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Mirizzi Syndrome: A Rare but Relevant Biliary Entity

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CASE REPORT

A 64 year-old man presented to our facility with a one-day history of right upper quadrant pain, scleral icterus, and intermittent fever and chills. The patient's vital signs included a temperature of 97.8, a pulse of 71, a respiration rate of 14, and a blood pressure of 124/80. On physical exam, he was mildly uncomfortable with key physical exam findings of right upper quadrant abdominal pain to palpation and on deep inspiration, scleral icterus, and jaundice. An abdominal ultrasound demonstrated mild intrahepatic biliary ductal dilation with at least one stone visualized in the gallbladder. The wall of the gallbladder was found to be slightly thickened without pericholecystic fluid and the common bile duct was measured at 11mm. A contrast-enhanced CT of the abdomen and pelvis was obtained and revealed prominent intrahepatic ductal dilation and what was interpreted as choledocholithiasis. Notably, the common bile duct had more distension proximally near the stone and less distension distally. GI and surgery consultations were obtained. A plan of preoperative ERCP followed by laparoscopic cholecystectomy was agreed upon.

ERCP revealed intrahepatic ductal dilation and proximal extrahepatic ductal dilation. Initial cholangiogram revealed what appeared to be a single, round 30 mm filling defect consistent with a stone eccentrically obstructing at the level of the CHD (Figure 1). Immediately proximal to the stone, there was visible dilation of the left and right hepatic ducts as well as the intrahepatic ducts. An inflated 15-18mm occlusion balloon could be pulled across the site of the stone without any apparent movement of the stone itself. Of note, the cystic duct was never seen to fill and was presumed to be obstructed. At this point it became apparent that the stone was actually within the cystic duct and was extrinsically compressing the CBD, consistent with a Mirizzi syndrome. An 8.5Fr x 12cm

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plastic biliary stent was inserted into the CBD across the site of extrinsic compression, with the proximal end of the stent in the CHD. (Figure 2) The patient improved clinically over the next 24 hours following biliary decompression. The patient was then referred for his cholecystectomy.

At surgery, the gallbladder was noted to be inflamed and adherent to the CBD, with what appeared to be a cholecystocholedocho fistula between the two at the level of the gallbladder neck/proximal cystic duct. Opening of the gallbladder revealed the impacted stone at the level of the fistula, which was then removed. Cholecystectomy was then carried out with subsequent incision of the CHD and removal of the impacted stone. The CHD was felt to have been damaged too severely by the stone/fistula combination for simple T-tube placement. The patient then underwent biliary reconstruction via a Roux-en-Y hepaticojejunostomy, although the distal CBD was left in continuity. The plastic bile duct stent was left in as a guide during surgery. The patient did well postoperatively and without complication.

A follow-up ERCP 8 weeks later demonstrated brisk flow of contrast through the biliary tree as well as a patent hepaticojejunostomy with free flowing contrast and bile into the small bowel. No filling defects were noted, indicating an absence of any residual or recurrent stones. Overall, the patient was felt to have developed a Type IV Mirizzi syndrome.

DISCUSSION

In developed countries, the incidence of gallstone disease has been rising of late with the majority of cases involving cholesterol stones. In the U.S. alone, an estimated 20 – 25 million adults suffer from some form of gallstone disease. Epidemiological studies have found that gallstone disease correlates highly with obesity, diabetes and metabolic syndrome.[1] Though gallstones are understood to be multifactorial from an etiology point of view, one property these risk factors all share seems to be hypercholesterolemia: a condition that can allow supersaturation of bile by cholesterol with subsequent precipitation of gallstones.[1] Gallstones can lead to a variety of conditions including cholangitis, cholecystisis, gallstone pancreatitis, and even gallstone ileus.[2]

Mirizzi Syndrome (MS) is a rare complication of cholelithiasis.[3,4] Classically, the common hepatic duct (CHD) or the common bile duct (CBD) become

