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HISTORIA, ÉTICA Y FILOSOFÍA

ORIGINAL ARTICLE

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Primary choledocholithiasis in total *situs inversus*

Coledocolitiasis primaria en situs inversus *total*

Sergio Morales-Polanco,* Oscar I Ortiz-Ruvalcaba,* Juan de Dios Díaz-Rosales*,‡

Keywords:
Choledocholithiasis, *situs inversus*, endoscopic retrograde cholangiopancreatography, endoscopy.

Palabras clave:
Coledocolitiasis, situs inversus, *colangiopancreatografía retrógrada endoscópica*, *endoscopia.*

ABSTRACT

Situs inversus totalis is a rare congenital entity characterized by right-to-left transposition of the viscera of the thorax and abdomen. We present the case of a 58-year-old female patient with a history of cholecystectomy 18 years ago, when a diagnosis of *situs inversus* was made, who presented to the emergency department with obstructive jaundice. With the surgical history and prior knowledge of her condition, an imaging approach and successful endoscopic treatment was performed. Cholelithiasis and *situs inversus* are a rare combination of entities; this binomial reminds us that in medicine there are no absolute concepts.

RESUMEN

El situs inversus *totalis es una rara entidad congénita caracterizada por la transposición de derecha a izquierda de las vísceras del tórax y abdomen. Se presenta el caso de paciente femenino de 58 años con antecedente de colecistectomía hace 18 años (donde se realizó diagnóstico de* situs inversus*). Acudió a urgencias con un cuadro de ictericia obstructiva. Con el antecedente quirúrgico y el conocimiento previo de su condición, se realizó un abordaje por imagen y un tratamiento endoscópico satisfactorio. La colelitiasis y el* situs inversus *son una rara combinación de entidades; este binomio nos recuerda que en medicina no existen conceptos absolutos.*

INTRODUCTION

Situs inversus totalis is considered a non-pathologic congenital entity characterized by right-to-left transposition of the totality of the viscera of the thorax and abdomen.[1] It has a frequency of 1:5,000-10,000 live births.[2] This rare condition often puts physicians in clinical dilemmas in the face of a common emergency.

Cholelithiasis is a public health problem and could be considered as part of a metabolic and degenerative problem.[3] Choledocholithiasis is a frequent complication of cholelithiasis and generates more costs and other possible complications in its treatment.

We present the case of a patient with *situs inversus* and primary choledocholithiasis who was successfully treated by endoscopic retrograde cholangiography (ERCP).

PRESENTATION OF THE CASE

A 58-year-old female patient was admitted to the emergency department for jaundice and left upper quadrant pain of three days' evolution. She had been suffering from colicky pain for three months, which worsened after consuming (atty food and improved after taking antispasmodic drugs. On physical examination her temperature we 37.9 ºC, respiratory rate 18 per minute, heart rate 88 beats per minute, and blood pressure 145/97 mmHg. Laboratory test results on admission showed leukocytosis of 13 $\times 10^9$ with neutrophilia of 78.3%, a serum total bilirubin (TB) of 10.3 mg/dl, a direct bilirubin (DB) of 7.3 mg/dl and indirect bilirubin (IB) of 2.7 mg/dl; a serum aspartate aminotransferase (AST) of 189 IU/l, alanine aminotransferase (ALT) of 98 IU/l, alkaline phosphatase (ALP) of 350 IU/l, a gamma glutamyl transpeptidase

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(GGT) of 630 IU/l, and serum amylase of 148 IU/l and lipase of 47 IU/l.

The patient had a history of laparotomy for acute abdomen 18 years ago with the finding of *situs inversus* and cholecystitis, for which she underwent cholecystectomy without apparent complications. With the surgical history, the findings described by the patient and the time of evolution, obstructive jaundice was diagnosed and primary choledocholithiasis was suspected due to the time of evolution from the previous procedure to her current condition, so imaging studies were requested. An abdominal CT scan confirmed the diagnosis of *situs inversus*, dilatation of the bile duct and a single 15 mm bile duct stone in the common bile duct *(Figure 1)*.

The patient underwent endoscopic retrograde cholangiography (ERCP), under general anesthesia in prone position and with the endoscopist on the right side of the table. The duodenoscope was introduced up to the stomach, and a 180º counterclockwise rotation was performed and introduced into the pylorus. With the duodenoscope in the second portion of the duodenum and in a long loop (due to the difficulty for correct positioning) a careful visualization was performed, and a native papilla was found and cannulated with a one o'clock direction (clockwise) towards the bile duct. In this case, this "reverse" direction allowed a correct cannulation procedure. A cholangiography was performed, which showed dilatation of the common bile duct and filling defects, so a sphincterotomy, up to the transverse fold, and dilatation of the sphincter of Oddi were performed. Three sweeps were done with an extraction balloon catheter, obtaining abundant biliary detritus *(Figure 2)* and a correct emptying of the contrast medium at the end of ERCP procedure. No evidence of other organic cause of jaundice was found, so she was discharged the same day of the procedure. During subsequent evaluations for one whole year, she remained asymptomatic and with these lab results at her last follow-up: TB 1.2 mg/dl, DB 0.6 mg/dl, IB 0.6 mg/dl, AST 46 UI/l, and ALT 56 UI/l.

