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Cholelithiasis Secondary to Mirizzi Syndrome: An Overview

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Abstrcat

Mirizzi syndrome (MS) is a relatively rare condition, accounting for a small percentage of biliary disorders. Even though this complication of cholelithiasis has a low prevalence, its morbidity rates, reflecting the overall burden of the disease, have been reported to range from 10% to 50%. This narrative review aims to provide a comprehensive overview of this rare but potentially complex condition, including its epidemiology, pathophysiology, clinical presentation, diagnosis, and treatment options. Surgical options for MS include open surgical procedures and minimally invasive approaches. Laparotomy, despite its more invasive nature, high complication rate, and extended postoperative hospital stay, has been considered the technique of choice, mainly due to its relative safety compared with the laparoscopic technique, the advantage of better visualization, haptic feedback, and removal of gallbladder calculus before cholecystectomy. Subtotal cholecystectomy may be the best treatment for Mirizzi type I and most cases of type II and III. Recently, subtotal cholecystectomy has been described as laparoscopic cholecystectomy, following the exact technical details described for the open technique. Laparoscopic cholecystectomy in MS showed high conversion levels (31% to 100%), complication rates of zero to 60%, biliary damage rates of zero to 22%, and mortality ranging from zero to 25%. This modality is expected to become more secure with technical advances, new materials, and greater surgeon experience. However, the conventional approach is still the gold standard.

Keywords: Mirizzi syndrome; Gallstones; Cholecystitis; Treatment; Surgery; Laparoscopic cholecystectomy; Biliary tree

Abbreviations: MS: Mirizzi Syndrome; CT: Computed Tomography; MRCP: Magnetic Resonance Cholangiopancreatography; ERCP: Endoscopic Retrograde Cholangiopancreatography; CBD: Common Bile Duct; LFT: Liver Function Tests; ALT: Alanine Transaminase; AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; CBC: Complete Blood Count; CA 19-9: Carbohydrate Antigen 19-9; CEA: Carcinoembryonic Antigen; ESWL: Extracorporeal Shockwave Lithotripsy; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; EUS: Endoscopic Ultrasounds; LC: Laparoscopic Cholecystectomy

Introduction

Cholelithiasis is defined as the presence of gallstones within the gallbladder or bile ducts. When gallstones become impacted in the cystic duct or gallbladder neck, generating a compression of the common bile duct, and leading to obstruction and subsequent inflammation, the condition is known as Mirizzi syndrome [1,2]. This complication of cholelithiasis has a low prevalence, estimated to occur in approximately 1-2% of patients with gallstones. It is more commonly seen in women and individuals over the age of 60. Pathophysiology involves the mechanical obstruction of the common bile duct by a gallstone impacted in the cystic

duct or gallbladder neck. This obstruction leads to bile stasis, inflammation, and subsequent pressure effects on the adjacent biliary tree, resulting in symptoms and potential complications. The clinical presentation can vary but typically includes right upper quadrant abdominal pain, jaundice, and signs of cholangitis or biliary obstruction, such as fever and elevated liver function tests [3].

The diagnosis of Mirizzi syndrome involves a combination of clinical evaluation, imaging studies such as ultrasound, computed tomography (CT) scan, or magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP) to visualize the biliary tree and identify the site and extent of the obstruction [4,5]. The treatment typically involves a surgical intervention to relieve the obstruction, remove the impacted stone, and reconstruct the biliary anatomy if necessary [4,6,7]. In some cases, a two-stage procedure may involve an initial intervention to drain the bile duct and reduce inflammation, followed by a definitive surgical procedure to address the underlying pathology [8]. This narrative review aims to provide a comprehensive overview of this rare but potentially complex condition, including its epidemiology, pathophysiology, clinical presentation, diagnosis, and treatment options.