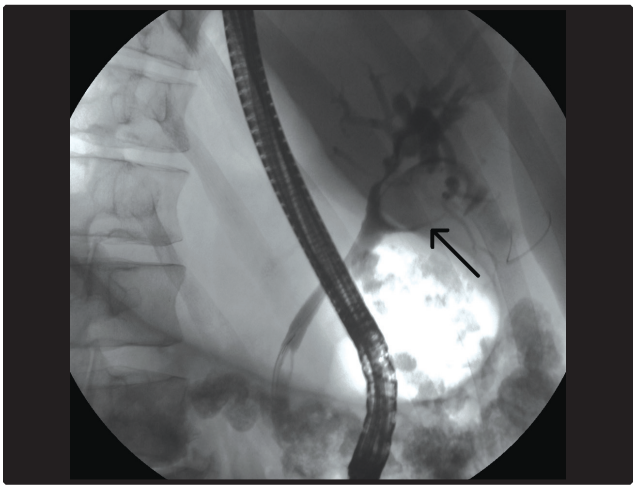

Figure 1. ERCP image of a large stone extrinsically compressing the CHD. (Arrow)

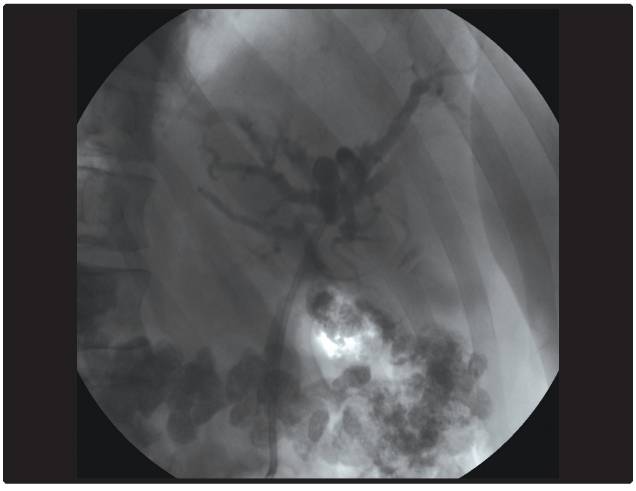

Figure 2. ERCP image of same patient following placement of a plastic biliary stent to decompress the biliary tree.

obstructed from mechanical compression and surrounding inflammation by gallstone impaction at either the cystic duct or the gallbladder neck.[2,5] Compression by the impacted stone results in biliary obstruction which can then cause obstructive jaundice and in some patients also lead to cholangitis. [4,6] From there, this process has the potential to further evolve into an internal biliary fistula, or even complete obliteration of the CHD.[3]

Overall, the incidence of Mirizzi Syndrome is rare, discovered only in 0.7 – 1.4% of patients undergoing cholecystectomy.[7] Management has historically been difficult due to the inadequacy of pre-operative diagnosis as well as the surgical challenge it presents given the

presence of active inflammation, dense adhesions, and distorted biliary ductal anatomy.[5,8]

The term Mirizzi Syndrome refers to a collection of four subtypes of the disease commonly acknowledged as the Csendes Classification model.[9] Type I is the most dominant form of MS and is characterized by extrinsic compression of the CBD due to an impacted stone at the cystic duct or the gallbladder neck.[4,10] Types II, III and IV all include cholecystocholedochal fistulas.[11] Type II describes a fistula where 1/3 of the CBD circumferential wall has eroded.[4,9] Type III refers to a larger fistula with erosion of 2/3 of the circumferential wall of the CBD.[4,9] Finally, Type IV denotes a fistula that has caused circumferential damage to the CBD and thus requires reconstruction of the CBD.[4,9]

Pathophysiology

Mirizzi Syndrome begins when a gallstone becomes impacted at the cystic duct or gallbladder neck and causes an inflammatory response. The offending stone then applies external pressure on the bile duct, eventually leading to erosion of the CBD with possible fistulization.[12]

Once this situation is established, episodes of biliary colic cause fibrosis and gallbladder atrophy.[12,13] Ongoing inflammation and proximity allow the gallbladder and/or the cystic duct and/or the CBD to fuse together.[12] An impacted gallstone at this location likely causes a pressure ulcer which then develops necrosis. The necrotic tissue can enable partial stone migration into the CBD and ultimately the production of a chronic fistula.[12] Such cholecystocholedocal fistulas are the hallmark of Type II, III and IV Mirizzi Syndrome, but they are still exceedingly rare. In fact, most biliary fistulas are actually cholecystoduodenal, joining the gallbladder to the small bowel.[11] Despite advanced imaging, most fistulas are found intra-operatively during cholecystectomy.[4,11]

