

## Primary Lymphoma of the Common Bile Duct A Case Report

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### Abstract

Primary gastrointestinal involvement of non-Hodgkin's lymphoma is frequently reported, but primary lymphoma of the common bile duct is extremely rare. Only fifteen cases have been recorded in the literature. In this paper, a 48-year-old male with obstructive jaundice and a primary lymphoma of the common bile duct is described. The cholangiogram disclosed stricture of the common bile duct. Pathological studies of the surgical specimen revealed that the wall of the common bile duct was transmurally infiltrated by non-Hodgkin's lymphoma of follicular cell type of B-cell lineage, with positivity for Bcl-2. Periductal and peripancreatic lymph nodes were replaced by metastatic lymphomatous involvement. The patient received postoperative chemotherapy according to the CHOP regimen. There is no evidence of lymphoma recurrence 3 months after the surgery. The analysis of the reported cases supports that a complete surgical resection of the lymphoma followed by chemotherapy has shown a promising result.

**Key words :** Common bile duct, Primary lymphoma

### INTRODUCTION

The malignant neoplasms obstructing the extrahepatic bile duct (EHBD) are usually intraductal or periductal carcinomas, including pancreatic carcinoma and ampullary carcinoma. But occasionally malignant lymphoma obstructs the extrahepatic bile duct due to compression by enlarged, lymphomatous lymph nodes in the periductal or peripancreatic region<sup>1,2)</sup> or by lymphomatous involvement of the pancreas or periampullary region<sup>3,4)</sup>, and is estimated to occur in 0.2 to 2.0 % of the patients with this disease as a late manifestation.<sup>4)</sup> Extranodal non-Hodgkin's lymphoma (NHL) primarily involving the EHBD is extremely rare. To our knowledge, only 10 or more cases have been documented in the literature, including one case reported in Korean literature.<sup>5-16)</sup> In this report an additional case of a middle-aged man who

developed acute obstructive jaundice and generalized itching sensation secondary to NHL of the common bile duct is documented, with review of the reported cases.

### CASE REPORT

This 48-year-old man developed icteric sclera and itching sensation on October 1st week, 2003. He had decreased appetite, but no nausea or vomiting. His urine became dark and his stools clay-colored. A few day later, he revealed generalized jaundice and complained of pruritus. He visited regional hospital and computerized tomography (CT) of the abdomen revealed marked diffuse dilatation of gallbladder and both intrahepatic bile ducts. He stated no weight loss over recent 6 months. He had a 30 pack-year history of cigarette smoking and also had taken 200cc/day of 'soju' for 30 years.

On admission to the Kosin University Gospel Hospital, he was PTBD state. His abdomen was soft and not

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distended, but was tender to deep palpation in the right upper quadrant. He had normal vital signs. His physical examination was otherwise unremarkable, except for icteric whole body surface and sclera. Any cervical, axillary, and inguinal lymph nodes were not palpated. Laboratory examination revealed serum alkaline phosphatase to be 545 U/L (normal, 100-280 U/L), total bilirubin 8.1 mg/dl (normal, 0.2-1.2 mg/dl), AST 72 U/L (normal, 5-45 U/L), ALT 64 U/L (normal, 5-40 U/L),  $\gamma$ -GTP 326U/L (normal, 1-63 U/L).

Percutaneous transhepatic cholangiography showed marked dilatation of both intrahepatic ducts and proximal segment of the common hepatic duct, with no visible EHBD distal to the common hepatic duct (Fig.1). Abdominal CT scan performed at the regional hospital revealed a 2.5x2 cm soft tissue mass involving EHBD from distal segment of the common hepatic ducts to proximal and middle segment of the common bile duct. Preoperative biopsy was not performed.

At laparotomy, a nodular segment involving the wall of the proximal and middle segment of the common bile duct was noted. Intrapancreatic common bile duct was relatively not thickened. The wall of the gallbladder was not thickened. Some enlarged lymph nodes were detected next to the common bile duct and in the superior pancreatic and celiac region. Ascites was not found. Resection of the common bile duct, including the nodular segment, pancreatic head, duodenum and jejunum, cholecystectomy, subtotal gastrectomy, radical superior pancreatic and celiac lymphadenectomy, and pancreaticojejunostomy, Roux-en-Y choledochojejunostomy and Roux-en-Y gastrojejunostomy were carried out. Fifteen days after surgery, his total bilirubin was down to 1.2 mg/dl, alkaline phosphatase to 316 U/L,  $\gamma$ -GTP to 75 U/L, AST to 14 U/L, and ALT to 13 U/L.