DISCUSSION

Situs inversus is a rare condition that involves diagnostic and therapeutic difficulties in common diseases. Although this condition is not *per se* a risk factor for cholelithiasis, it does increase the difficulty and risks while performing invasive procedures, such as ERCP, because the anatomy must be mirrored.[4]

There is no consensus on how to perform ERCP in these cases, nor is there a gold standard

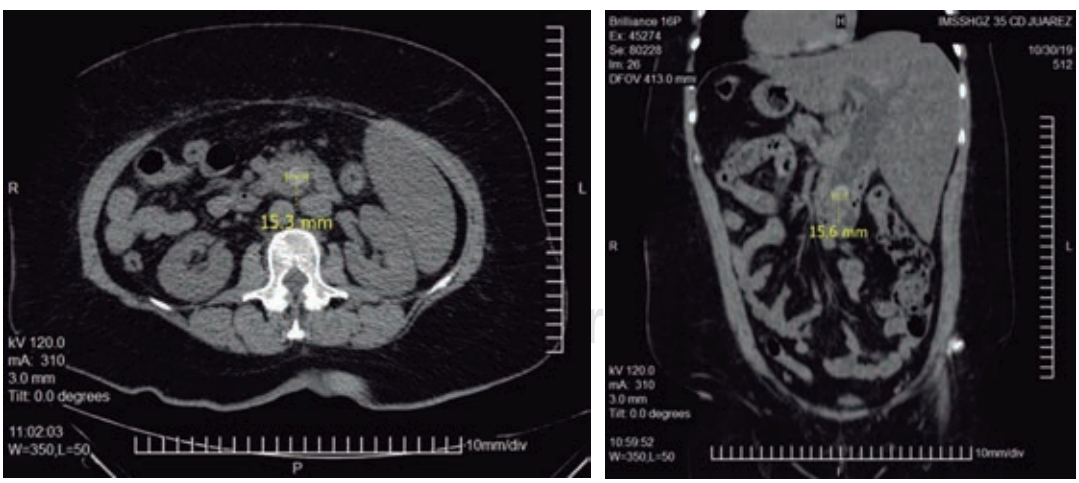

Figure 1: *Axial and coronal CT scan confirming the diagnosis of* situs inversus *totalis and showing dilatation of the bile duct and a 15 mm lithiasis.*

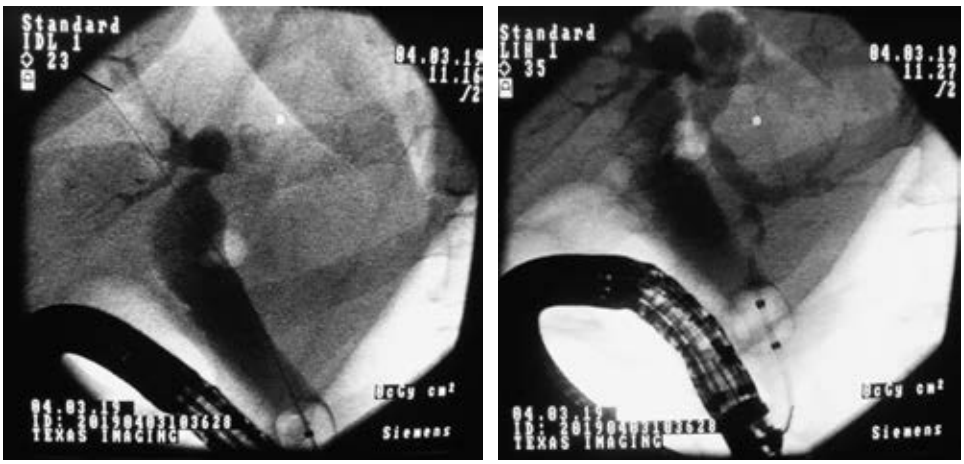

Figure 2: *Cholangiography showing bile duct dilatation and balloon probe sweep.*

technique for treating choledocholithiasis in *situs inversus*. The ERCP will be performed by an endoscopist or surgeon who feels most confident or as conditions allow the procedure at that time.

