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ORIGINAL ARTICLE

Role of ERCP in Diagnosis and Treatment of Type I Mirizzi Syndrome: A Case Series with Review of Literature

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ABSTRACT

AIM: Mirizzi syndrome is a rare condition complicating long-standing gallstones disease. The aim of this study is to define, through a 17 year-experience, the role of Endoscopic Retrograde Cholangiopancreatography in the diagnosis and the treatment of Mirizzi syndrome type I according to Csendes classification.

MATERIALS AND METHODS: A retrospective study including patients diagnosed with Mirizzi syndrome type I, between 2002 and 2019 was conducted in the department of digestive endoscopy of our university hospital. Data collected included demographic, clinical, biological and imaging findings. Endoscopic characteristics and procedures used for treatment were collected. Statistical analysis was performed using SPSS 20.0.

RESULTS: Type I Mirizzi syndrome was diagnosed during

ERCP in 0,48% of patients with gallstone disease, the median age was 55.5 (46-69.5) without gender difference. 50% of our cases were diagnosed before surgery. Endoscopic therapeutic procedures included biliary decompression techniques using nasal bile drainage or plastic stents, balloon sweeping after selective catheterization of cystic duct and large balloon papillary dilation with double cannulation. The success rate of endoscopic management was 66,6%. Surgical treatment was performed at the same time as laparoscopic cholecystectomy in patients with lithiasic gall bladder.

CONCLUSIONS: Mirizzi syndrome remains a fascinating and rare condition complicating gallstone disease with no uniform guidelines to date. Our study emphasizes the role of ERCP as a diagnostic and therapeutic procedure in the management of type I Mirizzi syndrome.

Key words: Olmesartan; Enteropathy

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Abbreviation

ALT: Alanine Amino Transaminases;

CBD: Common Bile Duct;

CD: Cystic Duct;

CHD: Common Hepatic Duct;

CRP: C Reactive Protein;

ENBD: Endoscopic Nasal Bile Drainage;

ERCP: Endoscopic Retrograde Cholangiopancreatography;

ES: Endoscopic Sphincterotomy;

GB: Gall Bladder;

MRCP: Magnetic resonance cholangiopancreatography;

MS: Mirizzi Syndrome;

NBD: Nasal bile drain;

US: Ultra-sonography.

INTRODUCTION

Mirizzi syndrome, also known as "extrinsic bile compression syndrome" is an uncommon condition complicating gallstone disease^[1]. It's characterized by the compression of common bile duct caused by a single large or multiple smaller gallstones impacted at the gallbladder infundibulum (Hartmann's pouch) or at the cystic duct, resulting to a partial or complete obstruction of hepatic duct, and finally triggering the hepatic function^[2]. Historically, Mirizzi syndrome was described for the first time by a surgeon from Argentina named Mirizzi Pablo Luis^[3]. Afterwards, numerous studies have been published about the pathophysiology of this condition^[4,5,6], and reporting other complications related to long-lasting gallstones including biliary fistulas. Mirizzi syndrome is nowadays encountered in 0,3 to 3% of patients undergoing cholecystectomy for gallstone disease^[7-12]; However, its incidence is more important in underdeveloped countries ranging between 4,7 to 5,7% in Latin America for example^[13,14]. There is no gender difference regarding the syndrome incidence, and it is known to be more common in subjects between the fifth and seventh decade^[1,15,16,17]. To date, the current hypothesis of Mirizzi syndrome pathophysiology starts with an external compression of the bile duct by impacted gallstones until it eroded through the gallbladder wall into the bile duct with later development of cholecysto biliary or cholecysto enteric fistulas as evolution of the disease^[1]. Although clinical symptoms of Mirizzi syndrome are non-specific, the most common clinical presentation is obstructive jaundice, abdominal pain over the right upper quadrant and fever in a patient with suspected or known gallstone disease^[1]. The preoperative diagnosis of Mirizzi syndrome is very difficult which is challenging for surgeons and leads to an important postoperative morbidity and mortality. The final diagnosis is based on clinical characteristics, surgical intuition, aided with imaging and endoscopic features[18]. The treatment of Mirizzi syndrome has traditionally been surgical, though it is considered as a real challenge with an increased risk of bile duct injury and other morbidities due to the severe inflammation process and anatomic variants of the biliary tree encountered in MS[8]. Endoscopic Retrograde Cholangio-Pancreatography (ERCP) is an invasive method which is useful for the positive diagnosis of Mirizzi syndrome with or without biliary fistula, but is also a therapeutic procedure allowing stones retrieval, and bile tract decompression especially in type I MS according to Csendes classification^[7]. The diagnostic accuracy of MS with ERCP is ranging from 55 to 90%[19,20]. The purpose of this study was to review our department experience in the endoscopic diagnosis and treatment of type I Mirizzi syndrome, and to assess the role of ERCP as a diagnostic and therapeutic tool in the management of type I Mirizzi syndrome.