Clinical Presentation

Mirizzi Syndrome is difficult to diagnose clinically because of its non-specific symptom profile.[5,6] Because MS resembles several other conditions, its differential diagnosis includes choledocholithiasis, cholecystitis, cholangitis, gallstone ileus, and gallbladder cancer.[5,11,12,14] Clinical presentation is non-specific, but obstructive jaundice is a common symptom – especially for types II, III and IV.[4] RUQ pain is also frequently seen, along with a fever. Laboratory values often reflect elevated liver enzymes, hyperbilirubinemia, leukocytosis, and a high CA-19-9.[12]

A reported 28% of MS types II, III and IV cases also have also been found to have concurrent gallbladder cancer.[11,12] Notably, longstanding gallstones is one of the primary risk factors for both MS and gallbladder cancer.[12] Average age of onset for MS is around 61 years.[9] Most MS patients have had gallstone disease for a mean of 29 years.[12]

Diagnosis

Lack of pathognomonic patterns or reliable clinical or laboratory indicators have made the diagnosis of MS difficult to distinguish from common choledocholithiasis.[5,15] Optimal management of MS and avoidance of iatrogenic bile duct injury during cholecystectomy depends on accurate preoperative diagnosis, although this cannot be made in all circumstances.[10] Several modalities are available for biliary imaging including transabdominal ultrasound, CT, MRCP, endoscopic ultrasound (EUS) and ERCP.[12] Transabdominal ultrasound (US) is typically the initial imaging test ordered for suspected biliary disease because it is non-invasive, although it's ability to detect choledocholithiasis is limited and the test is highly operator dependent.[2] US has high sensitivity to findings consistent with MS such as gallstones in the gallbladder neck, acute cholecystitis, a shrunken gallbladder and a dilated CHD.[10] CT scans have the capacity to demonstrate dilated intra and extrahepatic ducts with gallstones in the biliary tree, but in general are a poor test to detect MS or choledocholithiasis.[5] EUS is ideal for detecting choledocholithiasis but may fail to detect MS if the stone is located too proximally for the EUS transducer to visualize.[16] MRCP (Magnetic Resonance Cholangiopancreotography) is noninvasive and has a high sensitivity for finding pericholicystic inflammation and cholecystobiliary fistulas.[11] However, ERCP (Endoscopic Retrograde Cholangiopancreotography) is the gold standard for diagnosis of MS.[9] The sensitivity of ERCP for diagnosis of MS approaches 90%.[11,12] ERCP is both diagnostic and therapeutic.[11] Diagnostically, ERCP identifies ductal abnormalities and can distinguish with precision the cause, level and degree of biliary obstruction.[10] Therapeutically, ERCP is used for stone clearance if the stone is endoscopically accessible.[8] It also facilitates biliary decompression prior to cholecystectomy in patients with MS via

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stent placement, as was the case in our patient.[6,8] If a preoperative diagnosis of MS is not obtained, most experienced surgeons would recognize the entity in the operating room.

Treatment

The goals of treating patients with MS include: removal of the impacted stone and gallbladder, restoration of bile drainage and repair of the anatomical defect.[6,11] Preoperative ERCP can confirm the presence of MS.[9] It also allows for placement of a temporary stent – providing critical decompression of the obstructed biliary duct.[12] Such decompression alleviates progression of any fistulas.[14] Moreover, the stent will serve as a landmark in subsequent surgery to help minimize the risk of ductal injury.[4] Preoperative ERCP is also a viable alternative for patients who are not candidates for open cholecystectomy (OC).[12]