Although it is a rare entity, the adult patient may be aware of his/her condition and give it the required importance in case another common disease, such as appendicitis, cholecystitis, diverticulitis, for example, occurs.[5]

The icteric patient with *situs inversus* should undergo the same diagnostic and therapeutic approach as a patient with normal anatomy. Imaging studies such as abdominal ultrasound and CT scan will make the diagnosis in most cases. However, if prior knowledge of the biliary anatomy is required, a magnetic resonance cholangiography imaging will give detailed information to plan the most convenient therapeutic approach.[6]

Although there is no consensus on the therapeutic approach, ERCP is the initial treatment most authors claim and, therefore, it may be considered it as the treatment of choice. Although some authors consider that the position of the endoscopist on the right side of the table is not necessary for performing ERCP in *situs inversus*,[7] the true is that there is no consensus, so it is advisable to perform the procedure as the endoscopist or surgeon feels more confident with the technique or the conditions at that moment allow it. This practically justifies all the maneuvers performed to achieve the objective, meaning extracting the biliary stone or cleaning the biliary tract with the greatest safety. We must emphasize that, due to the technical difficulty, an unsatisfactory endoscopic procedure should not be considered as a failure,[8] and in that case the patient must be approached surgically.[9-11]

In conclusion, cholelithiasis and *situs inversus* are a rare combination of entities, and this binomial reminds us that in medicine there are no absolute concepts.

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ORIGINAL ARTICLE

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Management of gallbladder edema mistaken as cholecystitis in the Emergency Department

Manejo del edema de vesícula biliar confundido como colecistitis, en el Departamento de Urgencias

Jair Díaz-Martínez*

Keywords:
Gallbladder edema, cholecystitis, cholecystectomy, misdiagnosed.

Palabras clave:
Edema de vesícula biliar, colecistitis, colecistectomía, confusión diagnóstica.

ABSTRACT

Introduction: Different acute systemic diseases such as heart disease, cirrhosis, hepatitis can produce gallbladder wall edema and may be mistaken for acute cholecystitis. The aim of this study is to analyze patients sent for cholecystectomy due to gallbladder wall thickening mistaken for acute cholecystitis in an emergency department. **Material and methods:** An observational, retrospective study was performed from December 2016 to November 2019 in a regional referral center. Patients admitted to the emergency department for possible acute cholecystitis were studied. **Results:** Of 3,393 patients suspected of cholecystitis, 31 were mistaken for acute cholecystitis because of gallbladder wall thickening secondary to various acute illnesses and sent for cholecystectomy. Gender distribution was equal (male 51%). In all patients, gallbladder wall thickening of more than 5 mm (mean 8.96 mm, range: 5-16 mm) without signs of acute cholecystitis was corroborated. Diagnoses that were mistaken for cholecystitis were liver disease, dengue fever, cardiovascular disease, pneumonia, and pancreatitis. Seven patients (22.6%) underwent cholecystectomy for suspected cholecystitis. Two patients presented postsurgical complications (6.5%) and none died. In the histopathological study no signs of biliary cholecystitis were found. Patients who received surgical treatment had a longer hospital stay than those who did not undergo surgery, showing a statistical significance difference ($p = 0.004$). **Conclusion:** In the emergency assessment of patients with suspected cholecystitis, it is mandatory to rule out gallbladder edema secondary to systemic diseases. Surgical treatment in patients mistaken for acute cholecystitis may increase unnecessary hospital stay and costs.

RESUMEN

Introducción: *Diferentes enfermedades sistémicas agudas (cardiopatías, cirrosis, hepatitis) pueden producir edema de la pared de vesícula biliar y ser confundidas con colecistitis aguda. El objetivo de este estudio es analizar los pacientes presentados para colecistectomía, por engrosamiento de pared de vesícula biliar confundidos como colecistitis aguda en el Departamento de Urgencias.* ***Material y métodos:*** *Se realizó un estudio observacional, retrospectivo de diciembre 2016 a noviembre 2019 en un centro regional de referencia. Se revisaron pacientes admitidos al Servicio de Urgencias por posible colecistitis aguda.* ***Resultados:*** *De 3,393 pacientes sospechosos de colecistitis, 31 fueron confundidos con colecistitis aguda por presentar engrosamiento de la pared vesicular secundario a enfermedades agudas diversas, y presentados para colecistectomía. La distribución por sexo fue igual (varones 51%). En todos los pacientes, el engrosamiento de pared de vesícula biliar de más de 5 mm sin signos de colecistitis aguda fue corroborado (media: 8.96 mm, rango: 5-16 mm). Los diagnósticos que se confundieron con colecistitis fueron enfermedades hepáticas, dengue, enfermedades cardiovasculares, neumonía y pancreatitis. En siete pacientes (22.6%) se realizó colecistectomía por sospecha de colecistitis. Dos pacientes presentaron complicaciones postquirúrgicas (6.5%) y ninguno falleció. En el estudio histopatológico no se encontraron signos de colecistitis biliar. En el análisis, los pacientes que recibieron tratamiento quirúrgico tuvieron una estancia hospitalaria mayor que los no operados mostrando significancia estadística ($p = 0.004$).* ***Conclusión:*** *En la evaluación de urgencia en pacientes con sospecha de colecistitis es obligatorio descartar edema de vesícula biliar secundario a enfermedades sistémicas. El tratamiento quirúrgico en pacientes confundidos con colecistitis aguda puede incrementar la estancia hospitalaria y los costos.*

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INTRODUCTION

Acute cholecystitis is common in the emergency department, and the diagnosis is based on clinical signs and radiological findings.[1-3] However, different acute systemic diseases (heart failure, cirrhosis, hepatitis) can produce symptoms and even alterations in complementary diagnostic studies, such as gallbladder wall thickening resembling cholecystitis.[4,5] In acute systemic diseases, surgical treatment can produce a higher systemic inflammatory response, increasing morbidity and mortality.[6-8] Despite this, many of these pathologies are still confused with cholecystitis and continue to be sent to emergency cholecystectomy, representing a challenge for the surgeon.[7] Despite this, few articles explain this entity, persisting the fact that gallbladder edema may be mistaken for cholecystitis.