MATERIALS AND METHODS

Patients

Over a period of 17 years, from January 2002 to July 2019, a retrospective descriptive and analytical study was conducted in our department of Gastroenterology and digestive endoscopy at our university hospital analyzing all patients who underwent ERCP for gallstones disease.

Among 1240 ERCP performed, six patients had a type I Mirizzi syndrome according to Csendes Classification confirmed by two modalities including ERCP. The medical records of these patients were evaluated for patient medical and surgical history, demographic

data, clinical symptoms, laboratory findings, imaging features including hepatobiliary ultrasound (US) and MRCP findings. Finally endoscopic findings were recorded and endoscopic procedures were abstracted and reviewed. Exclusion criteria were represented by patients managed by exclusive surgery.

All patients had a pre-ERCP standard evaluation, laboratory tests included routine blood tests and liver function measurements. All patients underwent an hepatobiliary ultrasound as well as MRCP.

Finally, a clear informed consent was obtained from all patients before endoscopic procedures.

During endoscopic cholangiography, findings recorded were the common bile duct diameter, presence and location of lacunar images evoking gallstones, and anatomic variations of cystic duct (long cystic duct, low insertion of cystic duct, normal short cystic duct) had to be assessed.

The use of alternative endoscopic approaches namely nasal bile drainage, biliary plastic stent placement, large balloon papillary dilation and double cannulation were evaluated and their indications specified.

Statistics

Data were reported as means and medians with standards deviations for continuous variables and percentages and frequencies for categorical variables.

All patients data were assessed in a database using SPSS version 20.0 software for Mackintosh (SPSS, Chicago IL).

RESULTS

The incidence of Mirizzi syndrome was 0,48% among all patients who underwent ERCP for cholelithiasis in our department during the study period. The median age at the presentation in our series was 55.5 (46-69.5) year-old (Range 40 to 74). There were 3 women and 3 men with a sex ratio of 1.

50% of our patients (n = 3) had a history of cholecystectomy for gallstone disease. The most common clinical symptoms were abdominal pain over the upper right quadrant and evident obstructive jaundice which were present in all cases, whereas fever was present in half of them (n = 3). Laboratory findings were characterized by liver tests disruption in all patients, with elevation greater than 2 times the normal of Alanine amino transaminases, and conjugated hyperbilirubinemia with mean bilirubinemia at 107.7 +/-23.8 mg/L. Other laboratory findings were represented by inflammatory syndrome with elevated C-reactive protein and leukocytosis in 50% of cases (n = 3).

Patients demographic data, clinical characteristics and laboratory data are summarized in table 1.

Imaging findings

Pre-ERCP diagnostic procedures included hepatobiliary US and MRCP for 83,3% of our patients (n = 5), while one had a percutaneous cholangiography using T-tube left from surgery (case 6).

Hepatobiliary US findings are reported in table 2.

After hepatobiliary US, all patients had undergone MRCP interpreted by an expert radiologist. MRCP findings are detailed in table 3.

The diagnosis accuracy of Mirizzi syndrome using hepatobiliary US and MRCP was 20% (1/5) and 60% (3/5) respectively.

Case 6 was admitted 15 days after cholecystectomy and had a T-tube from which a percutaneous cholangiography was performed revealing the presence of 3 gallstones on the cystic remnant and evoked a Mirizzi syndrome

Table 1 Clinical characteristics and laboratory findings.

Cases	Age (year-old)		History of cholecystectomy	Clinical presentation	Laboratory findings		
					Total bilirubin (mg/L)	ALT (UI/L)	CRP (mg/L)
1	40	Female	No	Obstructive jaundice, abdominal pain	96	6N	5
2	74	Male	No	Abdominal pain, nausea and vomiting, obstructive jaundice one week later	110	3N	
3	53	Male	5 years before	Abdominal pain, obstructive jaundice and fever	85	4N	140
4	68	Male	No	Abdominal pain, obstructive jaundice and fever		3N	156
5	48	Female	15 days before admission	Obstructive jaundice and abdominal pain	140	3N	
6	58	Homale	one month before admission	Obstructive jaundice, abdominal pain and fever		4N	

Table 2 Hepatobiliary ultrasonography findings.

