A CASE REPORT

# Diffuse Large B-cell Lymphoma Presenting with Obstructive Jaundice from a Biliary Stricture: A Case Report and Review of Literature

by Mark S. Friedman, Ishwaria M. Subbiah, Geeta Arora, Gregg Brodsky, Vinay Sood

**Diffuse large B cell lymphoma (DLBCL) is the most common histologic subtype of Non-Hodgkin's lymphoma (NHL), accounting for approximately twenty five percent of cases. Forty percent of patients with DLBCL present with the primary lesion in an extranodal site. The gastrointestinal tract is the most frequent site of extranodal lymphoma, with the stomach and intestines most often involved. Involvement of the pancreas by NHL has been reported infrequently, and rarely does DLBCL present as obstructive jaundice from a biliary stricture or a pancreatic mass. The following report describes an unusual case of DLBCL of the pancreas presenting as obstructive jaundice from a biliary stricture.**

## INTRODUCTION

Diffuse large B cell lymphoma (DLBCL) is the most common histologic subtype of Non-Hodgkin's lymphoma (NHL), accounting for approximately twenty five percent of cases (1). As with most other NHLs, DLBCL has a male predominance, and the incidence increases with age; the median age at presentation is 64 (3). Patients with DLBCL commonly present with rapid swelling of a lymph node in the neck, axillae, or groin. Systemic 'B' symptoms, such as fever, night sweats, or unexplained weight loss of greater than 10 percent of body weight six months prior to diagnosis, are also common presenting features.

About 40% of DLBCL cases present with the primary lesion in an extranodal site. The gastrointestinal tract is the most frequent site of extranodal lymphoma, with the stomach and intestines most often involved (2). Gastrointestinal lymphomas typically present with nonspecific signs and symptoms attributable to the site of involvement. The most prominent symptoms, independent of site of disease, include abdominal pain, loss of appetite, weight loss, vomiting, and night sweats (4). Rarely, DLBCL presents as obstructive jaundice from a biliary stricture or a pancreatic mass. Based on the literature, a primary DLBCL in the head of the pancreas producing a biliary stricture and obstructive jaundice has only been reported 3 times.

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## CASE REPORT

A 34-year-old woman presented to the emergency room with one month of progressive right upper quadrant (RUQ) abdominal pain and one week of jaundice. Upon review of systems, the patient also reported dark urine and light brown stools. She denied any fevers, chills,

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pruritis, nausea, vomiting, or weight loss. The patient had no known medical problems and took no medication, including herbal supplements or acetaminophen. She denied any alcohol, tobacco, or drug use. She did have one tattoo that she received at age 19 from a "reliable source." Her family history was remarkable for two grandparents with colon cancer; there was no family history of liver or gallbladder disease.

Physical examination was significant for scleral icterus and jaundice of the skin. There was tenderness to deep palpation of the right upper quadrant of the abdomen. Liver and spleen span were within normal limits. Notable laboratory values were a total bilirubin of 6.3 (normal: 0.1–1.2 mg/dl), a direct bilirubin of 3.8 (normal: 0.0–0.3 mg/dl), an alkaline phosphatase (AP) of 317 (normal: 30–115 U/L), an AST of 86 (normal: 5–45 U/L), and an ALT of 159 (normal: 560 U/L). A viral hepatitis panel was drawn and was subsequently negative. RUQ ultrasound showed intrahepatic and extrahepatic ductal dilatation. The common bile duct (CBD) measured 1.3 cm, without pancreatic ductal dilatation. Endoscopic retrograde cholangiopancreatography (ERCP) was performed and a 4 cm biliary stricture was seen in distal third of the bile duct. Proximal to that, the upper third and middle third of the main bile duct was locally dilated. The largest diameter was 10 mm (Figure 1). A 10-mm biliary sphincterotomy was made and the biliary tree was swept with a balloon. Sludge was found, and dilation of the CBD stricture with the 6 mm balloon was performed. Cells for cytology were obtained by brushing the CBD stricture. A single 7 Fr by 7 cm biliary stent was placed into the bile duct and bile flow through the stent was observed.