The objective of this study is to identify and analyze the patients presented for cholecystectomy with gallbladder edema secondary to acute diseases, mistaken as cholecystitis in the emergency department of a regional reference center.

MATERIAL AND METHODS

Study design: a retrospective study in a regional reference center was conducted from December 2016 to November 2019. Patients admitted to the emergency department due to suspected acute cholecystitis were analyzed. All patients underwent radiological studies (abdominal ultrasound and CT-scan), and acute cholecystitis was ruled out. Inclusion criteria were patients older than 18 years, with signs, symptoms (colicky pain in the right hypochondrium, nausea, vomiting), and radiological findings like cholecystitis but without cholecystitis. Patients with radiological findings compatible with lithiasis cholecystitis according to Tokyo 2018 guidelines criteria, like microlithiasis, anatomical gallbladder alterations (polyps, scleroatrophy, in a Phrygian cap, etc.) or increased gallbladder diameters were excluded.[9]

Clinical evaluation: the patient's files with surgical assessment for suspected cholecystitis were retrospectively reviewed. In all patients, comorbidities, medical history, clinical symptoms, laboratories were evaluated, as well as radiographic signs seen in the abdominal ultrasound or in the abdominal tomography. Surgical indication for suspected cholecystitis, histopathological findings after surgery, the primary cause of gallbladder edema, hospital stay, follow-up, morbidity, and mortality were evaluated.

Statistical analysis: we used descriptive statistics, as well as the t-Student test, for continuous variables, χ^2, and non-parametric tests for categorical variables to perform the analysis. A p-value ≤ 0.05 (95% confidence interval) was considered statistically significant. The statistical analysis was performed using the IBM Statistical Package for Social Sciences (SPSS, Statistics version 24.0, Inc, Chicago, IL).

RESULTS

Of 3,393 patients analyzed, 31 patients were sent for cholecystectomy with gallbladder edema mistaken as cholecystitis, representing 0.91% of the total population. Mean age was 43.94 years (range, 18-81) with an equal gender distribution most of them being males (n = 16, 51%). Ten patients (32.3%) presented comorbidities, being the most common diabetes and systemic arterial hypertension. Of these, two patients (6.5%) had type II diabetes, four type II diabetes and systemic arterial hypertension (12.9%), one had cerebral vascular disease and arterial hypertension (3.2%), and one had antiphospholipid syndrome (3.2%). The remaining 21 patients (67.7%) had no comorbidities. The characteristics of the study population are shown in *Table 1*.

Upon admission, all patients underwent imaging studies for suspected acute cholecystitis (abdominal ultrasonography and/or abdominal tomography). In all patients, the gallbladder wall thickening of more than 5 mm (mean 8.96 mm, range 5-16 mm) was corroborated, and signs of acute cholecystitis (criteria TG-18) or structural alterations were ruled out. Differences between acute cholecystitis and gallbladder edema in the abdominal ultrasound are shown in *Figure 1*,

and differences in the CT scan are shown in *Figure 2*, respectively.

The admission diagnoses of these patients were mostly liver diseases (n = 17, 55%). Ten patients presented with acute viral hepatitis corroborated by elevated transaminase levels and a positive viral hepatitis profile. Five patients presented with decompensated cirrhosis in Child-Pugh B class, one patient had non-alcoholic liver disease, and one patient had a left lobe liver tumor who subsequently showed to be a left lobe hepatocellular carcinoma (HCC). Ten patients (32.25%) presented hemorrhagic dengue with abdominal involvement subsequently corroborated in their hospitalization with IgM and IgG antibodies. Two patients had an acute myocardial infarction. One patient presented with fungal pneumonia and one patient with severe acute non-biliary pancreatitis Balthazar D.

Table 1: Characteristics of study population (N = 31).

Variable	n (%)
Age (years)*	43.94 ± 18.28
Gender (male)	16 (51.6)
Comorbidities	
DM	2 (6.5)
DM, AH	4 (12.9)
AH, CVA	1 (3.2)
APS	1 (3.2)
Operated patients	7 (22.5)

* Mean ± standard deviation.
DM = diabetes mellitus; AH = arterial hypertension; CVA = cerebrovascular accident; APS = antiphospholipid syndrome.

