cholangiocarcinoma of the main hepatic duct junction. The intraoperative diagnosis of frozen sections of the resected edge was chronic nonspecific inflammation. The biliary tract was reconstructed with a Roux-en-Y hepaticojejunostomy.

Macroscopic examination of the resected specimen revealed a dense white nodular mass, 5.0 cm × 2.5 cm, in the main hepatic duct junction (Fig. 2). There was no lymph node involvement. Histological examination of the tumor revealed the diffuse growth of small-sized lymphoid cells, with lymphoepithelial lesions involving bile ducts and scattered lymphoid follicles (Fig. 3), which infiltrated a small number of regional lymph nodes. Immunohistochemical studies were positive for

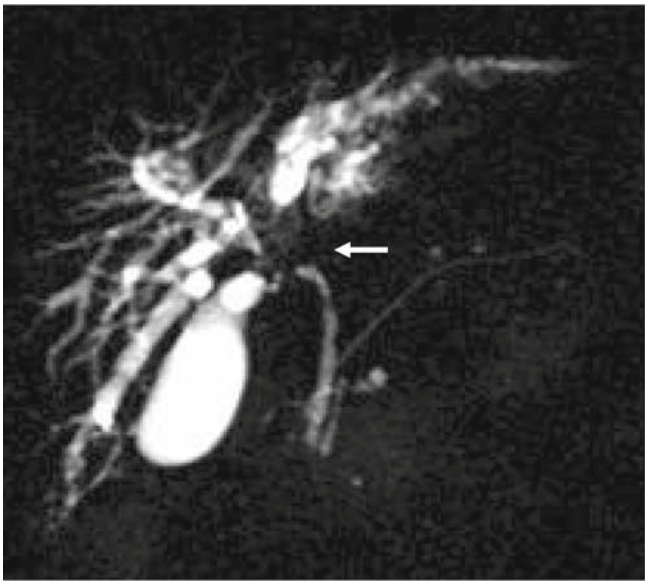


Fig. 1. Magnetic resonance cholangiopancreatography (MRCP) shows stenosis of the main hepatic duct junction (*arrow*) with dilatation of intrahepatic bile ducts

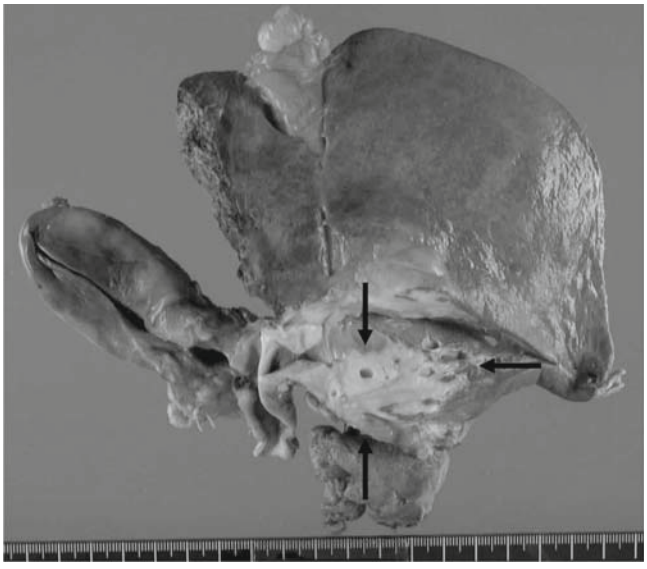
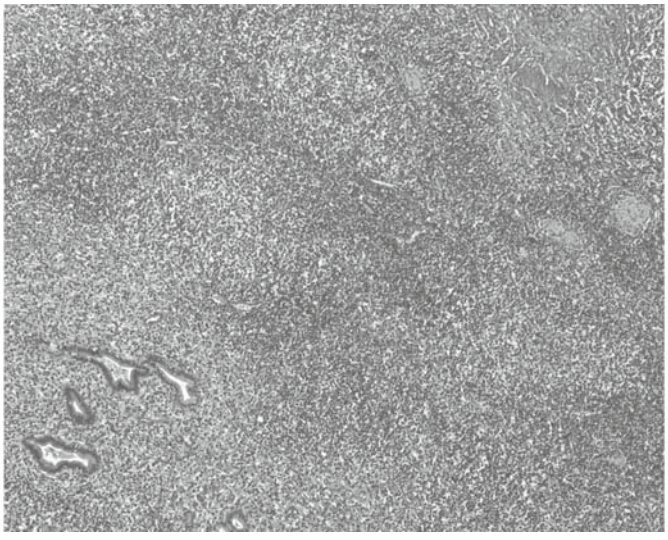
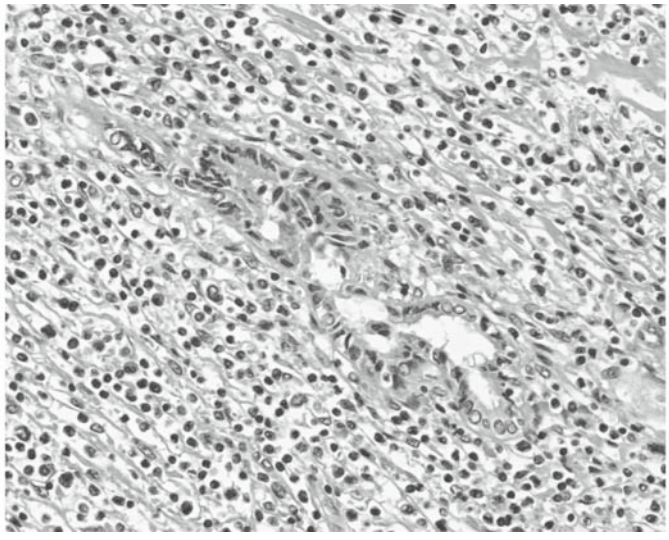