Epidemiology & Risk Factors

Mirizzi syndrome is a relatively rare condition, accounting for a small percentage of biliary disorders. The prevalence of Mirizzi syndrome varies across different populations and geographical regions, with reported rates ranging from 0.7% to 1.4% of all cholecystectomy cases [9]. Incidence data are limited but estimated to be less than 1% of all gallstone-related cases. Morbidity and mortality rates associated with this syndrome depend on various factors, including the severity of the condition, the presence of complications, and the promptness of diagnosis and management. Morbidity rates, reflecting the overall burden of the disease, have been reported to range from 10% to 50%. Complications such as bile duct strictures, biliary leaks, or fistulas can increase morbidity and may require surgical interventions. Mortality rates are relatively low but can occur due to complications or associated factors such as gallbladder cancer [10].

It's important to note that the epidemiology, prevalence, incidence, morbidity, and mortality rates of Mirizzi syndrome may vary among different studies and populations due to factors such as diagnostic challenges, regional variations, and differences in healthcare resources [9,10]. Several risk factors have been identified for developing Mirizzi syndrome. The most significant risk factor is the presence of gallstones, especially large or impacted stones in the cystic duct or gallbladder neck. Other risk factors include chronic cholecystitis, anatomical variations in the biliary system, such as a low cystic duct insertion, and the presence of a porcelain gallbladder (calcification of the gallbladder wall). Additionally, older age, female gender, and certain ethnic groups have been associated with an increased risk of developing Mirizzi syndrome [11,12].

Pathophysiology

Gallstones occur when substances in the bile reach their limits of solubility. As bile becomes concentrated in the gallbladder, it becomes supersaturated with these substances, precipitating into tiny crystals in time. These crystals, in turn, become stuck in the gallbladder mucus, resulting in gallbladder sludge [13]. The neck of the gallbladder is connected to the cystic duct, which empties into the common bile duct. Gallstones can get impacted in the neck of the gallbladder, causing inflammation with recurrent episodes of cholangitis and obstruction of the CBD. Chronic inflammation may lead to bile duct wall necrosis and erosion into the CBD, forming a cholecystobiliary fistula. In 1984 Csendes et al. [14] classified Mirizzi syndrome based on the presence and extent of a cholecystobiliary fistula, which was helpful in guiding surgical therapy. Type I: external compression of the common hepatic duct due to stone impacting at the neck or cystic duct. There is no fistula. 11% of individuals with Mirizzi syndrome. Type II: fistula involves less than 1/3 of the circumference of the CBD. 41% of individuals with Mirizzi syndrome. Type III: fistula between 1/3 to 2/3 of the circumference of the CBD. 44% of individuals with Mirizzi syndrome. Type IV: disruption of the entire CBD. 4% of individuals with Mirizzi syndrome.

Later in 1989, Csendes et al. classified type II Mirizzi syndrome into three subgroups (II, III, and IV), considering the entity of the involvement of the CBD. In type II of Csendes classification, the fistula involves 1/3 of the CBD circumference; in type III, it involves 2/3, and in type IV, the CBD is no longer recognizable and represents a whole entity with the gallbladder [15]. Multiple classifications of Mirizzi syndrome have been postulated; However, many authors continue to use the first classification of Csendes, which, by allowing a better distinction about the entity of the CBD wall involved in the fistula, could be useful to establish the right preoperative workup and surgical management [14].

Clinical Presentation

The presentation of Mirizzi syndrome is usually that of acute or chronic cholecystitis with the addition of jaundice. Patients with chronic cholecystitis usually present with dull right upper abdominal pain that radiates to the mid back or right scapular tip [16]. It is usually associated with fatty food ingestion. Nausea and occasional vomiting also accompany complaints of increased bloating and flatulence. Often the symptoms occur in the evening. Prolonged, less acute symptoms are usually present over weeks or months. Increased frequency and severity of acute exacerbations (acute biliary colic) are usually seen in the presence of more prolonged chronic symptoms [16].