After surgical assessment in these 31 cases, an emergency surgical treatment was performed in seven of them (22.58%). These patients underwent emergency cholecystectomy for suspected acute cholecystitis. Of these, four patients underwent open cholecystectomy, and three patients underwent laparoscopic cholecystectomy. One of these patients also had a liver biopsy was performed due to elevated transaminase in the presence of negative viral panel. In operated patients, the primary diagnosis that produced the gallbladder edema was viral hepatitis in four (12.9%), cirrhosis Child-Pugh A class in one (3.2%), non-alcoholic liver disease in one (3.2%), and non-biliary pancreatitis (3.2%) in one. In *Table 2*, he definitive diagnosis of patients who underwent cholecystectomy is shown.

After surgery, two patients (6.5%) had surgical-related complications, and none died. Complications were one hemoperitoneum and one abortion secondary to transuterine bleeding. The patient with hemoperitoneum was submitted to open cholecystectomy and had 1,500 cc of hepatic bleeding. In this patient reoperation for hemostatic control was

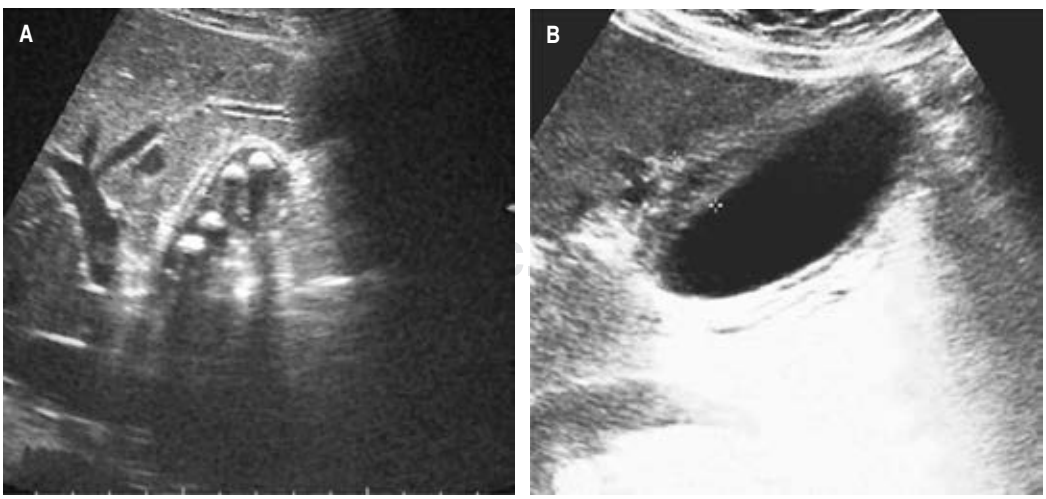

Figure 1:

Abdominal ultrasound scan showing differences between acute cholecystitis and gallbladder wall thickening without cholecystitis. ***A)*** *Wall thickening of the gallbladder due to acute cholecystitis with multiple lithiasis.* ***B)*** *Simple gallbladder edema due to dengue without cholecystitis.*

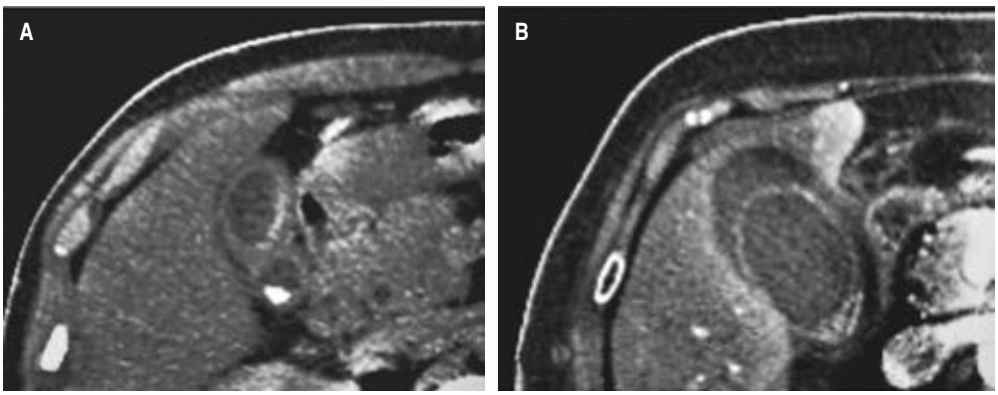

Figure 2:

Tomographic differences between typical cholecystitis and simple gallbladder wall thickening. ***A)*** *Typical cholecystitis gallbladder wall thickening.* ***B)*** *Gallbladder edema in a patient with viral disease without cholecystitis.*

needed. Clinical evolution after reoperation was satisfactory, and the patient was discharged without any other complication. The other patient presented transuterine bleeding with the subsequent abortion of nine weeks gestation. This patient was managed by the gynecology service for hemostatic control and subsequently discharged without any other complication. In the histopathological study, no signs of cholesterolosis or gallbladder inflammation secondary to gallstones were founded. During the hospital follow-up, two patients without surgical treatment died (6.5%). One patient was secondary to an acute transmural myocardial infarction and the other patient due to multiorgan failure after massive hemorrhagic dengue with antiphospholipid syndrome.