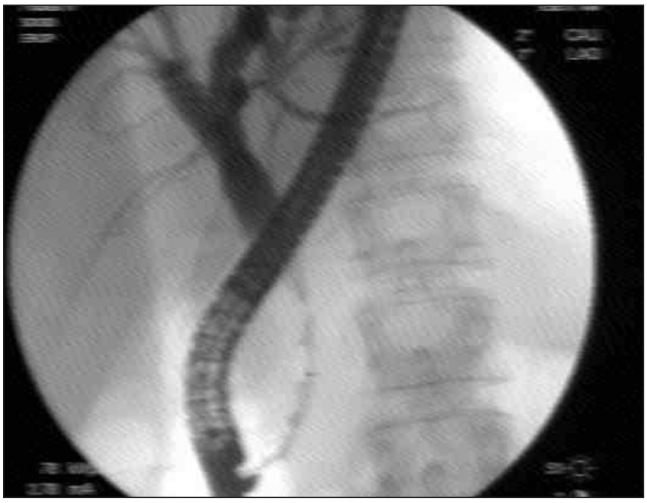

**Figure 1.** ERCP showing a dilated distal and middle bile duct. The proximal duct is narrowed.

Magnetic resonance cholangiopancreatography (MRCP) was performed after the procedure and noted a 3.5 cm mid-distal CBD stricture with extrahepatic and intrahepatic biliary dilatation. No focal masses or enlarged lymph nodes were identified. Over the course of the next week, the patient's RUQ pain dissipated and her total bilirubin decreased to 2.6. CBD brushings from the ERCP showed a hypocellular specimen consisting of rare benign ductal cells and bile. A CA19-9 drawn during the hospital stay was 8.

One week later, the patient presents to clinic reporting passage of the biliary stent in her stool, low-grade fevers, and generalized malaise and fatigue. There was no obvious recurrence of jaundice, and no change in the color of her urine or stools. However, there was concern for a recurrent biliary obstruction. Repeat laboratory values revealed a total bilirubin of 1.7, direct bilirubin of 0.8, AP of 551, AST of 188 and ALT of 179. ERCP was repeated, and the middle third of the main bile duct and upper third of the main bile duct were moderately dilated. The lower third of the main bile duct contained a single localized stenosis 4 cm in length. Dilation of the CBD stricture with the 8 mm balloon was successful. The stricture was biopsied with a cold forceps for histology. Cells for cytology were again obtained by brushing the CBD stricture. A single 10 Fr by 7 cm biliary stent was placed 7 cm into the bile duct with bile flow through the stent noted. Pathology of the CBD brushings showed mild atypical change, and the CBD biopsy showed fragments of benign fibrous tissue and glandular epithelium.

One month later, the patient presented to the emergency room again with abdominal pain, nausea, darkened urine and an 8 lb weight loss over the last week. On physical exam, the patient had mild midepigastric tenderness but no scleral icterus or jaundice. Laboratory data was remarkable for an amylase of 150 IU/L and a lipase of 254 IU/L, total bilirubin was 0.8, direct bilirubin was 0.2, AP was 110, AST was 25, and ALT was 20. An abdominal ultrasound showed two focal hypoechoic pancreatic lesions, the largest in the pan-

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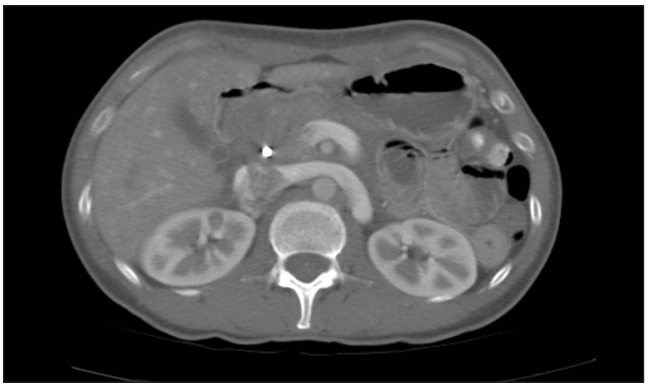

**Figure 2.** CT scan of the abdomen/pelvis showed interval development of a focal 3.3 × 2.5 cm pancreatic lesion with external duodenal displacement and mild pancreatic duct dilatation.

creatic head measuring 3.5 cm in diameter. Mild pancreatic duct dilatation and a common bile duct stent were also seen. A follow up computed tomography (CT) scan of the abdomen/pelvis showed interval development of a focal 3.3 × 2.5 cm pancreatic lesion with external duodenal displacement and mild pancreatic duct dilatation (Figure 2). Also seen was a right adrenal mass and left lower lobe lung mass; there was no bulky intra or retroperitoneal lymphadenopathy.

Endoscopic ultrasound (EUS) was performed. A 32 mm by 28 mm round, heterogeneous and hypoechoic mass was identified in the pancreatic head (Figure 3); fine needle aspiration (FNA) was performed. There was also an extrinsic deformity in the second part of the duodenum which was biopsied. FNA showed atypical large cells with high nuclear to cytoplasmic ratio, irregular nuclear membranes/cleaves, coarse chromatin, and frequent mitotic figures, suspicious for large cell lymphoma. Duodenal biopsy showed diffuse large B-cell lymphoma involving the small bowel. Cells from both samplings were strongly positive for BCL-6 and negative for BCL-2, CD10, CD30 and MUM-1. CD45 stain confirmed the hematolymphoid nature of the malignant infiltrate. CD20 confirmed the B-cell lineage of the malignancy. A bone marrow biopsy showed no evidence of marrow involvement. The patient was started on induction chemotherapy with rituximab and CHOP, (cyclophosphamide, doxorubicin, vincristine, and prednisolone) and is now in clinical remission.

