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Case Report

Biliar reflux by incompetence of the sphincter of oddi post endoscopic retrograde cholangiopancreatography, as cause of cholangiolar abscesses and cardiac vegetations

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ABSTRACT

The term sphincter of Oddi dysfunction (SOD) encompasses a heterogeneous group of patients with a clinical syndrome characterized by abdominal pain (biliary colic or pancreatic pain), attributed to motor alterations of the SO that cause obstruction of the flow of bile and pancreatic juice (intermittent or fixed acalculous obstruction) or reflux of the same through the sphincter. Its diagnosis and treatment are controversial. We presented the case of a patient with sphincter of Oddi incompetence as a rare cause of jaundice, abdominal pain and cholangiolar abscesses due to sphincter incompetence from multiple endoscopic procedures and a history of cholecystectomy. We review the epidemiology, etiology, diagnostic criteria and management, both conservative and surgical.

Keywords: SOD, Cholangitis, Hepaticojejunostomy

INTRODUCTION

SOD occurs in 1% of patients after cholecystectomy and in up to 23% of patients with post cholecystectomy syndrome with elevated liver enzymes.[1,2]

It occurs most commonly in cholecystectomized women between 20 and 50 years of age, although it can also occur in men and in patients with an intact biliary tree.

About 10-20% of cholecystectomy patients experience biliary colic, of which 9-51% meet diagnostic criteria.

Risk factors for SOD include gallbladder agenesis, preoperative cholelithiasis, lithotripsy, liver transplantation, alcohol use disorder, hypothyroidism, and irritable bowel syndrome.[5]

It commonly presents with intermittent or episodic epigastric or right upper quadrant pain lasting from 30 min to several hours according to the ROME III criteria.[1-3]

The underlying mechanism is not fully understood. Proposed causes include trauma from persistent passage of microlithiasis or crystals, increased pressure caused by a congenital hypertrophic sphincter, or paradoxical smooth muscle enlargement/response to neural or hormonal stimuli causing contraction. In other words, it can occur due to functional or mechanical obstruction. It can be the result of any process that leads to inflammation or scarring, such as pancreatitis, impaction of a biliary lithiasis in the papilla of Vater, surgical iatrogenesis, infection and adenomyosis. The latter is

characterized manometrically by abnormal sphincter of Oddi motility and elevated basal pressure.[2,3]

For the diagnosis of SOD, structural abnormalities and malignant neoplasms should be ruled out by imaging such as endoscopic ultrasound, abdominal ultrasound, computed tomography or magnetic resonance cholangiopancreatography (MRCP). Ampullary biopsy should also be considered to rule out ampullary tumors.

The treatment of this condition is complex and, so far, there is no clear recommendation on the optimal treatment.

CASE REPORT

A 29-year-old woman with a history of laparoscopic cholecystectomy on March 2021 for chronic calculous cholecystitis; 5 days after surgery she presented jaundice and residual choledocholithiasis, endoscopic retrograde cholangiopancreatography (ERCP) was performed with extraction of 2 stones and realization of endoscopic sphincterotomy. On postoperative day 15 he presented with jaundice and new extraction of residual lithiasis by ERCP with stent placement. One month after the surgical event, was readmitted to the hospital for abdominal pain and diagnosis of multiple hepatic abscesses, associated with dilatation of the intrahepatic and extrahepatic biliary tract, and was treated with meropenem and metronidazole for 14 days, and was discharged due to improvement. The stent was removed 4 months after its placement, with the finding during ERCP of intrahepatic and extrahepatic biliary tract dilatation without evidence of leaks, lithosclerosis or stenosis. Subsequently, she presented repeated episodes of cholangitis that required hospitalization; the last one 9 months after cholecystectomy, with fever, anorexia, jaundice, pain in the right hypochondrium and septic shock secondary to cholangiolar abscesses, biochemically with glucose: 89 mg/dl, urea: 15.0 mg/dl, cr: 0.59 mg/dl, BT: 1.05 mg/dl, BD: 0.67 mg/dl, BI: 0.38 mg/dl, ALT: 14 u/l, AST: 21 u/l, FA: 647 u/l, LDH: 136 u/l, GGT: 379 u/l, albumin: 2.7 g/l, amylase: 20 u/l, Ca: 9.2 mg/dl, Na: 132 mEq/l, Cl: 102 mEq/l, K: 3. 6 mEq/l, P: 4.3 mg/dl, Mg: 1.8 mg/dl, leukocytes: 22.7 thousands/microliter, Hb: 7.0 g/dl, Hto: 24.2%, MCV: 95.7 fl, MCH: 27.7 pg, platelets: 774×103, PT: 16.6 s, TTP: 32.1 s, INR: 1.2.

