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CASE REPORT | BILIARY

Disseminated Histoplasmosis Presenting as Obstructive Jaundice

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ABSTRACT

Gastrointestinal manifestations in systemic fungal infection are not uncommon; however, obstructive jaundice due to lymphadenopathy is considered rare. We present a case of a 16-year-old male patient who presented with painless jaundice. Laboratory tests revealed direct hyperbilirubinemia with cholestatic liver injury. Chest and abdominal computed tomography showed mediastinal and porta hepatis lymphadenopathy, with severe biliary ductal dilatation proximal to an obstructing lymph node near the head of the pancreas. Endoscopic ultrasound showed a 22 × 35-mm lymph node with a mass effect on the common bile duct leading to obstructive jaundice. Infectious workup confirmed the diagnosis of disseminated histoplasmosis.

KEYWORDS: histoplasmosis; obstructive jaundice; lymphadenopathy; endoscopic ultrasound; ERCP

INTRODUCTION

Histoplasmosis is one of the common fungal infections that can present with gastrointestinal (GI) manifestations in the disseminated form of the infection.[1] Severe manifestations of histoplasmosis are often seen in immunocompromised patients, whereas most of the immunocompetent patients can be asymptomatic with a self-limiting infection.[2] The GI manifestations of disseminated histoplasmosis (DH) include luminal (ulceration, polyps, masses, colitis, and perforation) and extraluminal involvement (hepatomegaly, splenomegaly, lymphadenopathy, or pancreatic involvement).[1,3–5] It is rare for biliary obstruction to be the presenting manifestation of DH. We present a case of a 16-year-old immunocompetent patient with obstructive jaundice as the only manifestation of DH due to large lymphadenopathy obstructing the biliary tract.

CASE REPORT

A 16-year-old male patient presented to the emergency department with a 2-week history of jaundice that was progressively getting worse with uptrending liver enzymes. He had no previous medical conditions or chronic illnesses. Three weeks before presentation, he experienced nonbloody diarrhea and dark urine color, followed by jaundice without abdominal pain. There was no fever, chills, nausea, vomiting, decreased appetite, chest pain, cough, or shortness of breath. He also reported some fatigue and malaise.

On examination, diffuse jaundice was noticed. There was no pallor, palpable lymph nodes, hepatomegaly, or splenomegaly. There were direct hyperbilirubinemia and elevated liver enzymes (Table 1). Chest and abdominal computed tomography (CT) with contrast showed multiple pulmonary nodules, multiple splenic lesions, and a mass near the head of the pancreas with severe intrahepatic and extrahepatic biliary ductal dilatation. No pancreatic duct dilatation was seen on the CT scan.

Endoscopic ultrasound (EUS) revealed that the mass seen on the CT is an enlarged 22 × 35-mm lymph node near the head of the pancreas causing external compression on the common bile duct (CBD) with dilatation up to 21 mm (Figures 1 and 2). There were minimal pancreatic parenchymal changes with a normal pancreatic duct with a 2 mm diameter. Fine needle aspiration (FNA) of this lymph node near the pancreatic head was performed using a 22-gauge needle. Endoscopic retrograde cholangiopancreatography showed a single moderate biliary stricture in the lower third of the CBD with significant CBD dilatation; therefore, a sphincterotomy was performed and a

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Table 1. Laboratory test results at presentation and follow-up

	On presentation	After 2 days (after ERCP)	After 4 wks	After 5 mo (stent removal)
White blood count ($10^3/\mu L$)	13.4	19.4	8.8	7.5
Hemoglobin (g/dL)	13.4	12.1	14.0	14.3
Platelets ($10^3/\mu L$)	535	427	319	226
ALT (U/L)	360	215	30	17
AST (U/L)	260	104	29	16
Total bilirubin (mg/dL)	16.9	8.6	1.3	0.3
ALP (U/L)	1,366	1,105	205	126
Lipase (U/L)	286			11
CRP (mg/dL)	1.8		<0.5	

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transferase; CRP, C-reactive protein; ERCP, endoscopic retrograde cholangiopancreatography.