Cases	US findings	Mirizzi syndrome diagnosis
1	Dilated hepatic duct in its extra and intra hepatic portions. Dilated CBD above a large gallstone of 9 mm. Lithiasic gallbladder	No
2	Dilated hepatic duct in its extra and intra hepatic portions. Lithiasic gallbladder. Hepatic steatosis	No
3	Moderate dilation of intrahepatic bile ducts. Dilated CBD (11 mm) with doubt about one large stone impacted on the cystic stump	Yes
4	Contracted gallbladder with thin walls. Moderate dilation of intrahepatic ducts and CBD without visible obstacle	No
5	Extra and intrahepatic bile ducts dilation. CBD measured at 13 mm above a 8.5 mm gallstone impacted in its distal part. Dilated choledochus to 17 mm in its distal part	No

Table 3 MRCP findings in different patients.

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Cases	MRCP findings	Mirizzi syndrome diagnosis				
1	Dilation of intrahepatic and extrahepatic bile ducts. CBD gallstone of 9mm.Lithiasic gall bladder	No				
2	Important dilation of common hepatic duct, intrahepatic ducts and cystic duct above 2 gallstones: one large stone (20mm) impacted in the cystic insertion which is low and narrowing the CBD, and a second non obstructive gallstone in the retro pancreatic portion of CBD (Figure 1A)	Yes				
3	Moderate dilation of CHD in its intra and extrahepatic portions, containing a non-obstructive gallstone. Large gallstone of 20mm in the cystic stump narrowing the CBD. Low insertion of the cystic duct (Figure 1B)	yes				
4	Contracted gallbladder with extremely thin walls. An impacted 5mm gallstone in the distal part of the cystic duct which is narrowing the CBD (Figure 1C)	yes				
5	Dilation of the CBD in its intra and extra hepatic portions (13 mm) above a 8.5 mm gallstone impacted in its lower part 17mm from its duodenal opening (Figure 1D)	No				

ERCP findings and endoscopic treatment

ERCP was carried out in all cases. Mean CBD diameter was 14+/-5.14mm (Range 5 to 18 mm).

Case 1: cholangiography showed a dilated CBD to 16 mm containing a lacunar image on its distal part. Cystic duct was long and parallel to CBD with a low insertion into the hepatic duct. Balloon sweep after endoscopic sphincterotomy (ES) showed there was no stones. A second opacification under pressure allowed to redress the diagnosis by revealing stones on the cystic insertion which is low, narrowing the CBD. A nasal bile drain was then placed (Figure 2).

Case 2: cholangiogram confirmed imaging findings by identifying a large stone on the cystic duct compressing the biliary junction and narrowing the common hepatic duct, with common hepatic duct dilation above the compression level, and a lacunar image of 8mm on the distal part of CBD. An ES was performed allowing the clearance of CBD and the placement of a plastic biliary stent of 8 cm/10fr (Figure 3).

Case 3: endoscopic cholangiography showed a frank dilation of CBD measured to 15mm which contained a lacunar image of 8mm. CBD was compressed and narrowed by a large 20mm stone impacted on the cystic stump which was low inserted (Figure 4). After endoscopic sphincterotomy and clearance of CBD, a plastic biliary stent was placed.

Case 4: Cholangiography confirmed MRCP findings by showing an impacted 5mm gallstone in the distal part of the cystic duct which is narrowing the CBD. After endoscopic sphincterotomy, a plastic biliary stent of $8\text{cm} \times 10\text{fr}$ was placed.

Case 5: Cholangiography showed a lacunar image of a stone impacted in the cystic stump, which is dilated and low inserted. CBD was narrowed by the cystic stone with dilation of CHD above. (Figure 5 A) Choledocus had a normal caliber. After ES, and initial failure of cystic stone retrieval using balloon sweep, a large papillary dilation using a 15mm balloon was performed allowing the stone extraction (Figure 5, B, C).

Case 6: ERCP was performed 20 days after cholecystomy showing a dilated CBD to 16mm with a dilated cystic stump to 14mm containing 2 lacunar images. After ES, a large balloon dilation of papilla was performed with a selective catheterism of cystic stump allowing the extraction of 2 stones and assuring the clearance of cystic stump.

