Unusual Case of Mirizzi Syndrome Presenting as Painless Jaundice

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Patient: Male, 60-year-old
Final Diagnosis: Mirizzi syndrome
Symptoms: Dark stools • jaundice • painless jaundice
Medication: —
Clinical Procedure: ERCP with stent placement • spyglass cholangioscopy
Specialty: Gastroenterology and Hepatology

Objective: Unusual clinical course
Background: Isolated painless jaundice is an uncommon presenting sign for Mirizzi syndrome, which is typically characterized by symptoms of acute or chronic cholecystitis. We report a rare case of Mirizzi syndrome with an acute onset of painless obstructive jaundice.

Case Report: A 60-year-old man with an unremarkable prior medical history presented with 1 week of jaundice, dark urine, and acholic stools. His laboratory studies revealed a pattern of cholestasis with marked direct hyperbilirubinemia. Ultrasound and magnetic resonance imaging studies demonstrated intrahepatic ductal dilation and cholelithiasis, including a stone within the cystic duct. Endoscopic retrograde cholangiopancreatography with SpyGlass cholangioscopy confirmed the diagnosis of Mirizzi syndrome.

Conclusions: An atypical presentation of Mirizzi syndrome should be suspected in the setting of biliary obstruction without pain. The differential diagnosis is broad and includes choledocholithiasis, ascending cholangitis, and hepatobiliary malignancy. Evaluation should include laboratory studies and biliary tract imaging. Noninvasive biliary tract imaging can help exclude malignancy and confirm ductal dilation but is not sensitive for Mirizzi syndrome. Endoscopic retrograde cholangiopancreatography can serve both diagnostic as well as therapeutic purposes via stone extraction and stent placement. SpyGlass cholangioscopy can also augment management in the form of Electrohydraulic lithotripsy. Although therapeutic biliary endoscopy can be very effective, cholecystectomy remains the definitive treatment for Mirizzi syndrome.

Keywords: Cholangiopancreatography, Endoscopic Retrograde • Cholestasis • Endosonography • Jaundice, Obstructive • Lithotripsy • Mirizzi Syndrome

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Background

Mirizzi syndrome (MS) is a rare complication of gallstones, affecting approximately 0.1% of the 20 million people afflicted with cholelithiasis in the United States [1]. It is defined by obstruction of the hepatic duct due to external compression from a gallstone impacted within the cystic duct or gallbladder infundibulum [1]. Patients typically present with characteristic clinical findings of biliary colic or cholecystitis, such as abdominal pain, as well as signs of obstructive jaundice [2]. We present a case of MS with an atypical presentation, in which a patient without a prior history of symptomatic gallstones presented with acute onset of painless jaundice.

Case Report

A 60-year-old man with no significant prior medical history presented to the Emergency Department with 1 week of painless jaundice and dark brown urine. The patient reported associated acholic stools and generalized pruritus for 3 days. He denied any abdominal pain, nausea, vomiting, fevers, or weight loss. His medical history included a negative colonoscopy 2 years prior. He endorsed smoking marijuana daily, having a 10 pack-year history of tobacco use, and drinking 12 cans of beer a week.

The physical examination revealed scleral icterus and full-body jaundice. The patient’s abdomen was nondistended without shifting dullness, was nontender, and had no appreciable organomegaly. No skin lesions, including palmar erythema or spider angiomas, were visualized. Laboratory values showed transaminitis (aspartate aminotransferase of 85 IU/L [reference range, 0-37 U/mL]; alpha fetoprotein and carcinoembryonic antigen were within normal limits. Urinalysis showed 3+ bilirubin, confirming the suspected bilirubinuria. Abdominal ultrasound showed cholelithiasis with intra- and extrahepatic biliary duct dilation. The patient was admitted for further evaluation.