The classic physical examination will demonstrate right upper abdominal pain with deep palpation (Murphy's sign). Patients

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are usually not acutely ill but are uncomfortable. Patients with advanced Mirizzi syndrome or more severe acute cholecystitis may present with more pronounced symptoms and findings. Jaundice is usually present, and significantly elevated bilirubin can sometimes be identified [17]. All three main symptoms are only present in 44 to 71 percent of patients. Pain is the most common presenting feature (54-100%), followed by jaundice (24-100%) and cholangitis (6-35%). Up to one-third of patients have acute cholecystitis on presentation and, in rare cases, acute pancreatitis [16].

Rapidly diagnosing Mirizzi syndrome is crucial to avoid potentially fatal complications because this condition can lead to severe complications that may endanger the patient's life. Prompt diagnosis allows for the timely initiation of appropriate treatment, which can help prevent further progression of the condition and reduce the risk of complications. Early intervention can also lead to better outcomes for the patient [18,19]. Mirizzi syndrome can lead to several complications, including cholecystitis, bile duct injury, biliary strictures, abscess formation, and even liver failure. Rapid diagnosis enables early intervention to prevent or manage these complications effectively. In conclusion, rapid detection of Mirizzi syndrome is essential for timely intervention, prevention of complications, and improved patient outcomes [20-22].

Diagnosis

The diagnosis of Mirizzi syndrome involves a combination of clinical evaluation, imaging studies, and differential diagnosis to differentiate it from other similar conditions. Several diagnostic tools are employed to confirm Mirizzi syndrome's presence and determine the obstruction's extent. One of the initial steps in diagnosing Mirizzi syndrome involves a thorough clinical evaluation [22,23]. The patient's medical history is reviewed to identify symptoms such as jaundice, right upper quadrant pain, fever, and weight loss. Physical examination may reveal tenderness in the upper abdomen or a palpable mass. However, clinical evaluation alone cannot definitively diagnose Mirizzi syndrome, and further diagnostic tools are required [23,24].

Laboratory tests are an essential component in the diagnostic workup of Mirizzi syndrome. While these findings alone cannot confirm the diagnosis of Mirizzi, they can provide supportive evidence and help evaluate the patient's overall health. Some commonly performed laboratory tests in Mirizzi syndrome include liver function tests (LFTs), which can indicate the presence of biliary obstruction or liver dysfunction. Parameters such as bilirubin levels, liver enzymes (e.g., ALT, AST), and alkaline phosphatase (ALP) are typically included in LFTs. Elevated levels of total bilirubin, especially direct (conjugated) bilirubin, can indicate biliary obstruction [24,25]. Liver enzymes may be elevated in cases of associated liver inflammation or injury. Elevated ALP levels are commonly seen in biliary obstruction, including Mirizzi syndrome. Moreover, a complete blood count (CBC) may show leukocytosis or thrombocytosis (i.e., platelets act as biomarkers of inflammation) [26]. Other tests, such as the carbohydrate antigen 19-9 (CA 19-9) or carcinoembryonic antigen (CEA), may be measured to rule out gallbladder malignancy as a differential. However, it's important to note that these tumor markers are not specific to Mirizzi syndrome [27]. It's important to note that laboratory findings in Mirizzi syndrome are non-specific and can overlap with other biliary pathologies. Therefore, a comprehensive evaluation combining clinical findings, imaging studies, and laboratory results is essential for accurate diagnosis and appropriate management [26,27].

Lastly, imaging studies play a crucial role in diagnosing Mirizzi syndrome. Ultrasonography is often the first-line imaging tool used to evaluate biliary pathologies. It helps identify gallstones, the presence of biliary dilation, and the level of obstruction. The US can also visualize the impacted stone in the cystic duct or gallbladder neck, providing critical diagnostic clues. Secondly, magnetic resonance Cholangiopancreatography (MRCP) is a non-invasive imaging technique that uses magnetic resonance to visualize the biliary system. It provides detailed images of the bile ducts and helps identify the level and extent of the obstruction caused by Mirizzi syndrome. MRI can demonstrate the dilatation of the intrahepatic bile ducts and the common bile duct proximal to the site of obstruction [23,28]. Also, MRCP can visualize the impacted gallstone in the cystic duct or gallbladder neck, causing compression and obstruction of the common hepatic duct or common bile duct. The stone may appear as a low-signal intensity structure on T2-weighted images and may show acoustic shadowing on other imaging sequences. In severe cases, the gallbladder may appear atrophic or contracted.

