

# Primary biliary non-Hodgkin's lymphoma

## A case report

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### Abstract

**Rationale:** Primary biliary non-Hodgkin's lymphoma (PBNHL) is a rare disease with only 41 cases reported since 1982. The incidence of PBNHL in patients with malignant cholangiocarcinoma was 0.6%, and PBNHL accounted for 0.4% of extranodal non-Hodgkin's lymphoma, and only 0.016% of all non-Hodgkin's lymphoma cases.

**Patient concerns:** We present a rare case of PBNHL in a 59-year-old female who had jaundice for 3 days with weight loss and Epstein-Barr virus infection. Initial computed tomography and magnetic resonance imaging showed diffuse thickening wall of bile ducts with corresponding lumen stenosis, blurred fat space around the portal vein, lymphadenopathy, and a normal spleen. These manifestations and images were similar to hilar cholangiocarcinoma. So, the diagnosis of hilar cholangiocarcinoma was initially considered.

**Diagnoses:** Postoperative pathology confirmed the final diagnosis was PBNHL.

**Interventions:** The patient and her family requested to clarify the histologic diagnosis by laparotomy biopsy. Because the biopsy result could not be defined during operation, then right hemihepatectomy and choledochojejunostomy were performed. She did not receive any antitumor treatment.

**Outcomes:** One month after the patient's first examination, both computed tomography and magnetic resonance images showed diminished stenosis of common bile duct and left hepatic duct, but a new mass in segment IV of liver was observed. Unfortunately, the patient died due to disease progression.

**Lessons:** This case reminds us that although PBNHL is rare, making accurate diagnosis difficult preoperatively, PBNHL should be considered when encountering a case with Epstein-Barr virus infection and those typical imaging findings.

**Abbreviations:** IAC = immunoglobulin G4-associated cholangitis, LDH = lactate dehydrogenase, PBNHL = primary biliary non-Hodgkin's lymphoma.

**Keywords:** biliary tract, case report, cholangiocarcinoma, cholangitis, non-Hodgkin's lymphoma

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The Ethics Committees approved this case report of the First Affiliated Hospital of Chongqing Medical University (Chongqing, China).

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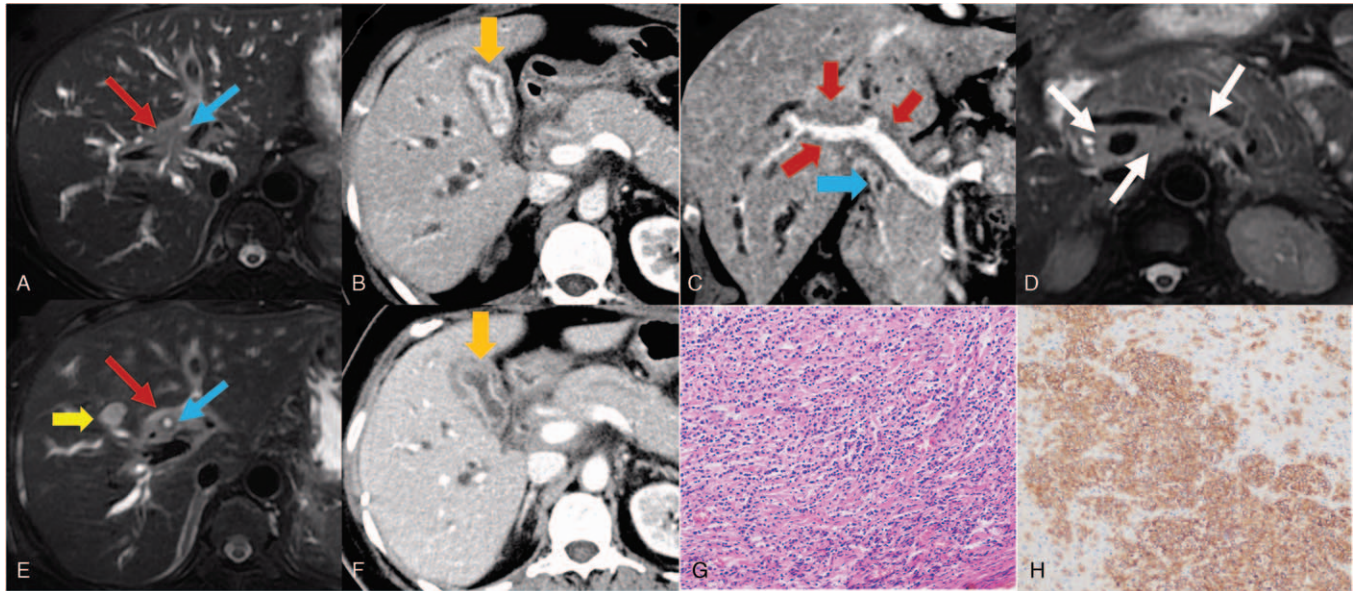
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## 1. Introduction