The study protocol included abdominal US, abdominal CT and CMR, without identifying the origin of the cholangiolar abscesses; after the finding of pneumobilia in the abdominal CT, a cholangiogammagraphy and SEGD were requested to identify the site of communication with the digestive tract.

Imagological findings

Abdominal US (changes in the echogenicity of the hepatic parenchyma with suspicion of cholangiolar abscesses); Cholangioresonance; abdominal CT; cholangiogram (data compatible with enterobiliary fistula located towards the descending segment of the duodenum); esophagogastroduodenal series; endoscopic ultrasound (EUS): multiple diffuse hypoechoic images in hepatic parenchyma; ERCP: intrahepatic and extrahepatic biliary tract dilatation with predominantly peripheral saccular images compatible with cholangiolar abscesses. Biliary aspirate and culture were performed (Figure 1-4).

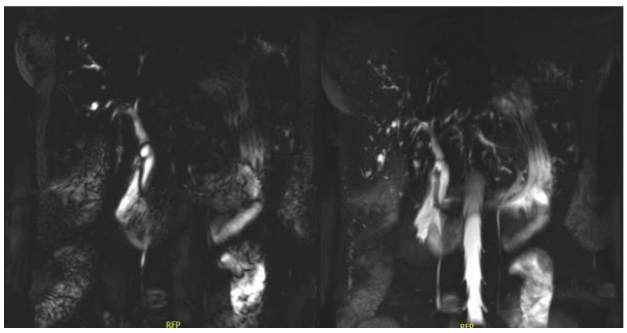

Figure 1: Cholangioresonance: findings in relation to cholangiolar abscesses associated with intrahepatic and extrahepatic biliary tract dilatation and pneumobilia; surgical absence of gallbladder.

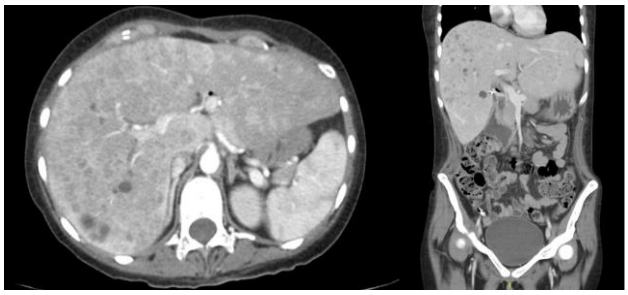

Figure 2: Simple and contrasted thoracoabdominal CT: cholangiolar abscesses; pneumobilia: surgical absences of gall bladder.

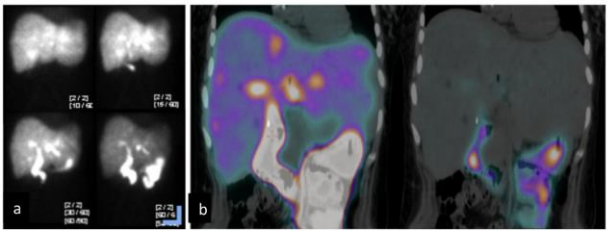

Figure 3: Cholangiogammagraphy with 99mTc-mebrofin; (a) the biliary tract is observed from minute 10, with transit to the intrahepatic biliary tract, common bile duct (CBD) and choledochus at minute 15, which are prominent due to dilatation and statis of bile, with subsequent flow to the gastric cavity and intestine, which is visualized from minute 30; the prominence of the CBD persists upto 60 minutes presenting greater activity than in the liver; (b) single photon emission tomography (SPECT/CT) which corroborated dilatation of the biliary tract, bile reflux towards the CBD and stomach.