MRCP can help identify any associated complications of Mirizzi syndrome, such as biliary strictures, bile leaks, or fistulas. These complications may be visualized as irregularities, strictures in the bile ducts, or abnormal fluid collections in the surrounding area. Lastly, computed tomography (CT) scan may also be performed to assess the biliary system and adjacent structures. It can help identify the presence of gallstones, dilated bile ducts, and the compression of the common bile duct. CT scan provides detailed cross-sectional images that aid in the evaluation of the extent of the obstruction and any associated complications [25,29]. Differential diagnosis is crucial in distinguishing Mirizzi syndrome from other conditions that may present with similar symptoms. Conditions that should be considered in the differential diagnosis include gallstone-related diseases (acute cholecystitis, choledocholithiasis, or cholangitis, where gallstones cause inflammation or obstruction of the gallbladder or bile ducts), biliary strictures, and gallbladder cancer [25,26]. Imaging studies, such as CT scan or MRCP, can help differentiate between the two conditions.

Medical Treatment

Mirizzi syndrome is managed without well-developed, internationally recognized clinical guidelines. Furthermore, for patients with poor medical candidates for surgery, treatment

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presents a medical conundrum that revolves around alleviating the acute symptoms at presentation and maintaining long-term patency hepatobiliary tree [30]. Non-Surgical gallstone treatment options exist and can be considered based on the patient's clinical presentation [31]. Observation and dietary advice are recommended for asymptomatic gallstones to reduce the chances of recurrent episodes and improve patient outcomes [33]. Medical treatment with Urso deoxycholic acid may be considered for patients with small gallstones and high cholesterol. However, it is essential to note that achieving dissolution may take several months, and success rates are around 50%. Extracorporeal shockwave lithotripsy (ESWL) can be an option for non-calcified gallstones [32].

Antibiotic therapy plays a crucial role in the management of gallstones. Prompt administration of antibiotics is recommended in cases of acute cholecystitis with signs of sepsis, cholangitis, abscess, or perforation [33]. Additionally, antibiotics may be beneficial in reducing the incidence of wound infection in high-risk patients [31,33]. Pain control is a vital aspect of gallstone management. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the preferred choice for pain relief in acute biliary colic due to their effectiveness and fewer adverse effects than narcotic pain relievers (Surgical and Nonsurgical Management of Gallstones, 2014). In cases of severe pain, spasmolytics or nitroglycerin may be added to the pain management regimen [31]. Surgical intervention becomes necessary when nonsurgical approaches are insufficient or contraindicated [33,34].

Laparoscopic Treatment

Surgical options for Mirizzi syndrome include open surgical procedures and minimally invasive approaches. The choice of surgical technique depends on the severity of the condition, the extent of biliary obstruction, and the surgeon's expertise. Laparoscopic surgery for Mirizzi syndrome is a minimally invasive surgical procedure to treat this rare condition characterized by extrinsic compression of the common hepatic duct due to an impacted gallstone in the cystic duct or gallbladder neck. This compression leads to obstructive jaundice and can result in bile duct injury [34]. The laparoscopic approach offers several advantages over traditional open surgery, including reduced postoperative pain, shorter hospital stays, faster recovery, and improved cosmetic outcomes.