After the pathologic diagnosis of non-Hodgkin's lymphoma was established (see below), the patient received two cycles of chemotherapy according to the CHOP regimen. For each cycle of therapy, he received

cyclophosphamide 900 mg, Adriamycin 50 mg, vincristine 2 mg, and prednisolone 15 mg. The patient tolerated the chemotherapy well. Four cycles of chemotherapy will also be done. At present his liver enzymes were within normal limits, and he is well without evidence of disease recurrence.

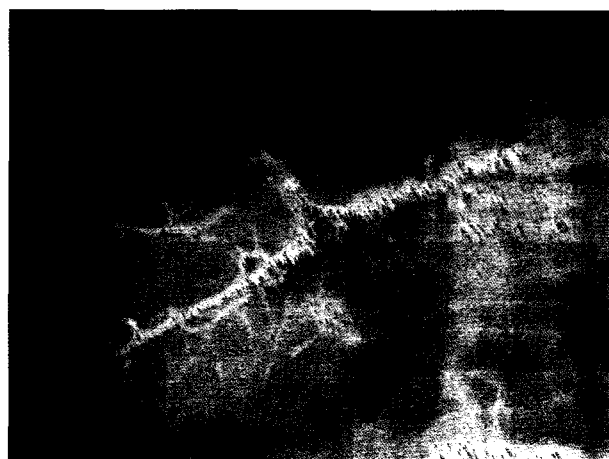


Fig. 1 Percutaneous transhepatic cholangiography revealing dilatation of both intrahepatic ducts and total obstruction involving the common bile duct.

### Pathologic Findings

The common bile duct was stenotic and its wall was markedly thickened by diffuse neoplastic infiltration. Proximally the neoplasm extended proximal to the site of cystic duct insertion without involvement of the cystic duct or gallbladder. The gallbladder wall was not thickened. The pancreas and intrapancreatic common bile duct is pathologically unremarkable. Histopathologically, the wall of the involved common bile duct was diffusely and transmurally infiltrated by neoplastic large and small lymphoid cells, with some nodules of neoplastic lymphoid cells (Fig 2 and 3). The neoplastic lymphoid cells extend just beyond the boundary of the duct. The large lymphoid cells appeared to be noncleaved or often cleaved, with prominent nucleoli. The bile duct lining epithelium is focally intact, and some glands were surrounded by neoplastic small and large lymphoid cells. Of 6 lymph nodes adjacent to the involved bile duct and in the superior pancreatic and celiac region, 4 were enlarged (3

periductal, and 1 superior pancreatic) and the enlarged lymph nodes showed diffusely replaced by the markedly enlarged neoplastic follicles. The largest node was located next to the common bile duct and measured 2x1.5x1.5 cm in size. Immunohistochemical studies showed that these neoplastic lymphoid cells were positive for CD45 and CD20, and they were of B-cell phenotype with a scattering of T-cells (as shown by CD45Ro) throughout the lesion. The neoplastic large lymphoid cells were also positive for Bcl-2, but negative for CD5, CD10, CD43, cyclin D1, and epithelial markers. The pathological diagnosis is follicular center cell lymphoma according to WHO classification.<sup>17)</sup>

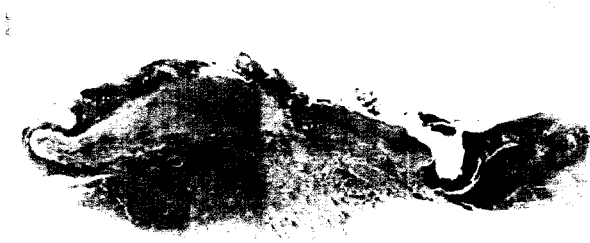


Fig. 2 Whole mount of the common bile duct revealing transmural involvement of neoplastic lymphoid follicles in diffuse and nodular form, with extending just beyond the boundary of the duct.