Fig. 2. Macroscopic examination of the resected specimen reveals a dense white nodular mass in the main hepatic duct junction (*arrows*)



a



b

Fig. 3a,b. Histological findings of the tumor reveal the diffuse growth of small-sized lymphoid cells with lymphoepithelial lesions involving bile ducts, and scattered lymphoid follicles. **a** H&E, ×20; **b** H&E, ×100

both B-cell (CD20) and T-cell (CD45RO) markers, indicating tumor cells and reactively infiltrating T-lymphocytes, respectively. Therefore, histology and immunohistochemistry confirmed MALT lymphoma of the main hepatic duct junction. The patient received three courses of combination chemotherapy [cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP)] after the surgery. He has been well and there was no evidence of recurrence 45 months after the surgery.

Discussion

Obstructive jaundice often occurs as a secondary manifestation of NHL, but primary NHL of the bile duct initially presenting as obstructive jaundice is extremely rare. In both NHL and cholangiocarcinoma, obstructive jaundice is the major presenting symptom, as the similarity of the clinical and radiological findings in both cases. Therefore, a primary diagnosis of NHL is very difficult, and in most cases diagnoses of NHL have been made postoperatively. In our patient, US, CT, ERCP, and MRCP were performed for the diagnosis of the lesion, but they provided nonspecific findings of stenosis of the main hepatic duct junction, which was diagnosed preoperatively as cholangiocarcinoma. Cytological examination, such as brush and bile cytology, should have been performed to reach a histological diagnosis preoperatively, although these diagnoses may not always be complete.

We reported a patient presenting with a transient icteric episode probably due to localized thickening of the bile duct. This cholestasis, in association with the features identified on imaging, suggested a diagnosis of cholangiocarcinoma, primary sclerosing cholangitis, or some other rare disease.[5–7] Surgical resection for carcinoma of the main hepatic duct junction can be performed safely and effectively, as our colleagues have described before;[8] therefore, if there is any possibility of carcinoma, an operation should be undertaken.

In previous reports of NHL, the intraoperative diagnoses of frozen sections were chronic nonspecific inflammation and nonepithelial malignant neoplasm;[9–11] in the present patient, the intraoperative diagnosis of frozen sections was chronic nonspecific inflammation in the resected edge. In a patient in whom the intraoperative diagnosis of frozen sections for stenosis of the bile duct is chronic nonspecific inflammation, primary NHL should be suggested. Surgical resection for primary NHL is necessary not only to have a correct diagnosis but also to adequately determine subsequent chemotherapy.