In the rest of the patients misdiagnosed as cholecystitis and sent for cholecystectomy, the gallbladder edema was reevaluated, and no indication for surgical treatment was found. Subsequently, the patients evolved satisfactorily and were discharged. The mean hospital stay was 9.38 days (range, 3-21 days). In those patients without surgical treatment, the mean hospital stay was 8.7 days (range: 3-12 days), and with surgical treatment was 17 days (range: 14-21 days). The causes of gallbladder edema misdiagnosed as cholecystitis were analyzed with the different diagnosis and pre-surgical variables, and no statistically significant difference was found. Besides, postsurgical complications were analyzed comparing with the pre-surgical diagnosis and no significant difference was found. In operated patients, the analyst of hospital stay was significantly larger than in patients without surgery with a statistical significant difference ($p = 0.004$). No complications after 30 days of follow-up were found.

Table 2: Definitive diagnosis of study patients underwent cholecystectomy.

Diagnosis	Surgery, n (%)
Viral hepatitis	4 (12.9)
Cirrhosis	1 (3.2)
Non-alcoholic liver disease	1 (3.2)
Hepatocellular carcinoma	0
Hemorrhagic dengue	0
Acute myocardial infarction	0
Pneumonia	0
Non-biliary pancreatitis	1 (3.2)
Total	7 (22.5)

DISCUSSION

Different systemic diseases may produce gallbladder wall thickening due to edema demonstrated by ultrasonography or CT scan which may be confused with acute cholecystitis. Some of these diseases are self-limited such as hepatitis A or dengue, but other may be fatal, so recognizing them on time can improve

the prognosis of these patients.[6,7,10,11] The presentation of these diseases is not that clear sometimes, and experience is required to rule out surgical treatment. In addition, there is a lack of evidence worldwide, especially in Latin America, where this diagnostic confusion has been less reported, making recognition of this situation more difficult.

Lithiasis cholecystitis is a prevalent disease reported in up to 10% of the population. Unlike lithiasis cholecystitis, gallbladder edema without lithiasis is a rare condition. In our series, the frequency of gallbladder wall thickening without cholecystitis was only 0.95% of all patients submitted to cholecystectomy. Due to this low frequency of wall thickening presentation in patients with typical symptoms, many surgical teams prefer to perform a cholecystectomy procedure due to the risk implying a silent lithiasis, with its subsequent complications.[12-14]

Unlike the mechanism seen in lithiasis cholecystitis where the luminal obstruction of the cystic duct produces mucous distention, ulceration, and infiltration of leukocytes, in patients with non-lithiasis gallbladder edema the mechanism occurs due to vascular permeability, inflammation, and increased portal venous pressure, although the exact pathophysiology is not clearly identified.[7,15]

In viral diseases such as hepatitis, viral infiltration as well as direct cellular liver damage are the cause of gallbladder edema. Hepatitis A, a common cause of acute viral disease, causes acute liver failure in 0.5% as well as thickening of the gallbladder wall as an extrahepatic involvement. In the study patients, the pathologies that were most mistaken for acute cholecystitis were liver diseases. In these cases, viral hepatitis was mostly self-limited, but in 12.9% of those submitted to surgical treatment, two had complications, and in one patient the complication was graded as severe due to 1,500 cc hemoperitoneum.[16]

In other viral diseases like dengue, it has been reported that in the early stages, capillary plasma leakage occurs, leading to thickening of the gallbladder wall in up to a third of them.[17] In this series, dengue cases occurred with a frequency of 32.25%, in all of them with thrombocytopenia and the presence of spontaneous hemorrhage; one patient with dengue hemorrhagic fever and antiphospholipid syndrome died. In these patients, the indication for surgical treatment was not clarified, probably due to the high risk of spontaneous hemorrhage induced by severe thrombocytopenia in the initial stage of the disease. In all these patients, the gallbladder edema decreased after the initial stage, and indication for surgical treatment was not subsequently mentioned.

Cardiovascular diseases also occur due to hepatic venous congestion. However, their relationship has not been fully established. In most cases, a relationship between cardiovascular diseases and gallbladder edema has been reported.[18] In this series, only two patients without surgical treatment had an acute myocardial infarction. One of them died from an acute transmural myocardial infarction, and the other patient had congestive heart failure as a sequel. In addition, one patient had fungal pneumonia. This etiology has not been reported as a cause of gallbladder wall thickening until now.

After the statistical analysis, the gallbladder wall thickening was evaluated, and no relation to surgical treatment was found. Regarding this finding, some studies show that gallbladder thickening due to edema is a direct indicator of plasma capillary leakage, especially in patients with dengue.[17] In present report, the relationship between the wall thickening and other variables showed no statistical significance.