## DISCUSSION

This is an unusual case of diffuse large B cell lymphoma presenting as obstructive jaundice from a biliary stricture. This case is also atypical because initial CBD brushings and abdominal imaging were negative for any malignancy or lesions. However, within 8 weeks, the lymphoma had progressed to a 3.5 cm lesion with extension into the duodenum. Non-Hodgkin's Lymphoma is rarely considered in the differential diagnosis for patients presenting with obstructive jaundice as only 1–2% of adults with NHL have been shown to have biliary obstruction due to their malignancy. Of those cases, the cause is commonly secondary to the direct compression of the ducts by the enlarged hepatic hilar and periportal lymph nodes (5). A review of the literature revealed only 3 cases in which a primary DLBCL in the head of the pancreas caused a biliary stricture and obstructive jaundice.

Malignant lymphoma infrequently involves the pancreas, accounting for less than 1% of NHL cases and between 0.2–4.9% of all pancreatic tumors (6, 7). The presenting symptoms of pancreatic lymphoma are usually non-specific and include abdominal pain (83%), abdominal mass (58%), weight loss (50%), jaundice (37%), acute pancreatitis (12%), small bowel obstruction (12%) and diarrhea (12%) (8). More commonly seen gastrointestinal sites of DLBCL are the stomach, duodenum, ileo-cecal region, and rectum (9,10). These patients typically present with a variety of symptoms including watery diarrhea and severe weight loss (7).

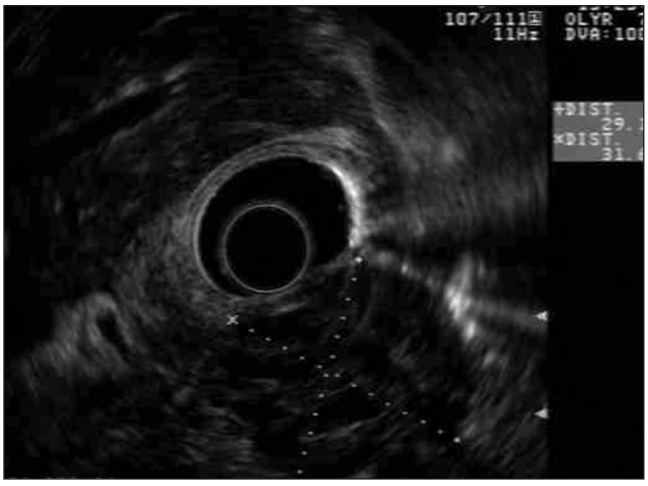

**Figure 3.**

Imaging plays an important role in the diagnosis and staging of pancreatic masses. This is particularly true for pancreatic lymphoma, as treatment and prognosis are significantly different from those for pancreatic adenocarcinoma (8). CT scan is the modality commonly used for the detection of pancreatic lymphoma. Ultrasound- or CT-guided fine needle biopsy of the pancreatic mass can also help distinguish pancreatic lymphoma from pancreatic adenocarcinoma (8). Definitively diagnosing primary pancreatic lymphoma without a tissue diagnosis is difficult since the clinical signs and symptoms are remarkably similar to those of pancreatic ductal adenocarcinoma.

Regardless of the presenting symptoms, the cornerstone of DLBCL treatment remains chemotherapy with or without radiotherapy. In order to determine the appropriate management direction, the International Prognostic Index (IPI) is used to select the appropriate therapeutic approach. In a trial of 294 DLBCL patients treated with a median of 6 cycles of CHOP chemotherapy with or without involved-field radiotherapy, lower IPI scores (0–2) correlated with improved outcomes in five-year progression-free survival, cause-specific survival, and overall survival rates (11). Our patient's IPI score places her in the high-intermediate risk group on account of her Ann Arbor stage III, >1 site of extranodal involvement (primary pancreas lesion with extension into duodenum), and an elevated serum lactate dehydrogenase level (LDH = 256 [normal = 90–225]) (12). A 2002 phase III study compared elderly patients managed with CHOP alone to those treated with CHOP plus rituximab, a chimeric monoclonal antibody against the CD20 B-cell antigen (13). The CHOP plus rituximab group demonstrated a higher rate of complete response than the group receiving CHOP alone (76 percent vs. 63 percent, P = 0.005). Also noted was a significant increase in the overall survival times and a decrease in treatment failure and death (13). Accordingly, our patient was treated with neoadjuvant CHOP plus rituximab.

The role of surgery in the management of DLBCL is evolving. About 40% of DLBCL patients present with localized disease that can be contained in one radiation field (14). With the advent of the ERCP, obstructive lesions are being increasing managed with biliary balloon dilatation and stenting rather than a radical procedure to resect the mass. Additionally the exuberant response of the tumor to the first line chemotherapy regimen makes surgery a less necessary option. In conclusion, although rare, DLBCL should be considered within the differential with patients that present with obstructive jaundice with a biliary stricture. ■

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