There are two main laparoscopic techniques commonly employed for the management of Mirizzi syndrome: the antegrade technique and the retrograde technique. The choice of technique depends on the extent of biliary obstruction and the surgeon's expertise. During the antegrade technique, the impacted gallstone or gallbladder is removed first in this approach. The common bile duct is explored and cleared of other stones or impacted material. Finally, a T-tube or a biliary stent may be placed to ensure adequate bile drainage. On the other hand, the retrograde technique involves clearing the biliary tree before removing the impacted gallstone or gallbladder. A cholangiography is performed to identify the anatomy and location of the obstruction. The gallbladder is dissected and removed once the bile duct is cleared of stones or impacted material. A choledochoplasty (enlargement of the common bile duct opening) may be necessary to ensure proper bile flow [35,36].

Indications for laparoscopic surgery in Mirizzi syndrome include symptomatic patients with obstructive jaundice, cholecystitis, or cholangitis. The procedure is also suitable for patients with favorable anatomy without extensive fibrosis or dense adhesions. Complications associated with laparoscopic surgery for Mirizzi syndrome can include bile duct injury, bleeding, bile leak, retained stones, infection, and conversion to open surgery. Diligent preoperative imaging and careful surgical technique can help reduce these risks. Some contraindications to laparoscopic surgery in Mirizzi syndrome include patients who are unsuitable candidates for general anesthesia or laparoscopy due to severe comorbidities, significant peritoneal adhesions, or extensive intra-abdominal malignancies [36].

Endoscopic Treatment

Endoscopic surgery is another suitable approach for Mirizzi syndrome. The primary goal is to relieve the bile duct obstruction caused by an impacted gallstone or extrinsic compression. Endoscopic procedures offer a less invasive approach than traditional open surgery, resulting in reduced postoperative morbidity, shorter hospital stays, and faster recovery. Two main endoscopic techniques are commonly employed for managing Mirizzi syndrome: endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound-guided interventions [37].

During an endoscopic retrograde cholangiopancreatography (ERCP), an endoscope is inserted into the bile duct, and contrast material is injected to visualize the biliary anatomy. Once the site of obstruction is identified, various therapeutic interventions can be performed, including sphincterotomy (cutting of the sphincter muscle to facilitate bile flow), balloon dilation of the bile duct, and stone extraction using baskets or balloons. On the other hand, ultrasound-guided interventions, or endoscopic ultrasounds (EUS) are used to visualize the bile ducts and surrounding structures with high-resolution imaging. It allows for more precise localization of the obstruction. EUS-guided interventions include gallbladder drainage, plastic or metal stents placement across the obstruction, and stone removal using specialized tools [38,39].

Endoscopic approaches are particularly suitable for patients with favorable anatomy, smaller stones, and less extensive fibrosis or adhesions. Complications associated with endoscopic surgery for Mirizzi syndrome may include pancreatitis, bleeding, perforation, infection, and bile duct injury. The risk of complications is generally lower than open surgery, but careful technique and experienced endoscopists are essential to minimize

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these risks [37,40]. Contraindications to endoscopic surgery may include significant comorbidities, uncorrectable coagulopathies, or anatomical factors that make endoscopic access challenging, such as altered gastrointestinal anatomy or extensive scarring [38,40].

Open Surgery

Laparotomy is usually chosen as the first-line treatment method in patients with Mirizzi syndrome. This usually involves total or partial cholecystectomy of the fundus and neck to repair compromised biliary structures. Due to the association with gallbladder carcinoma, all excised tissue should undergo a pathologic examination to rule out unsuspected carcinoma. The insertion of a T-tube or nasociliary decompression is usually done pre and postoperatively to prevent further biliary leaks, strictures, or the development of cholangitis [41].

Subtotal cholecystectomy may be the best treatment for Mirizzi type I and most cases of Mirizzi type II and III. Recently, subtotal cholecystectomy has been described as laparoscopic cholecystectomy, following the exact technical details described for the open technique. After identification of the anatomical repairs and having determined the presence of Mirizzi syndrome, the gallbladder is approached by an incision running from the fundus to the Hartmann's pouch, or if possible, in selected cases, directly over the Hartmann's pouch to remove the impacted gallstone. Surgery began laparoscopically twice; on both occasions, the intense inflammatory procedure prompted conversion [42,43].