Primary biliary non-Hodgkin's lymphoma (PBNHL) is a rare disease with only 41 cases reported since 1982.<sup>[1]</sup> In 2007, Odemiş et al<sup>[2]</sup> reported that the incidence of PBNHL in patients with malignant cholangiocarcinoma was 0.6%, and PBNHL accounted for 0.4% of extranodal non-Hodgkin's lymphoma and only 0.016% of all non-Hodgkin's lymphoma cases. Hepatitis B virus, hepatitis C virus, human immunodeficiency virus Epstein-Barr virus infection, elevated lactate dehydrogenase (LDH), or low immunity are associated with the development of PBNHL.<sup>[3–5]</sup> This paper reports a case of PBNHL that appeared like hilar cholangiocarcinoma.

## 2. Case presentation

A 59-year-old woman was admitted to our hospital with a 3-day history of jaundice associated with generalized itching, pale stools, and dark urine. There was no history of nausea or vomiting. Oil aversion, anorexia, abdominal pain, or fever was also absent. History of weight loss was present which was about 5 kg in the past 3 months. Past medical history was unremarkable. Laboratory tests showed elevated total bilirubin, direct bilirubin, alkaline phosphatase, and LDH. Routine blood tests were regular. Immunoglobulin M antibody to Epstein-Barr virus (EBV-IgM) was positive. Immune-related laboratory tests



**Figure 1.** A 55-year-old woman with pathology confirmed primary hepatobiliary lymphoma. A–D, The initial abdominal images of the patient. A, Axial T2-weighted MRI showed intermediate homogeneous intensity mass surrounding the hilar bile duct (red arrow) with dilated intrahepatic ducts. B, Axial contrast-enhanced CT demonstrated thickening gallbladder wall with marked enhancement (yellow arrow). C, Coronal reconstruction contrast-enhanced CT showed blurred fat space around the portal vein and hepatic artery in hepatic hilum without lumen stenosis (red arrow). And the diffuse thickening wall of CBD was noted (blue arrow). D, Axial T2-weighted MRI showed lymphadenopathy (white arrows) around the celiac trunk and portal vein. Figures E and F were the following-up images 1 month later without any antitumor therapy. E, Axial T2-weighted MRI showed that the common hepatic duct diminished in stenosis than the initial image (blue arrow), but a new parenchyma lesion was observed (yellow arrow). F, Axial contrast-enhanced CT demonstrated a thinner gallbladder wall (yellow arrow) and enlarged cavity. G, HE staining showed medium-large lymphoid cell infiltration in the gallbladder wall. H, The tumor cell membranes were positive for CD20. CBD = common bile duct, CT = computed tomography, HE = hematoxylin-eosin, MRI = magnetic resonance imaging.

revealed immunoglobulin G4 level was average. Tumor marker showed elevated carbohydrate antigen 19–9 (CA 19–9) and normal alpha-fetoprotein and carcinoembryonic antigen.

Initial computed tomography (CT) and magnetic resonance imaging images showed diffuse thickening wall of bile ducts (including common bile duct, common hepatic duct, and intrahepatic ducts) with corresponding lumen stenosis and blurred fat space around portal vein. Thickening of the gallbladder wall was also noted. All of these lesions above exhibited significantly diffusion restricted and moderately homogeneous enhancement. Lymphadenopathy was found around the celiac trunk and its branches. The spleen was normal (Fig. 1 A–D). One month after the patient's first examination, without any antitumor treatment, both computed tomography and magnetic resonance imaging images showed diminished stenosis of common bile duct and left hepatic duct, but a new mass in segment IV of liver was observed (Fig. 1 E, F).

The diagnosis of hilar cholangiocarcinoma was first considered because it was combined with elevated tumor marker CA19–9 and images showing gallstones with cholecystitis.

One month later, the patient and her family requested to clarify the histologic diagnosis by laparotomy biopsy. Because the biopsy result could not be defined during operation, then right hemihepatectomy and choledochojejunostomy were performed. During the operation, significant contracture of the first porta hepatis, thickening of the hepatoduodenal ligament and the wall of the right hepatic duct, stenosis of the right posterior bile duct was observed. Moreover, lymphadenopathy at the portal vein, antrum, and proper hepatic artery could be found. The postoperative pathology report showed atypical cells in group

8 of the lymph nodes were observed. Furthermore, the surgical margin was negative. The immunohistochemistry of bile duct tissue suggested that FOXP1 (80%), Ki-67 (70%), Bcl-6 (60%), MUM-1 (70%), c-myc (3%), CD38 Kappa, CD43, CD20, and CD79a were positive, and Lambda and Bcl-2 were negative (Fig. 1 G). So, the final pathologic diagnosis was diffuse large B-cell lymphoma, stage IV. Unfortunately, the patient died 2 months later after the operation due to disease progression. Important milestones related to the diagnoses and interventions are listed in Figure 2.