Removal of the gallbladder and the impacted stone along with repair of the malformed anatomy is performed laparoscopically or by open surgery. OC has historically been the surgical standard of care for MS.[4] However, LC is fast gaining acceptance as a viable alternative to OC.[6,11] The main advantage conferred by OC is a lower risk of iatrogenic bile duct injury than LC.[14] This is large part due to the feasibility of a fundus first approach enabled by OC.[17] Morbidity from OC has been reported to be 3% for MS type I. However, OC performed on types II and III correlate with a higher morbidity rate (15 – 26%) due to more complicated anatomical deformities.[4] The biggest risk associated with OC is iatrogenic injury to the CBD.[5] Such risk stems from the technical challenge presented by anatomical distortions, cholecystocholedocal fistulas, and adhesions in Calot's triangle encountered in MS patients undergoing OC.[4,5] Disadvantages of OC include a larger incision which provides a higher risk of infection and wound dehiscence.[8] Additionally, OC entails a longer recovery.[6]

Laparoscopic Cholecystectomy (LC) for treatment of MS has been somewhat controversial.[10] Indeed, some surgeons still consider MS as a contraindication to laparoscopic cholecystectomy.[4,6,9] Nonetheless, LC has become a viable alternative to OC as experience and enhanced instruments continue to improve outcomes with this procedure.[6] LC involves removal of the gallbladder, the impacted stone and suturing the biliary defect.[8] Its advantages are that it is minimally invasive and by extension entails a lower risk of infection, produces less blood loss, and offers a shorter hospital stay.[8] Some disadvantages are that it is technically demanding, requires a high degree of expert skill and thus a longer duration for the procedure.[8]

In general, LC is indicated for the less complicated MS as in Type I. Open surgery is indicated for higher risk cases of MS, difficult dissections (due to anatomical malformations or acute inflammation), and patients who have failed LC.[8] In some cases, higher grades of MS: Type II, III and IV, may require open biliary-enteric bypass to repair extensive destruction of the bile ducts or strictures.[11] Such complete biliary reconstruction is termed a Roux-en-Y hepatico-jejunostomy and involves anastomosis of the jejunum with the fistula to close the eroded duct.[18] Lastly, postoperative ERCP after complete healing of the site removes the temporary stent.[8] The incidence of iatrogenic complications is reported to range between 0 – 14%.[3] Such adverse events can be severe and include cholangitis, bile leakage from perforation of the CBD or perforation of the gallbladder, bile duct strictures from fistula repair, post-ERCP pancreatitis, and sepsis.[3] Regardless of the intervention, a high risk of morbidity exists with treatment of MS.[9]

CONCLUSION

Mirizzi Syndrome is a rare clinical entity that presents a formidable challenge when encountered. The constellation of a contracted gallbladder, obstructive jaundice, gallstones, pain and cholecystitis should arouse suspicion of MS. A preoperative diagnosis is critical to optimal management and is best confirmed by cholangiography during ERCP, although not all patients have the diagnosis made prior to interventions. Once a definitive diagnosis of MS is made, a multidisciplinary team approach including a skilled endoscopist and surgeon offers the best outcome. Treatment for each patient must be individualized, as specific MS types necessitate distinct surgical approaches. Preoperative ERCP with stenting can restore bile flow and mitigate cholangitis, thus enhancing safety of subsequent surgery. ■

References

1. Shaffer EA. Gallstone disease: Epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol. 2006;20(6):981-96. Review. PubMed PMID: 17127183.