The reflux of bile indicates the presence of a fistula between the gallbladder and the bile duct because the cystic duct is usually occluded. If no fistula is macroscopically evident or diagnosed by intraoperative cholangiography, a partial cholecystectomy leaving the gallbladder neck or infundibulum is performed, and the gallbladder stump is closed with absorbable monofilament sutures over the bile duct. However, it must be remembered that a classic cholecystectomy could sometimes be performed. If a fistula is present (Mirizzi III and IV), besides partial cholecystectomy, a biliary-enteric anastomosis could sometimes be performed between the duodenum and bile duct or between the bile duct and a loop of jejunum (Roux-en-Y gastric bypass) [42].

Work on laparoscopic cholecystectomy in MS shows high conversion levels (31% to 100%), complication rates of zero to 60%, biliary damage rates of zero to 22%, and mortality ranging from zero to 25%. With technical advances, new materials, and greater surgeon experiences, this modality may become more secure. However, the conventional approach is still the gold standard [43].

Laparotomy has been considered the technique of choice for managing Mirizzi Syndrome. This is mainly due to its relative safety compared with the laparoscopic technique, which is associated with high conversion rates (31-100%) and an increased incidence of bile duct injury. However, laparotomy has the advantage of better visualization, haptic feedback, and removal of gallbladder calculus before cholecystectomy despite its more invasive nature, high complication rate, and extended postoperative hospital stay. Patients with MS should be evaluated comprehensively based on MRI/MRCP. Open surgery or timely conversion to open surgery should be selected when preoperative evaluation or LC intraoperative exploration shows that laparoscopic surgery is unsuitable [44,45]. However, most surgeons do not recommend LC as a viable standard of treatment due to the increased risk of bile duct injury and a high conversion rate with this condition. Open surgery was still the favorite treatment modality, accounting for 40% to 100% of cases [44].

Conclusion

Mirizzi syndrome is characterized by the extrinsic compression of the common hepatic duct or common bile duct due to impacted gallstones in the cystic duct or neck of the gallbladder, leading to a series of clinical manifestations. It predominantly affects middle-aged females, although it can occur in any age group or gender. Although Mirissa syndrome is relatively uncommon, accounting for approximately 1-2% of all cases of cholecystitis, it may lead to potentially fatal complications if left untreated. The clinical presentation of Mirissa syndrome is diverse and can range from mild abdominal pain and jaundice to severe complications such as cholangitis, biliary fistula, or abscess formation. Due to the nonspecific symptoms, diagnosis can be challenging and requires a comprehensive evaluation, including clinical examination, laboratory tests, imaging studies (such as ultrasound, magnetic resonance cholangiopancreatography, or endoscopic retrograde cholangiopancreatography), and sometimes even exploratory surgery. Medical strategies are used in conjunction with surgical procedures to manage the condition.

Medical treatment primarily focuses on controlling infection and relieving symptoms and typically involves intravenous antibiotics, biliary drainage, and supportive care. Minimally invasive treatment options, such as endoscopic retrograde cholangiopancreatography with stent placement or balloon dilatation, can also be crucial in managing bile duct obstruction. Regarding surgery modalities, in recent years, laparoscopic management has emerged as the preferred approach for treating Mirizzi syndrome. It offers advantages such as minimal invasiveness, shorter hospital stays, and faster recovery. However, laparotomy may be necessary in complex cases or instances of severe inflammation to ensure adequate visualization and safe biliary reconstruction. Early recognition of Mirizzi syndrome is vital for improving patient outcomes. Prompt diagnosis allows for timely intervention, preventing further complications and reducing the risk of morbidity and mortality associated with this condition. Additionally, it emphasizes the need for further research to develop better surgical strategies to minimize surgical complications and reduce mortality rates. Advances in surgical techniques, improved imaging modalities, and a better

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understanding of the pathophysiology of Mirizzi syndrome are essential for refining treatment algorithms and enhancing patient care in the future.

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