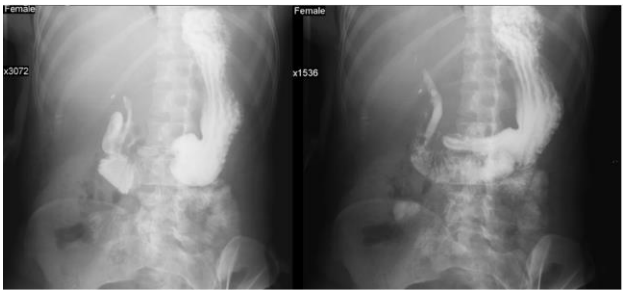

Figure 4: SEGD with findings related to SOD and duodenocholedocholedochal reflux.

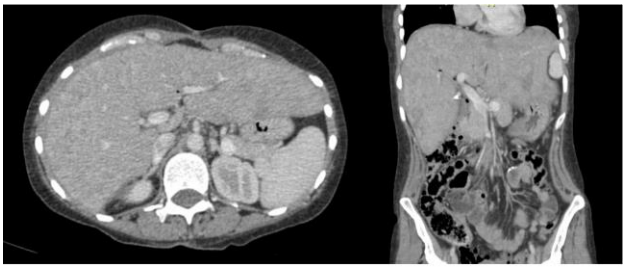

Figure 5: Andominal CT with surgical changes due to hepatojejunostomy without evidence of stenosis, without dilatation of the intrahepatic and extrahepatic biliary tract; pneumobilia due to surgical history.

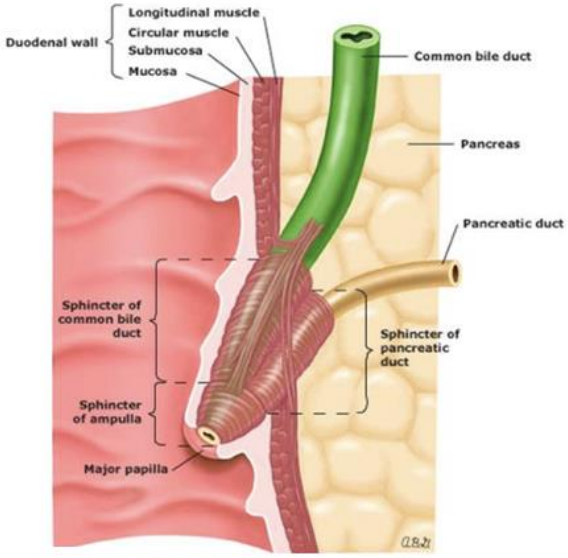

Figure 6: Sphincter of oddi anatomy.

She received treatment with imipenem+linezolid for 15 days, then meropenem+colistin+amphotericin B due to the development in biliary fluid of pseudomonas aeruginosa with carbapenemase expression and *E. faecium* resistant to ampicillin, completing 14 days.

During her hospitalization with torpid evolution secondary to infective endocarditis (vegetation of 19×20 mm in the roof of the right atrium), multiple liver abscesses (*Pseudomonas aeruginosa* and *Enterococcus faecium*), pleural effusion of 15% bilaterally, tubulopathy associated with the use of antimicrobials.

Due to the integrated diagnosis of sphincter of Oddi incompetence and the finding of reflux of gastroalimentary content to the biliary tract, with persistent cholangiolar abscesses and the development of infectious endocarditis despite medical and endoscopic treatment, it was decided to perform a biliodigestive bypass when hemodynamic conditions and septic shock improved.

Intraoperative findings

Multiple grade IV adhesions, 12 mm common bile duct, 6 mm hepatic artery, a hepatojejunostomy was performed with an anastomotic surface of 2 cm, the jejunojejunal anastomosis at 60 cm from the Treitz angle and 40 cm from the biliary loop, liver biopsy was performed without eventualities, trans operative bleeding 500 ml.