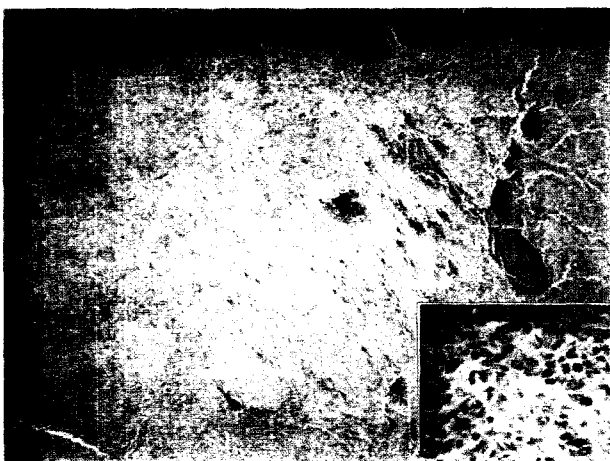


Fig. 3 Neoplastic lymphoid follicles mainly composed of large non-cleaved or cleaved cells, with some apoptotic bodies. (H-E stain, x100; inset, x400)

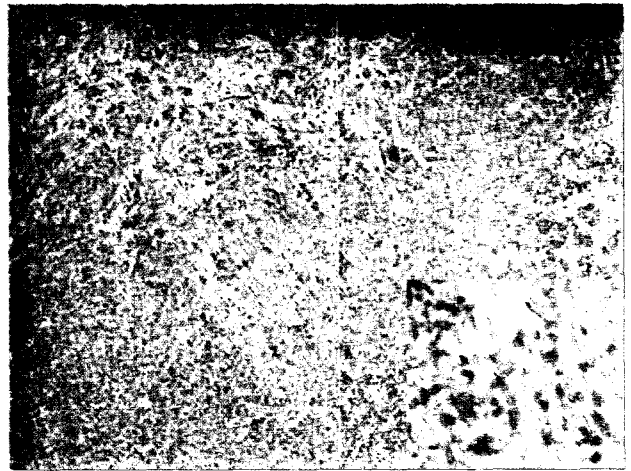


Fig. 4 Neoplastic large and small lymphoid cells showed positive staining for CD20 along the cell membrane. (Immunostain, x100; inset x400)



Fig. 5 Neoplastic large lymphoid cells showed positive nuclear and/or cytoplasmic staining for Bcl-2. (Immunostain, x100; inset x400)

## DISCUSSION

The segmental stricture and nodular thickening of the common bile duct due to primary NHL always manifests acute onset of obstructive jaundice as seen in the previous and present reports of primary NHL of common bile duct. Preoperative radiologic diagnosis of NHL involving EHBD is very difficult because the neoplastic thickening of common bile duct is carcinomatous involvement, with extremely rare lymphomatous involvement, although

Japanese investigators<sup>7,9)</sup> emphasized the presence of a homogenous hypoechoic mass filling the lumen of the bile ducts, which was retrospectively reported to be similar to the ultrasonic appearance of other extranodal lymphoma. Whether or not such a specific diagnosis can be made with certainty simply based on the ultrasonic findings remains to be verified. Also preoperative or intraoperative pathological diagnosis of NHL involving EHBD is also difficult because the biopsy specimen obtained from common bile duct wall often revealed severe infiltration of mononuclear inflammatory cells and some degree of fibrosis, although some cases revealed neoplastic lymphoid cell infiltration.<sup>5,6,9)</sup>

Because primary extranodal NHL differs from metastatic involvement of nodal NHL in therapeutic regimens and prognosis, the differential diagnosis of both extranodal lymphomatous involvement is important. The diagnosis of primary NHL of the common bile duct was based on the segmental, intramural, or transmural lymphomatous involvement of the common bile duct without evidence of NHL in the lymph nodes, liver, spleen, bone marrow, or other organs. Thirteen of fifteen cases reported previously seem to fulfill this requirement.<sup>5-7,9,11-16)</sup> The remaining two cases revealed lymphomatous involvement in the bone marrow and cerebrospinal fluid<sup>8)</sup> or in liver.<sup>10)</sup> However, when NHL was demonstrated in both the common bile duct and the adjacent lymph nodes as in the present case, the diagnosis of primary common bile duct NHL might be questioned. In the present case, four lymph nodes were replaced by NHL (3 periductal and 1 peripancreatic). The periductal lymph node was the largest and practically replaced by NHL with mild extracapsular extension; it was separated from the adjacent lymphomatous common bile duct by fibrous tissue. No lymph nodes were enlarged at other sites on CT. In primary gastrointestinal (GI) lymphoma positive mesenteric lymph nodes are regarded as localized metastases when they occur at the time diagnosis and do not invalidate a diagnosis of primary GI lymphoma.<sup>18)</sup> The segmental,