2. Wong CS, Al-Ajami AK, Crotty JM, Naqvi SA. Benign biliary stricture and its rare association-Mirizzi syndrome: A case series and literature review. International Journal of Case Reports and Images 2012;3(10):1–7.
3. Bassi M, Muratori R, Larocca A, Cennamo V. Gallbladder endoscopic drainage plus extracorporeal shock wave lithotripsy for Mirizzi syndrome type I complicated by acute cholecystitis. Dig Liver Dis. 2014 Oct;46(10):961-2. doi: 10.1016/j.dld.2014.06.001. Epub 2014 Jul 5. PubMed PMID: 25008144.
4. Tung KL, Tang CN, Lai EC, Yang GP, Chan OC, Li MK. Robot-assisted laparoscopic approach of management for Mirizzi syndrome. Surg Laparosc Endosc Percutan Tech. 2013 Feb;23(1):e17-21. doi: 10.1097/SLE.0b013e3182724f9f. PubMed PMID: 23386165.
5. Xu XQ, Hong T, Li BL, Liu W, He XD, Zheng CJ. Mirizzi syndrome: our experience with 27 cases in PUMC Hospital. Chin Med Sci J. 2013 Sep;28(3):172-7. PubMed PMID: 24074620.
6. Li B, Li X, Zhou WC, He MY, Meng WB, Zhang L, Li YM. Effect of endoscopic retrograde cholangiopancreatography combined with laparoscopy and choledochoscopy on the treatment of Mirizzi syndrome. Chin Med J (Engl). 2013;126(18):3515-8. PubMed PMID: 24034100.
7. Donatelli G, Dhumane P, Dallemagne B, Ludovic M, Delvaux M, Gay G, Marescuax J. Double-cannulation and large papillary balloon dilation: key to successful endoscopic treatment of mirizzi syndrome in low insertion of cystic duct. Dig Endosc. 2012 Nov;24(6):466-9. doi: 10.1111/j.1443-1661.2012.01312.x. PubMed PMID: 23078442.
8. Lee KF, Chong CN, Ma KW, Cheung E, Wong J, Cheung S, Lai P. A minimally invasive strategy for Mirizzi syndrome: the combined endoscopic and robotic approach. Surg Endosc. 2014 Sep;28(9):2690-4. doi: 10.1007/s00464-014-3529-3. Epub 2014 Apr 16. PubMed PMID: 24737533.
9. Zheng M, Cai W, Qin M. Combined laparoscopic and endoscopic treatment for Mirizzi syndrome. Hepatogastroenterology. 2011 Jul-Aug;58(109):1099-105. doi: 10.5754/hge11069. PubMed PMID: 21937357.
10. Cui Y, Liu Y, Li Z, Zhao E, Zhang H, Cui N. Appraisal of diagnosis and surgical approach for Mirizzi syndrome. ANZ J Surg. 2012 Oct;82(10):708-13. doi: 10.1111/j.1445-2197.2012.06149.x. Epub 2012 Aug 20. PubMed PMID: 22901276.
11. Shenoy S. Spontaneous internal biliary fistulas from gallstones: Mirizzi's syndrome, cholecystoenteric fistula, and gallstone ileus. Am Surg. 2014 Apr;80(4):409-11. PubMed PMID: 24887676.
12. Beltrán MA. Mirizzi syndrome: history, current knowledge and proposal of a simplified classification. World J Gastroenterol. 2012 Sep 14;18(34):4639-50. PubMed PMID: 23002333; PubMed Central PMCID: PMC3442202.
13. Zhong H, Gong JP. Mirizzi syndrome: experience in diagnosis and treatment of 25 cases. Am Surg. 2012 Jan;78(1):61-5. PubMed PMID: 22273316.
14. Kelly MD. Acute mirizzi syndrome. JSLS. 2009 Jan-Mar;13(1):104-9. PubMed PMID: 19366554; PubMed Central PMCID: PMC3015902.
15. Erben Y, Benavente-Chenhalls LA, Donohue JM, Que FG, Kendrick ML, Reid-Lombardo KM, Farnell MB, Nagorney DM. Diagnosis and treatment of Mirizzi syndrome: 23-year Mayo Clinic experience. J Am Coll Surg. 2011 Jul;213(1):114-9; discussion 120-1. doi: 10.1016/j.jamcollsurg.2011.03.008. Epub 2011 Apr 3. PubMed PMID: 21459630.
16. Verma D, Kapadia A, Eisen GM, Adler DG. EUS vs MRCP for detection of choledocholithiasis. Gastrointest Endosc. 2006 Aug;64(2):248-54. Review. PubMed PMID: 16860077.
17. Ibrarullah M, Mishra T, Das AP. Mirizzi syndrome. Indian J Surg. 2008 Dec;70(6):281-7. doi: 10.1007/s12262-008-0084-y. Epub 2008 Dec 23. PubMed PMID: 23133085; PubMed Central PMCID: PMC3452351.
18. Trikudanathan G, Navaneethan U, Parsi MA. Endoscopic management of difficult common bile duct stones. World J Gastroenterol. 2013 Jan 14;19(2):165-73. doi: 10.3748/wjg.v19.i2.165. Review. PubMed PMID: 23345939; PubMed Central PMCID: PMC3547556.

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