Surgical treatment and follow-up

Patients with known lithiasic gallbladder (Cases 1, 2 and 4) had undergone laparoscopic cholecystectomy after CBD clearance. On cases 1 and 2, the cystic stones were extracted at the same surgical time with great outcomes. On case 4, cystic duct stone was not extracted during the surgical procedure because of the important inflammatory process on the gall bladder and the perivesicular space. A second ERCP was then performed allowing the clearance of cystic stump after extraction of biliary plastic stent. For the other 3 cases, endoscopic treatment was sufficient without necessity of surgical cure. On case 3, Plastic biliary stent was extracted 3 months after the initial procedure. Endoscopic cholangiography showed multiple



Figure 1 MRCP findings in cases 2, 3,4 and 5.

lacunar images on the CBD with disappearance of cystic stone which means a fragmentation of the cystic stone and its migration into CBD, balloon sweep allowed the clearance of CBD.

Patients were all discharged from hospital in good conditions, without morbidity. Clinical, biological and radiological followup using hepatobiliary US were satisfactory in all patients.

DISCUSSION

Through this case series, we confirm that ERCP plays an important role in the diagnosis and treatment of type I Mirizzi syndrome. ERCP confirmed the diagnosis in all cases in our series, but it also leads to an efficient treatment using endoscopic procedures in 66,6% (n = 4).

Mirizzi syndrome is defined as an impaction of gallstone in the Hartmann's pouch or in the cystic duct in close proximity with the common hepatic duct, causing obstruction of CHD by extrinsic compression^[10]. It's an uncommon complication of long-standing gallstone disease^[1], with an incidence ranging from 0,3 to 3% in patients undergoing cholecystectomy for lithiasic gallbladder^[12]. In our series, the incidence of type I MS was 0,48% among 1240 ERCP performed for gallstones disease confirming the rarity of the syndrome, compared to an incidence of 1,07% reported by Yonetci N. et al in a turkish series of 656 patients^[20].

The patophysiological process of Mirizzi syndrome has been described by McSherry et al^[21] and Csendes et al^[7], who also proposed a classification describing different types of MS. The type I lesion which was considered in our series is defined as the external

compression of the common bile duct due to a stone impacted at the neck of the gallbladder or at the cystic duct.

To date, there is no pathognomonic pattern of the clinical presentation of Mirizzi syndrome^[22]. In our experience, all patients with Mirizzi syndrome presented with obstructive jaundice and abdominal pain, which is in accordance with datas previously published by Young Erben et al. and Carmen Paya et al^[16,22].

The most common laboratory findings in the literatture in Mirizzi syndrome are represented by hyperbilirubinemia as well as elevation of aminotransaminases which was the case in all our patients^[1].

In patients presented with obstructive jaundice, the first recommended investigation is hepato-biliary US. However the diagnosis accuracy of MS using US was only 20% in our series, compared to 29% in litterature^[23], hence the indication of MRCP in all our cases. MRCP is a non invasive procedure with a reported diagnostic accuracy of 50% in Mirizzi syndrome^[23]. In our experience, it allowed the diagnosis of MS type I in 60% of cases, by showing typical features like a large stone impacted in the cystic duct narrowing the CBD, but also less typical ones like a contracted gallbladder with thin walls. Moreover, MRCP is a useful procedure to rule out other causes of biliary tract obstruction including malignancies and cholelithiasis. However, due to the MRCP low diagnosis accuracy of MS, all our patients underwent ERCP which is considered as the gold standart in the peroperative diagnosis of Mirizzi syndrome^[16]. ERCP is an invasive procedure which in addition to allow the diagnosis of Mirizzi syndrome, is a therapeutic procedure that enable the decompression of bile tract. In our series

the diagnosis accuracy using ERCP was 100% with no morbidity. The diagnosis sensitivity of ERCP in MS is reported to be 55-90%^[23]. Some typical ERCP findings of MS are widely recognized including midbile duct obstruction with dilated proximal CHD and intra hepatic ducts combined with normal duct caliber distal to the obstruction, insertion of the cystic duct at the point of obstruction and/or complete obliteration of the CD and finally a stone visualized at the point of obstruction either within the CD or the $CBD^{\scriptsize{[24]}}$. In our series, at least one of these characteristics was identified in every case, a low insertion of the cystic duct in CBD was noted in 50% of our cases, bile ducts dilation above the obstruction level in 66,6% (n = 4), a long CD parallel to CBD in one case and normal caliber of distal choledocus in one case. In addition of being a diagnostic procedure, ERCP is recognized as a therapeutic tool in the management of type I Mirizzi syndrome. Several case reports and small series have been published describing endoscopic procedures in management of MS starting with the standard ones as the passage of balloon catheter