Histological findings

Liver biopsy found ascending cholangitis with cholangiolar microabscesses. Parenchymal micro infarcts. Moderate intracytoplasmic cholestasis bile ducts showed pyknotic nuclei, hepatocytes with macrovesicular steatosis, mild hydropic and foamy degeneration, regeneration data, intracytoplasmic cholestasis, canalicular and bile lakes with some neutrophils. Final diagnosis was intense cholestasis due to bile duct obstruction.

Postoperative course

Good evolution, with adequate oral tolerance and normal bowel movements, serous discharge through drainage, which was removed and discharged due to improvement.

Two months after abdominal surgery she presented a vegetation in the right atrium; the CT reported an intracardiac nodular lesion, dependent on the posterior wall of the right atrium, measuring 11×11×10 mm with well-defined borders, isodense in simple phase and low attenuation in venous contrast phase, of heterogeneous composition secondary to the presence of peripheral linear calcifications. Due to the size and location of the tumor, she did not require surgical treatment, and was discharged with metoprolol 100 mg every 12 hours, ivabradine 5 mg every 12 hours and rivaroxaban 15 mg every 24 hours.

Currently asymptomatic (9 months after biliodigestive surgery), afebrile, without abdominal pain, with biochemical improvement, with decrease of leukocytosis and improvement of cholestasis in 50%. Biochemically with mild anemia, reactive thrombocytosis, mild hypoalbuminemia, without elevation of transaminases (total protein 9.9 g/l, albumin 2.8 g/l, total bilirubin 0.53 mg/dl, direct bilirubin 0.34 mg/dl, indirect bilirubin 0.19

mg/dl, AST 9 u/l, ALT 5 u/l, LDH 87 u/l, GGT 97 u/l, alkaline phosphatase 434 u/l, leukocytes 15.90 miles/microliter, hemoglobin 10.4 g/dl, hematocrit 34.3 %, MCV 98 fl, mean MCH 29.7 pg, platelets 624,000).

The last control CT scan reported surgical changes due to hepatojejunostomy without evidence of stenosis, without intrahepatic and extrahepatic bile duct dilatation; pneumobilia due to surgical history (Figure 5).

She is under medical management with pancreatin 3 tab every 8 hours and ursodeoxycholic acid 1-0-2 tab.

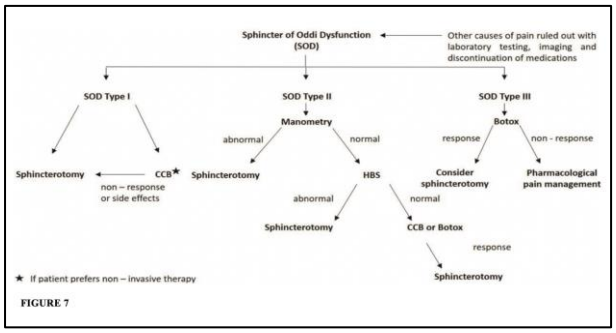

Figure 7: Diagnostic algorithm for sphincter of oddi dysfunction.

DISCUSSION

The sphincter of Oddi is composed of small circular and longitudinal muscle segments measuring 6 to 10 mm in total length that are mostly located in the thickness of the duodenal wall (Figure 6). Its physiology depends on the feeding or fasting state. It regulates bile and pancreatic flow into the duodenum and prevents bile and pancreatic reflux.

Basal sphincter pressure is 3 to 35 mmHg with an intermittent phasic increase in tone 2 to 6 times per minute from 50 to 140 mmHg.

The SOD encompasses a heterogeneous group of patients with a clinical syndrome characterized by abdominal pain, similar to biliary colic or pancreatic pain, attributed to motor disturbances of the SO that would cause obstruction of the flow of bile and pancreatic juice (sphincter abnormality causing intermittent or fixed acalculous obstruction). It is also known as biliary dyskinesia, but only denotes a motility disorder and not an anatomic obstruction.[1]

SOD is manifested by episodes of severe abdominal pain, localized in the epigastrium and right hypochondrium (in biliary-type dysfunction) or in the middle area of the upper hemiabdomen radiating to the back (in pancreatic-type dysfunction).[2]