NHL of the common bile duct appears to be a rapidly progressive disease after the initial diagnosis is made from surgical exploration.[11] Therefore, chemotherapy or radiotherapy, in addition to surgery, appears necessary. Chemotherapy is important; indeed it is essential for the postoperative treatment of NHL of the extrahepatic bile duct;[1,2,12] therefore, sequential chemotherapy, mainly CHOP, needs to be performed for there, to be a chance of cure. According to a recent report,[13] chemotherapy is the most appropriate treatment if the correct diagnosis is made before surgery, and surgical resection should be reserved to address complications of biliary obstruction or the failure of chemotherapy. In our patient, however, accurate diagnosis was not established preoperatively, and surgical intervention played an important role in the treatment and for the subsequent chemotherapy, based on the histological examination. Although there have only been a few such patients reported, they appear to have responded well to the chemotherapy following surgery.[14,15] Our patient is still alive and free of recurrence more than 3 years after surgery followed by chemotherapy, though continued close follow-up is essential. The role of radiotherapy remains to be clarified; it may be effective when the disease is very limited.[11] Particularly, the use of radiotherapy should be reserved for any residual disease after primary chemotherapy, or to relieve symptoms of pain caused by the disease.[2]

In conclusion, we treated a patient with primary NHL of the main hepatic duct junction. Although a diagnosis of NHL is very difficult to reach because of the rarity of this disease, surgical resection followed by chemotherapy holds out the prospect of a good prognosis.

References

1. Fidias P, Carey RW, Grossbard ML. Non-Hodgkin's lymphoma presenting with biliary tract obstruction. A discussion of seven patients and a review of the literature. Cancer 1995;75:1669–77.
2. Ravindra KV, Stringer MD, Prasad KR, Kinsey SE, Lodge JP. Non-Hodgkin lymphoma presenting with obstructive jaundice. Br J Surg 2003;90:845–9.
3. Suzuki S, Tanaka S, Suzuki M, Imazato M, Hayashi T, Hanyu F, et al. Mucosa-associated lymphoid tissue-type lymphoproliferative lesion of the common bile duct. Hepatogastroenterology 2004;51:110–3.
4. Shimura T, Kuwano H, Kashiwabara K, Kojima M, Masuda N, Suzuki H, et al. Mucosa-associated lymphoid tissue lymphoma of the extrahepatic bile duct. Hepatogastroenterology 2005;52: 360–2.
5. Brouland JP, Molimard J, Nemeth J, Valleur P, Galian A. Primary T-cell rich B-cell lymphoma of the common bile duct. Virchows Arch A Pathol Anat Histopathol 1993;423:513–7.
6. Tsushimi T, Enoki T, Harada E, Orita M, Noshima S, Masuda M, et al. Ectopic hepatocellular carcinoma arising in the bile duct. J Hepatobiliary Pancreat Surg 2005;12:266–8.
7. Kadono J, Hamada N, Higashi M, Ishizaki N, Nakamura N, Sakata R. Carcinosarcoma of the extrahepatic bile duct. J Hepatobiliary Pancreat Surg 2005;12:328–31.
8. Sugiura Y, Nakamura S, Iida S, Hosoda Y, Ikeuchi S, Mori S, et al. Extensive resection of the bile ducts combined with liver

resection for cancer of the main hepatic duct junction: a cooperative study of the Keio Bile Duct Cancer Study Group. Surgery 1994;115:445–51.
9. Nguyen GK. Primary extranodal non-Hodgkin's lymphoma of the extrahepatic bile ducts. Report of a case. Cancer 1982;50: 2218–22.
10. Kosuge T, Makuuchi M, Ozaki H, Kinoshita T, Takenaka T, Mukai K. Primary lymphoma of the common bile duct. Hepatogastroenterology 1991;38:235–8.
11. Maymind M, Mergelas JE, Seibert DG, Hostetter RB, Chang WW. Primary non-Hodgkin's lymphoma of the common bile duct. Am J Gastroenterol 1997;92:1543–6.
12. Dudgeon DJ, Brower M. Primary chemotherapy for obstructive jaundice caused by intermediate-grade non-Hodgkin lymphoma. Cancer 1993;71:2813–6.
13. Das K, Fisher A, Wilson DJ, dela Torre AN, Seguel J, Koneru B. Primary non-Hodgkin's lymphoma of the bile ducts mimicking cholangiocarcinoma. Surgery 2003;134:496–500.
14. Joo YE, Park CH, Lee WS, Kim HS, Choi SK, Cho CK, et al. Primary non-Hodgkin's lymphoma of the common bile duct presenting as obstructive jaundice. J Gastroenterol 2004;39:692–6.
15. Gravel J, Lallier M, Garel L, Brochu P, Champagne J, Alvarez F. Primary non-Hodgkin lymphoma of the extrahepatic biliary tract and gallbladder in a child. J Pediatr Gastroenterol Nutr 2001; 32:598–601.