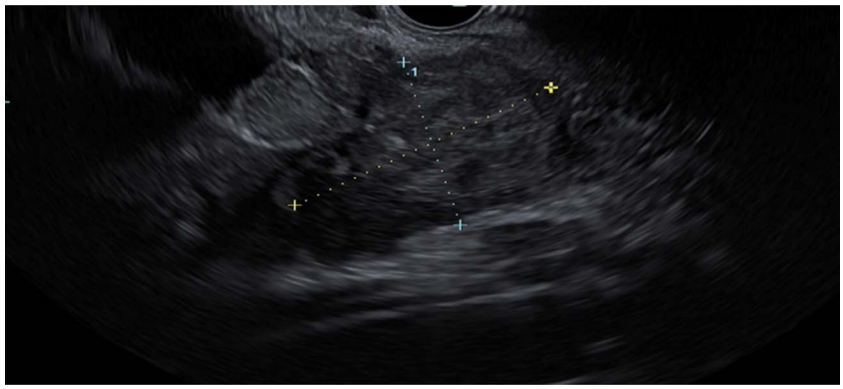

Figure 1. Endoscopic ultrasound of the large lymph node near the head of the pancreas causing biliary obstruction.

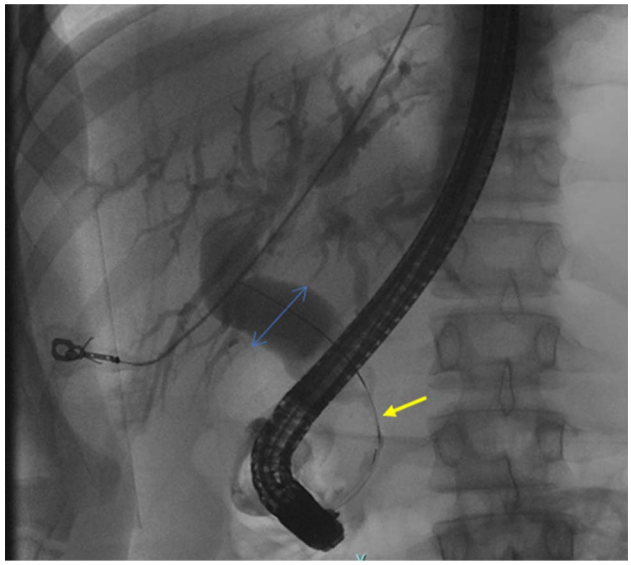

Figure 2. Fluoroscopic image from the endoscopic retrograde cholangiopancreatography showing the stricture (yellow arrow) and the dilated common bile duct (blue arrow).

plastic stent was placed across the stricture. FNA results showed acute granulomatous inflammation with hemorrhage and necrosis, but no organisms were identified on Grocott methenamine silver and acid-fast bacilli stains. An extensive infectious workup revealed positive histoplasmosis total antibodies (Table 2). The genomic testing (*Karius* test) was positive for *Aspergillus chevalieri*. The patient was treated with itraconazole to cover histoplasmosis and aspergillosis. After biliary drainage, the liver enzymes and bilirubin normalized (Table 1). The workup for immunodeficiency was unremarkable (Table 2). At 8 weeks follow-up, his liver enzymes remained normal, and there was improvement of the lymph node size, but they were still enlarged so the stent was exchanged. Two months later, abdominal CT showed improvement in the lymph nodes' size suggestive of treatment response. Endoscopic retrograde cholangiopancreatography showed marked improvement of the stricture and thus the stent was removed (Figure 3). The patient did well after the procedure without any recurrence of the symptoms or elevation of the liver enzymes.

DISCUSSION

Histoplasma capsulatum is a dimorphic fungus that causes histoplasmosis and is typically found in soil that contains bird

Table 2. Infectious and immunological workup

Bartonella henselae IgM/IgG	Negative
Bartonella henselae blood PCR	Negative
Blastomyces dermatitidis ID and CF	Negative
Coccidioides antibodies by CF	Negative
Chlamydia psittaci IgM/IgG	Negative
Gastrointestinal pathogen panel (stool)	Negative
Histoplasma antibodies CF (mycelia)	1:16
Histoplasma antibodies ID (yeast)	1:64
Genomic testing (Karius testing)	Positive for *Aspergillus chevalieri*, *Bacteroides fragilis* (*ovatus* and *uniformis*)
Mycoplasma pneumoniae IgM/IgG	Negative/positive
PPD test	0 mm after 48 h
QuantiFERON test	Negative
Serum IgG (mg/dL)	1,131 (normal)
Serum IgM (mg/dL)	64 (normal)
Serum IgA (mg/dL)	408 (high)
Serum IgE (kU/L)	9 (normal)
Total complement (CH50)	>60 (normal)
Neutrophil oxidative burst assay	Normal activity
Mannose-binding lectin	172 (normal)
Th17 enumeration	Normal

CF, complement fixation; ID, immunodiffusion; Ig, immunoglobulin; PPD, purified protein derivative; PCR, polymerase chain reaction.

or bat droppings. Histoplasmosis is considered an endemic in the Mississippi and Ohio valley areas but not limited to these areas.[6] In the past, the belief was that histoplasmosis causes severe infection only in immunocompromised patients, but emerging studies showed that immunocompetent patients can be affected as well and can have the disseminated form of the infection.[1,7] Histoplasmosis has a wide variety of presentations including GI manifestations from the disseminated disease or organ-specific involvement of the infection. In our case, the patient presented with obstructive jaundice as the only symptom for DH.