### 3. Discussion

PBNHL is a rare type of diffuse large B-cell lymphoma. Clinical manifestations are jaundice, epigastric pain, fever, weight loss, and abdominal mass. Biliary obstruction is a sign of poor prognosis.<sup>[2,6]</sup> Imaging features of PBNHL reported so far are very limited, and mainly include diffuse space-occupying lesions or irregular thickening of the bile duct, mild biliary stricture, and secondary biliary dilatation.<sup>[2,7,8]</sup> The diagnosis of lymphoma is mainly based on histopathology, immunohistochemistry, combined with clinical data and imaging findings. Positron emission tomography-computed tomography can be used to determine the extent of tumor invasion.<sup>[9]</sup> However, clinicians may misdiagnose PBNHL as cholangiocarcinoma or immunoglobulin G4-associated cholangitis (IAC).

IAC patients have elevated serum and bile immunoglobulin G4 levels with the imaging feature of homogeneous progressive enhancement of the symmetric thickening wall (including the stenotic area and nonstenotic area). The most common location

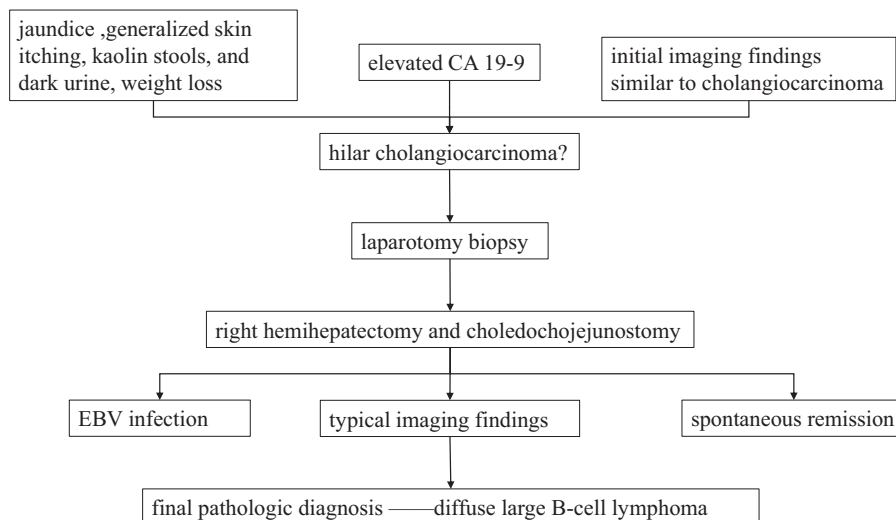


Figure 2. Important milestones related to the diagnoses and interventions.

of IAC is inferior portion of the common bile duct. IAC is frequently accompanied by pancreatic inflammation.<sup>[10,11]</sup> Cholangiocarcinoma presents that the tumor marker CA19-9 increases significantly, and the extent of lesion is more localized, and bile duct stenosis is severe and stiff. The biliary stricture in lymphoma is softer than cholangiocarcinoma. The patient without any antitumor treatment, the imaging showed relief of some biliary strictures, which has been reported in lymphoma, but it has not been reported in cholangiocarcinoma.<sup>[12-14]</sup>

However, establishing the diagnosis of PBNHL can be challenging by relying only on imaging and clinical manifestations. Even for biopsy, the results are often misdiagnosed as chronic nonspecific inflammation and other malignant tumors. So, surgery is inevitable to obtain enough tissue and achieve an accurate diagnosis.<sup>[15,16]</sup> At the same time, due to the rarity of PBNHL, unified treatment plan is uncertain. But it is believed that once the diagnosis is confirmed, chemotherapy is the basic and necessary treatment. Immunochemotherapy with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone or similar regimens is generally used.<sup>[7,17]</sup> And if biliary obstruction occurs, the biliary diversion is required.<sup>[2]</sup> Radiotherapy has been used in some patients and can be used for patients with residual disease after primary chemotherapy, or to relieve pain. However, whether radiation therapy is an essential treatment remains to be further studied because of the rarity of the disease.<sup>[16,18]</sup> Besides PBNHL also lacks studies to definite prognosis. The overall survival can be less than 1 year due to disease progression caused by adverse effects of surgery or the lack of chemotherapy.<sup>[1,19]</sup>

#### 4. Conclusion

Although it is difficult to diagnose PBNHL preoperatively, diagnosis of PBNHL should be considered when the bile duct is diffusely thickened without stenosis and the surrounding fat space is blurred. At the same time, factors such as infection with Epstein-Barr virus, elevated LDH, typical imaging findings, and spontaneous remission of the patient's condition are more suggestive of this disease.

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#### Author contributions

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