The Milwaukee classification of SOD is based on symptoms, biochemical abnormalities, and radiographic findings, and is the widely adopted classification: type I: pain, abnormal chemistry (that can include bilirubin, transaminases, alkaline phosphatase, or gamma-glutamyl transferase) and dilated bile duct or pancreatic duct on imaging; type II: pain plus abnormal biochemical markers or abnormal imaging; type III: pain without abnormal chemistry or abnormal images.[3]

Ten percent of patients who undergo cholecystectomy surgery may develop post cholecystectomy syndrome weeks or months later. Post cholecystectomy syndrome was first described in 1947 by Womack and Crider. It refers to the persistence of gastrointestinal symptoms after cholecystectomy and may occur in 5-47% of patients. The etiology can be broadly divided into biliary, extrabiliary, organic, and functional. SOD accounts for 1.8-31% of cases.[4]

The prevalence in the general population is about 1.5%, but in patients with idiopathic recurrent pancreatitis it is thought to be as high as 72%. SOD occurs in 1% of patients after cholecystectomy and in up to 23% of patients with post cholecystectomy syndrome with elevated liver enzymes.[1,2]

It occurs most commonly in cholecystectomized women between 20 and 50 years of age, although it can also occur in men and in patients with an intact biliary tree. About 10-20% of cholecystectomy patients experience biliary colic, of which 9-51% meet diagnostic criteria.

Risk factors for SOD include gallbladder agenesis, preoperative cholelithiasis, ERCP, lithotripsy, liver transplantation, alcohol use disorder, hypothyroidism, and irritable bowel syndrome.[5]

Commonly presents with intermittent or episodic epigastric or right upper quadrant pain lasting from 30 min to several hours according to ROME IV criteria.[1-3]

Pancreatic SOD usually presents with more prolonged pain that may radiate to the back and be associated with recurrent episodes of pancreatitis (pain commonly occurs after meals). SOD may present with intermittent biliary colic, recurrent pancreatitis, abnormal liver function tests, and/or ductal dilatation.[4,5]

The underlying mechanism is not fully understood. Proposed causes include trauma from persistent passage of microlithiasis or crystals, increased pressure caused by a congenital hypertrophic sphincter, or paradoxical smooth muscle enlargement/response to neural or hormonal stimuli that cause contraction. In other words, it can occur due to functional or mechanical obstruction.[6,7]

Clinically it is very difficult to differentiate SOD from other biliopancreatic diseases, especially lithiasis, as well as from other functional digestive disorders. The greatest difficulties lie in type III dysfunction whose only manifestation is pain, without other objective data to

support its biliary or pancreatic origin (e.g., alterations of the hepatic profile in laboratory tests or dilatation of the biliary tract).[1,4]

The diagnostic strategy should begin with an analytical study that includes the determination of bilirubin and liver enzymes, as well as amylase/lipase, both at baseline and during painful crises. A transabdominal ultrasound should also be performed. It is essential to demonstrate the absence of biliary lithiasis and organic biliopancreatic and papilla of Vater lesions.

For this purpose, imaging scans with a diagnostic sensitivity superior or equal to ERCP, but less invasive, such as cholangiopancreatography (CP) obtained by magnetic resonance imaging (MRCP) or endoscopic ultrasonography (EUS), and failing this, CP by helical tomography or computed axial tomography, are recommended.[4,5]

If SOD is suspected, structural abnormalities and malignant neoplasms should be ruled out by imaging such as endoscopic ultrasonography, abdominal ultrasonography, computed tomography, or MRCP. Ampullary biopsy should also be considered to rule out ampullary tumors.

Manometry

This is the gold standard for the diagnosis of SOD, although results vary depending on patient and operator experience. Medications such as hyoscyamine, midazolam, calcium channel blockers, anticholinergics, cholinergics, nitrates and opioids may also affect results and should not be used prior to procedures. Sphincter of Oddi hypertension is defined as manometry with a baseline biliary or pancreatic sphincter pressure of >40 mmHg (greater than three standard deviations above the mean pressure). Other criteria that have been used include increased frequency of phasic waves. SOD 1 does not require manometry for diagnosis; 35% of patients have normal manometry and sphincteric hypertension is only demonstrated in 55-65% of patients. Sphincter of Oddi manometry is rarely used, due to a high risk of complications (25%), especially acute pancreatitis in patients with SOD.