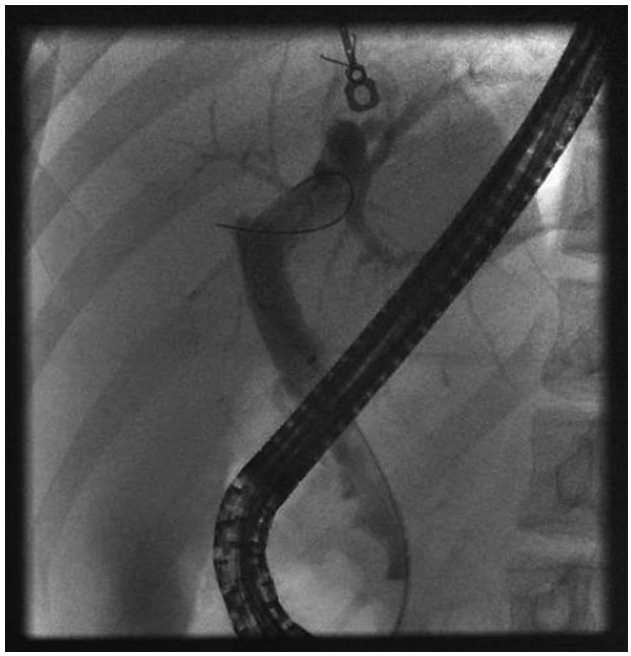

Figure 3. Fluoroscopic image from the endoscopic retrograde cholangiopancreatography after the patient received treatment showing improvement in the distal common bile duct dilatation.

GI manifestations of DH have a wide variety based on the severity of the infection and the organ involved. We divided these manifestations to luminal and extra luminal manifestations.

The main luminal manifestations include:

1. mucosal ulceration throughout the GI tract which can present as GI bleeding,[8,9]
2. polyps or mass-like lesions mimicking malignancy,[5,10]
3. colitis mimicking inflammatory bowel disease,[11] and
4. perforation.[12,13]

The main extraluminal GI manifestations can include:

1. hepatic involvement that can range from mild elevation of liver enzymes to acute liver failure,[14,15]
2. gallbladder involvement presenting as cholecystitis,[16,17] and
3. pancreas involvement can range from pancreatitis to mimicking a pancreatic mass,[3,18]

Lymphadenopathy is considered a common manifestation of histoplasmosis. Histoplasmosis-associated lymphadenopathy can be seen in acute or chronic histoplasmosis including DH. In rare cases, isolated lymphadenopathy can be the only presenting symptom.[19] Sampling by biopsy or FNA could be essential for the diagnosis.[20] However, culture sensitivities are variable in patients based on the disease involvement; therefore, non-invasive testing is the primary tool used in diagnosing histoplasmosis.[21] To the best of our knowledge, there are no cases reported on histoplasmosis-associated lymphadenopathy causing obstructive jaundice by mass effect on the common bile duct. EUS is an essential tool to establish the diagnosis in such cases; in our case, the lesion was believed to be a pancreatic head mass; however, EUS was essential to rule that out, which assisted in reaching the diagnosis of histoplasmosis-associated lymphadenopathy.

The treatment of histoplasmosis consists of systemic antifungal, with itraconazole considered the treatment of choice in mild to moderate disease.[22] The genomic test came back positive for aspergillosis, but the suspicion was low for that based on the patient's clinical presentation, and a treatment with itraconazole should cover for both pathogens. Fortunately, after treatment and decompression of the bile duct with biliary stent, the patient continued to improve, and he tolerated itraconazole well without any complications. Patients could require prolonged treatment, and the resolution of the lymphadenopathy could take time such as in our case which was around 5 months.[23]

In conclusion, this is the first case reported on disseminated histoplasmosis-associated lymphadenopathy presenting as obstructive jaundice. EUS is a safe and valuable tool to help rule out other etiologies and assist in establishing the diagnosis. Treatment with antifungal is effective, but resolution of the lymphadenopathy could take time.

DISCLOSURES

Author contributions: L. Numan reviewed literature, wrote, edited, and revised the manuscript. W. Hayajneh edited and revised the manuscript and provided intellectual input. W. Kiwan provided the endoscopic images, edited, and revised the manuscript, provided intellectual input, and is the article guarantor.

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