transmural lymphomatous involvement of the common bile duct and the drainage of lymph from common bile duct to the periductal lymph nodes,<sup>19)</sup> and regional nodal involvement of GI lymphoma support NHL originated in the common bile duct and spread to the adjacent lymph nodes.

Pathologically, segmental stenosis of the common bile duct is the common dominator due to transmural infiltration by a diffuse form of NHL in all cases except for one which exhibited a nodular form.<sup>11)</sup> The present case showed a nodular form of NHL. In contrast to GI lymphoma which usually reveals MALT-type lymphoma, various types of NHL were represented and only one MALT-type lymphoma.<sup>16)</sup> Among those with known phenotype, seven cases, including the present case, showed B-cell phenotype<sup>9,10,13,14,16)</sup>, two manifested T-cell phenotype.<sup>12,15)</sup> T-cell lymphoma appeared to be somewhat unusual compared with primary GI lymphoma, which is mostly B-cell lymphoma.

Although the common bile duct NHL appears to be a rapidly progressive disease, the prognosis of the patients suffering this disease usually depends on the therapeutic modalities.<sup>14)</sup> Ten cases, including the present case, were follow-up. Four patients who underwent surgical resection of the common bile duct lymphoma and received chemotherapy and/or radiation therapy shortly after surgery were well and alive 4 years, 6 months, 13 months, and three months, respectively, after surgery.<sup>10,11,14)</sup> However, four cases among six patients who underwent only surgery or chemotherapy were died during follow-up period from 4 months to 16 months.<sup>6,9,12)</sup>

In summary, the common bile duct NHL is extremely rare, but an aggressive neoplasm and recurs and spreads widely within 6 months after initial diagnosis by surgical exploration, if no additional chemotherapy and/or radiation therapy. The radiation therapy may be effective in a very limited disease. Surgical exploration is important in establishing the diagnosis, in removal of the lymphomatous mass, or in alleviating obstructive jaundice. When the bile

duct NHL is not resectable, surgical exploration with biopsy is needed in avoiding the potential complication of treatment-induced biliary failure, and bile duct NHL showed more response to other therapeutic modalities than biliary duct carcinomas. The analysis of the reported cases and the present case suggests that complete surgical resection of the bile duct lymphoma followed by sequential chemotherapy with CHOP regimen appears to be an effective therapeutic modality, although a long-term follow-up is needed.

## CONCLUSION

A very rare primary lymphoma of the common bile duct was experienced. This case clinically showed obstructive jaundice due to CBD stricture and pathologically was non-Hodgkin's lymphoma of follicular cell type of B-cell lineage, with positivity for Bcl-2. The patient received postoperative chemotherapy according to the CHOP regimen, with no evidence of recurrence 3 months after the surgery.

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## 국문초록

림프절의 림프종은 주로 위장관이나 두경부에 발생하며, 총담관의 원발성 림프종의 보고는 매우 드물다. 지금까지 문헌에는 15 증례만이 보고되어 있다. 48세 남자 환자가 급성 폐쇄성 황달을 주소로 내원하였으며, 담관 촬영술에서 총담관의 협착이 관찰되었다. 병리학적으로 총담관의 벽은 전층이 B-세포 계통의 비호지킨성 여포성 림프종에 이환되어 있었고, 담관주위 및 췌장 주위 림프절도 전이성 림프종에 대치되어 있었다. 환자는 CHOP 요법에 따라 수술 후 항암치료를 받았다. 수술 후 약 3개월 동안 림프종 재발의 증거는 관찰되지 않았다. 본 증례를 포함하여 보고된 증례를 분석한 결과 간외담관의 림프종의 완전한 절제 및 뒤이은 항암요법이 좋은 예후와 연관이 있다고 생각된다.

**중심단어:** 총담관, 원발성 림프종