Serum total bilirubin increased overnight to 26.1 mg/dL. An abdominal computed tomography (CT) scan, with and without intravenous contrast, was obtained, showing intra- and extrahepatic biliary dilatation and gallbladder wall thickening. This was followed by magnetic resonance cholangiopancreatography, which demonstrated moderate intrahepatic ductal dilation and cholelithiasis without dilation of the common bile duct (Figure 1). Owing to concern for malignancy, the decision was made to proceed with endoscopic ultrasound, which confirmed intrahepatic ductal dilation without common bile duct dilation; there were no pancreatic, liver, or ductal lesions and thus no biopsies were taken. Endoscopic retrograde cholangiopancreatography (ERCP) revealed a stone impacted within the cystic duct and dilation of the intrahepatic ducts upstream from the area of impaction, which confirmed a diagnosis of MS (Figure 2). A 10-French by 9-cm plastic biliary stent was placed, with resultant good bile flow (Figure 3).

The patient’s serum bilirubin trended down over the course of 2 days following stent placement but remained within an abnormal range. This raised concern for a proximal intraductal mass, such as cholangiocarcinoma, and a need for further characterization of the cystic duct calculus, which prompted a second ERCP in conjunction with SpyGlass cholangioscopy (Boston Scientific). Following removal of the stent using forceps, the cholangioscope was advanced to the intrahepatic bifurcation, which revealed no abnormality (Figure 4).

Table 1. Trends of inpatient laboratory studies throughout admission.

| Hospital day | Total bilirubin (mg/dL) | Direct bilirubin (mg/dL) | AST (IU/L) | ALT (U/L) | Alkaline phosphatase (U/L) |
|--------------|-------------------------|-------------------------|------------|-----------|---------------------------|
| 0            | 22.2                    | 16.5                    | 85         | 184       | 433                       |
| 1 (ERCP #1)  | 26.1                    | –                       | 71         | 156       | 438                       |
| 2            | 25.7                    | –                       | 52         | 119       | 383                       |
| 3            | 16.5                    | –                       | 39         | 84        | 295                       |
| 4 (ERCP #2)  | 15.0                    | –                       | 45         | 90        | 306                       |
| 5            | 14.7                    | –                       | 47         | 83        | 306                       |

ALT – alanine aminotransferase; AST – aspartate aminotransferase; ERCP – endoscopic retrograde cholangiopancreatography.

* All laboratory values exceeded institutional upper limits of normal.
The catheter was slowly withdrawn while the duct was irrigated with normal saline. Following cannulation of the cystic duct, the cholangioscope was advanced toward the gallbladder neck. A large cholelith was directly visualized at the junction of the gallbladder neck and cystic duct, with no evidence of fistula; no features suggestive of malignancy were identified in the biliary tree.

General Surgery was consulted for surgical evaluation. However, the patient expressed his wishes for early discharge and outpatient follow-up. Given his down-trending serum bilirubin levels and clinical stability, he agreed to be evaluated for cholecystectomy in the outpatient setting. The patient presented for his outpatient appointment with General Surgery but left before discussing the plan of care with the surgeon, opting against any surgical treatment at that time. Unfortunately, the patient did not return for follow-up and could not be evaluated further.

**Discussion**

MS is a rare complication of symptomatic cholelithiasis. It has an annual incidence of less than 1%, which increases to 2.7% in patients with a history of cholelithiasis, and up to 25% among patients undergoing gallbladder resection [1,3-6]. There may be a slight propensity for females and older populations [5,7,8],
but recent studies have shown no male or female predilection [2]. Over 25% of all patients diagnosed with MS are at risk for gallbladder cancer [9,10].

The pathogenesis of MS results from an impacted gallbladder calculus at the cystic duct or infundibulum [9,11]. Gallstone impaction leads to compression of adjacent biliary structures and extrinsic post-hepatic obstruction. A chronic, local inflammatory response can precipitate erosion into the ductal wall and lead to the formation of a fistula [9]. MS is classified into type I, defined as external compression of the bile duct by an impacted stone, and type II through V, which all have some degree of erosion into the common bile duct wall as well as fistulous formation between the gallbladder and adjacent structures (Table 2) [12,13].