Hepatobiliary scintigraphy

Scintigraphy uses a radionuclide tracer to quantify bile flow with the help of intravenous CCK infusion or opioids and measurement of the time of appearance in the duodenum, and the transit time from the hepatic hilum to the duodenum. It is a viable option in patients with previous cholecystectomy.[8] Visualization time of the common bile duct in a normal patient is 6.7±2.6 minutes vs. 12.5±2.2 minutes in patients with SOD. Transit time to the duodenum is 12.7 min vs. 30.1 min in SOD. Total visualization time of the common bile duct is 38.2 min vs. 60.1 min in SOD.[8]

SOD treatment aims to reduce basal pressure and sphincter resistance (Figure 7).

Medical treatment

Calcium channel blockers such as nifedipine and nicardipine have been used to cause smooth muscle relaxation with a significant decrease in the number of pain episodes, emergency visits and use of analgesics.[8,9]

Botox injection into the sphincter of Oddi has been shown to reduce basal sphincter pressure by up to 50% over a median of 5 months in a previous study. The randomized, multicenter, controlled PREBOT trial is currently ongoing.[10]

Previous studies have shown that up to 87% undergoing botulinum toxin treatment had improvement in pain at post-procedure examination. The severity of pancreaticobiliary pain attacks and the frequency of episodes were significantly improved in 75% of cases. Relapse of biliary pain after the initial Botox injection occurred in 56 % of cases at a median of 3 months (range 1 to 24 months).[11]

Endoscopic treatment

Type I SOD: Respond well to endoscopic intervention, regardless of sphincter of Oddi pressure.

Type II SOD: About 60 to 94% of patients have improvement after biliary sphincterotomy.

Type III SOD: Clinical response ranges from 8 to 62%. 12

In the EPISOD study, it was demonstrated that patients with type I and II SOD presented the best response to sphincterotomy. In addition, in this study a consensus was reached that type I SOD does not require manometry and therefore treatment should not be defined by this study.[13,14]

Surgical treatment

Surgical sphincteroplasty can be performed upfront or after failure of endoscopic therapy.[13] There are no reports in the literature on biliodigestive surgery for the management of SOD.

CONCLUSION

We present the case of a patient with a diagnosis of biliary reflux due to incompetence of the sphincter of Oddi after ERCP resulting in a dysfunction of the sphincter of Oddi manifested with abdominal pain and jaundice; this diagnosis was integrated due to the finding of reflux of gastro alimentary content into the biliary tract documented by the SEGD. This pathology can occur in 1% of cholecystectomized patients, mainly in women

between 20 and 50 years of age and in this case, it was secondary to an endoscopic procedure. This patient's SOD was type I with the pain, abnormal chemistry and dilated bile duct; type I SOD does not require manometry for diagnosis according to the latest EPISOD consensus, since up to 35% have normal results and the risk of performing it should be assessed, especially when there is already evidence of reflux in another study such as SEGD or scintigraphy. The study used for the diagnosis of SOD in this patient was scintigraphy, where we observed that the visualization time of the common bile duct was 15 minutes, the transit time to the duodenum was 30 minutes and the total visualization time of the common bile duct was greater than 60 minutes. The treatment of choice for this pathology is endoscopic, however, this patient underwent ERCP on 4 occasions without improvement, with progression to cholangiolar abscesses, infectious endocarditis, and sepsis without improvement with medical treatment, so it was decided to perform biliodigestive bypass with a good subsequent evolution. The literature suggests resorting to surgery after failure of endoscopic therapy; however, there are not case reports of patients who underwent Roux-en-Y hepaticojejunostomy for the treatment of this disease. We consider biliodigestive surgery as a safe alternative for the treatment of difficult to manage SOD as in this case, with low morbidity and good results since the success lies in the decrease of the bacterial load by reflux to the biliary tract.

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