In some cases of silent lithiasis, surgical treatment is indicated, which could be the cause of deterioration in these patients. In this series, there was no direct relationship between morbidity and mortality after surgical treatment, but a statistical significance difference with the hospital stay in postsurgical patients was found. In our experience, the indication of cholecystectomy must be very carefully chosen when dealing with these types of patients because the most important issue is the management of its underlying pathology. More prospective studies are required to increase information in this regard.

CONCLUSION

In the emergency surgical treatment of patients with suspected cholecystitis, it is mandatory to rule out gallbladder edema secondary to acute diseases. Surgical treatment in patients confused as acute cholecystitis can increase the length of hospital stay and therefore, costs.

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Ethical considerations: The Local Ethics Committee approved this protocol. Also, it was subjected to specific standards for these types of human studies. And it was also subjected to the regulations of the General Health Law on health research and with the Declaration of Helsinki, as well as institutional norms and instructions on scientific research.

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Puestow procedure: results in 19 years of institutional experience

Procedimiento de Puestow: resultados en 19 años de experiencia institucional

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ABSTRACT

Introduction: Chronic pancreatitis comprises a chronic progressive inflammatory syndrome of the pancreas, with irreversible damage and loss of exocrine and endocrine function. Pain is the most frequent symptom. Surgical treatment is superior compared to conservative or endoscopic therapies. **Objective:** To know the results obtained in the performance of a Puestow procedure for the management of chronic pancreatitis. **Material and methods:** All patients who underwent a Puestow procedure at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" in Mexico City, Mexico, between 2000 and 2019 were included. **Results:** We found 45 patients operated for a lateral pancreato-jejunal-anastomosis. The mean age was 46 years. There were 24 (53%) men and 21 (47%) women. In 42.2% of the patients there was a history of alcoholism and/or smoking. The most frequent indications for surgery were pain (46.7%) and recurrent acute pancreatitis (37.8%). Eighteen (40%) patients had recurrence of pain with a mean follow-up of 4.4 years. **Conclusions:** At present, there is no ideal surgical procedure for patients with chronic pancreatitis, the type of intervention to choose should reflect the balance between the success of the procedure and the inherent risks.

RESUMEN

Introducción: *La pancreatitis crónica comprende un síndrome inflamatorio progresivo crónico del páncreas, con daño irreversible y pérdida de la función exocrina y endocrina. El dolor es el síntoma más frecuente. El tratamiento quirúrgico es superior en comparación con terapias conservadoras o endoscópicas.* ***Objetivo:*** *Conocer los resultados obtenidos en la realización de un procedimiento de Puestow para el manejo de pancreatitis crónica.* ***Material y métodos:*** *Se incluyeron todos los pacientes que fueron sometidos a un procedimiento de Puestow, en el Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" en la Ciudad de México, México, entre los años 2000 a 2019.* ***Resultados:*** *Se encontraron 45 pacientes operados por una pancreatoyeyunoanastomosis lateral. La edad media fue de 46 años. Fueron 24 (53%) hombres y 21 (47%) mujeres. En 42.2% de los pacientes había antecedente de alcoholismo y/o tabaquismo. Las indicaciones más frecuentes para la cirugía fueron: dolor (46.7%) y pancreatitis aguda de repetición (37.8%). Dieciocho (40%) pacientes cursaron con recurrencia del dolor con un seguimiento medio de 4.4 años.* ***Conclusiones:*** *En la actualidad, no existe un procedimiento quirúrgico ideal para pacientes con pancreatitis crónica, el tipo de intervención a elegir debe ser el reflejo del equilibrio entre el éxito del procedimiento y los riesgos inherentes.*

INTRODUCTION

Chronic pancreatitis (CP) comprises a set of clinical manifestations secondary to a persistent inflammatory process of the pancreas.[1-3] The American Pancreas Association (AAP) defines CP as: "a chronic progressive scarring and inflammatory syndrome of the pancreas, with irreversible damage and loss of exocrine and endocrine function".[4]

CP shows an overall annual incidence of four to 23 cases per 100,000 population, and

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Table 1: General features of the study population. N = 45.