MS typically presents with abdominal pain and jaundice, with pain being the most reported feature [2,6,14]. Other associated signs or symptoms include fever, nausea, vomiting, anorexia, and weight loss [2,6]. Patients can demonstrate signs of obstructive jaundice such as dark-colored urine and acholic stools [15,16]. A small subset of patients presents asymptomatically [6].

Our case represents a rare presentation of MS with acute painless jaundice. Reports of MS presenting as painless jaundice have been seldom described in the literature and often include other associated symptoms such as weight loss and fatigue, which were absent in this case [17-20]. Our patient’s presentation with signs of painless biliary obstruction is unusual, as patients with MS characteristically present with acute abdominal pain or a history of previous episodes of biliary colic [1].

The differential diagnosis for painless jaundice should raise clinical suspicion for malignancy, namely cholangiocarcinoma, an adenocarcinoma of the pancreas or gallbladder. In our

Table 2. Classification, descriptions and management of Mirizzi syndrome subtypes.

| Type I | Type II | Type III | Type IV | Type V |
|--------|---------|----------|---------|--------|
| Description | Impacted stone at cystic duct or gallbladder neck | Stone erodes <1/3 of anterior or lateral CBD wall | Fistula eroding 1/3 to 2/3 of CBD circumference | Fistula completely involves/obliterates CBD wall | Cholecystoenteric fistula + any type + gallstone ileus |
| Cholecystobiliary fistula presence | No | Yes | Yes | Yes | Yes and no |
| Management | Partial or total cholecystectomy; CBD exploration not typically required | Cholecystectomy plus fistula closure (suture, T-tube or choledochoplasty) | Choledochoplasty or bilioenteric anastomosis depending on fistula | Bilioenteric anastomosis (typically choledocho-jejunostomy) | Cholecystectomy with excision of fistula |

CBD – common bile duct.
case, the absence of abdominal pain or fever decreased our suspicion for benign biliary diseases, such as cholelithiasis and ascending cholangitis. Inherited causes of hyperbilirubinemia should be considered after excluding life-threatening etiologies.

An initial evaluation of nonspecific symptoms of jaundice includes laboratory studies to discern between hepatocellular and cholestatic processes: liver enzyme panels and serum conjugated bilirubin levels [2]. Further workup of liver function should include serum levels of albumin, bilirubin, and prothrombin/international normalized ratio. CA 19-9 levels can be considered if there is concern for malignancy, although elevations have been reported in a few cases of MS, as in ours [17,19,21].

Ultrasonography is routinely performed for workup of acute cholecystitis, and CT scanning can aid in the diagnosis of malignancy; however, both lack sensitivity for MS (48% and 42-50%, respectively) [2,6]. Magnetic resonance cholangiopancreatography is more sensitive and can facilitate the identification of post-hepatic obstruction [2]. ERCP is highly accurate in diagnosing MS and offers potential therapeutic roles in the form of endoscopic retrograde cholangiopancreatography (ERCP) and stone extraction, and stent placement [1,9,22]. Over half of patients are diagnosed with MS intraoperatively, regardless of preoperative workup [9,10].

Direct cholangioscopy offers an alternative diagnostic modality in assessing for MS. In our patient, the SpyGlass direct visualization system, a single-use cholangioscope, allowed for direct visualization of the impacted gallstone at the gallbladder neck; this finding has been previously reported in the literature [23]. Use of cholangioscopy also offers a potential therapeutic advantage when used in conjunction with electrohydraulic lithotripsy to pulverize the impacted cholelith to relieve the obstruction [24-26].

**Conclusions**

A high index of suspicion for an atypical presentation of MS should be employed in the setting of painless biliary obstruction. Early identification can help prevent long-standing complications of MS, including the formation of fistulas. Noninvasive biliary tract imaging can help rule out an underlying malignant process but lacks the sensitivity to reliably identify MS. ERCP can serve both a diagnostic and therapeutic role in management. Cholangioscopy can serve to augment the diagnosis of MS as well as offer a potential therapeutic modality through electrohydraulic lithotripsy.

**Department and Institution Where Work Was Completed**

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**Declaration of Figures’ Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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