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Figure 2 First case cholangiogram showing a lacunar image on the cystic duct narrowing the CBD. Opacification performed using Nasal bile drainage.

beyond the obstruction level, use of stone extraction basket, as well as mechanical lithotripsy^[24]. The decompression of bile tract by the placement of a nasal bile drain or a plastic stent can be used as a bridge to a surgical treatment, but can also lead to a calculi fragmentation which facilitate an ulterior endoscopic treatment. Other techniques have been historically described in the form of case reports with great outcomes such as extracorporeal shock wave lithotripsy using an ENBD[25]. In our series, MS was diagnosed preoperatively in half of the cases and post-cholecystectomy in the other half. When the diagnosis was evoked before surgery, endoscopic procedures consisted in the bile tract decompression using endoscopic nasal bile drain or plastic stents that provided a temporary improvement; a laparoscopic cholecystectomy was then performed in all cases with surgical treatment of the biliary stones in two cases. In one case, the surgical retrieval of the cystic stone was difficult because of the inflammatory process and was thus assured postoperatively during ERCP with selective catheterisation of the cystic remnant and balloon sweeping. On the other hand, when the diagnosis of MS was made postoperatively, the purpose was a curative treatment which was possible in our 3 cases using a large balloon dilation of the

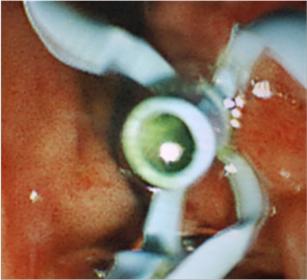


Figure 3 Plastic stent 8cm/10fr after clearance of CBD in case 2.



Figure 4 Endoscopic findings on case 3, CBD appears to be narrowed by a large cystic stone.

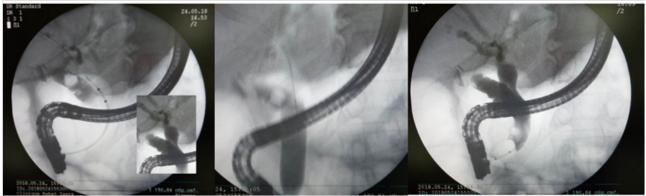


Figure 5 ERCP findings and endoscopic papillary dilation in case 5.

papilla with double cannulation of cystic stump and CBD in 2 cases. This technique was reported by Gianfranco Donatelli in 2012 with great outcomes^[26], and its results were confirmed in our series. On the last case, the calculi fragmentation was assured by plastic stent, and the clearance of CBD was then allowed by balloon sweeping at the same time as plastic stent extraction. Nowadays, the use of minimally invasive endoscopic procedures is widely recommended; thus the several procedures described. In addition of techniques cited above, Hong jun Kim et al reported the simultaneous use of endoscopic nasal gallbladder drainage and endoscopic NBD as a bridge to surgical laparoscopic treatment in 3 cases of type I MS^[27]. Recently, some case reports reported also the usefulness of per-oral cholangioscopy for the treatment of Mirizzi syndrome^[28]; However, these advanced methods remain unavailable in all centers and have to be developped as a next step in management of Mirizzi syndrome. Despite the endoscopic advancement and all the procedures developped, cholecystectomy remains todate the treatment of choice of type I Mirizzi syndrome.

Our study is evidently limited by its retrospective design, and the few number of patients, but it confirms and highlights the important role of ERCP as a diagnostic procedure as well as a therapeutic one that can provide a curative treatment of type I Mirizzi syndrome in well selected patients.

In conclusion, we confirm through our study the place of ERCP in the diagnosis, but also in the treatment of type I MS. Laparoscopic cholecystectomy remains therefore the standard treatment of these patients, but in type I post cholecystectomy MS, endoscopic procedures have a primordial role in the management to avoid further surgeries. However, due to the relatively few patients in our series, large and prospective multi-centric studies have to be conducted to provide equivocal guidelines in endoscopic management of type I Mirizzi syndrome.

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