Variable	n (%)
Age (years)	46.44 ± 14.59
Male sex	24 (53.3)
Weight (kg)	61.83 ± 12.29
Body mass index kg/m^2	22 ± 4.11
Background history	
Type 2 diabetes mellitus	5 (11.1)
Alcohol consumption	19 (42.2)
Smoking	19 (42.2)
Tobacco rate	22.7 ± 30.35
Acute pancreatitis	37 (82.2)
Number of episodes of acute pancreatitis	5.2 ± 5.38
Pancreatic insufficiency	
Endocrine	14 (31.1)
Exocrine	9 (20.0)
Diarrhea	19 (40.0)
Previous imaging studies	
Transendoscopic ultrasound	20 (44.4)
Magnetic resonance imaging	18 (40.0)
Computerized tomography scan	44 (97.8)
Preoperative findings	
Calcifications	32 (71.1)
Location	
Head	16 (50.0)
Neck	1 (3.1)
Body	2 (6.2)
Uncinate process	1 (3.1)
Multiple	12 (37.5)
Preoperative findings	
Stones	15 (33.3)
Location	
Head	11 (73.0)
Neck	1 (7.0)
Multiple	3 (20.0)
Atrophy	14 (31.0)
Duct diameter	8.03 ± 3.94
Previous interventions	
Endoscopy	15 (33.3)
Type of procedure	
Lithotripsy	2 (13.33)
Pancreatic stent	4 (26.66)
Failed	2 (13.33)
Pain management	1 (6.66)
Sphincterotomy	3 (20.00)
Combined	3 (20.00)
Drainage of pancreatic pseudocyst	4 (8.90)
Pancreatic necrosectomy	2 (4.40)
Use of pancreatic enzymes	23 (51.10)
Chronic opioid use	4 (8.90)

Data are presented as mean ± standard deviation or median (p25-p75).
Categorical variables are presented as frequencies and percentages.
Study data.

a prevalence of 13 per 100,000.[5] Patients have a four times higher mortality risk compared to the general population, and a ten times higher probability of pancreatic malignancy.[6] Multiple etiologies are attributed to the development of CP. In the United States, alcohol consumption is responsible for 45% of reported cases. Other causes are included in the acronym TIGAR-O (toxic/metabolic, idiopathic, genetic, autoimmune, recurrent severe acute pancreatitis, obstructive).[7]

One hypothesis linked to hereditary pancreatitis suggests that CP begins with an episode of acute pancreatitis. This model is known as SAPE (sentinel acute pancreatitis event).[8] Abdominal pain is the most frequent symptom of CP. Different causal mechanisms of pain have been proposed including inflammation, increased pressure within the duct or parenchyma, ductal stenosis and/or obstruction by calculi, complications such as pseudocysts or phlegmons, or extra-pancreatic complications such as portal thrombosis, biliary or duodenal stenosis and peptic ulcers.[9] It has been demonstrated that there are also central and peripheral sensitization mechanisms that cause changes at the level of pancreatic innervation.[10]

The World Health Organization (WHO) recommends, for pain management, to start with non-opioid medications, and if there is no improvement move upwards to weak opioids such as tramadol followed by stronger opioids.[11] Some groups suggest that endoscopic or interventional treatment is the first step in the treatment of patients with CP; however, not all patients are candidates for this type of approach.[12,13]

Recently, the surgical approach has been shown to be superior for the treatment of CP compared to conservative or endoscopic therapies.[14-16]

The Puestow procedure was first described in 1958 by Partington and Rochelle. It consists of a drainage procedure performing a longitudinal latero-lateral pancreato-jejunal-anastomosis. This type of surgery is the one of choice when the main pancreatic duct is dilated (5 mm minimum diameter),[17] in the absence of an inflammatory mass in the head of the pancreas or obstruction of the bile duct.[18]

Table 2: Perioperative and follow-up features.

	n (%)
Indication of Puestow procedure	
Pain	21 (46.7)
Conduit disconnected	3 (6.7)
Pancreatic insufficiency	2 (4.4)
Episodes of acute pancreatitis	17 (37.8)
Intraoperative findings	
Hard consistency of the pancreas	14 (31.1)
Stone extraction	20 (44.4)
Location	
Head	9 (45)
Neck	2 (10)
Tail	2 (10)
Multiple	7 (35)
Atrophy	16 (35)
Duct diameter	8.19 ± 2.29
Postoperative evolution	
Restart of oral feeding	
≥ 48 hours	12 (27)
≥ 72 hours	18 (40)
4 to 7 days	14 (31)
> 7 days	1 (2)
Use of drainage	45 (100)
Pancreatic fistulae	0 (0)
Days of postoperative hospitalization	7 (5-9)
Complications due to ACCORDION	14 (31.1)
Grade	
Mild	8 (58)
Moderate	3 (21)
Severe	3 (21)
Follow-up	
Recurrence of pain	18 (40)
Use of opioids	5 (11)
De novo pancreatic insufficiency	20 (44)
Endocrine insufficiency	8 (18)
Exocrine insufficiency	17 (38)
Use of pancreatic enzymes	33 (73)
Hospital readmission	4 (9)
Follow-up (years)	4.44 ± 2.29

Data are presented as mean ± standard deviation or median (p25-p75).
Categorical variables are presented as frequencies and percentages.
Study data

It has been described as technically safe and efficient procedure, with low morbidity (20%) and operative mortality (1%).[19] Pancreatic leaks develop in less than 5% of cases.[20] Endocrine and exocrine functions are usually not compromised because there is no major resection of pancreatic tissue. In Mexico, González and collaborators described in 1996 the results obtained in 49 patients submitted to a pancreato-jejunal-anastomosis because of CP. With a mean follow-up of 6.5 years, they found that 98% were pain free.[21]

Dite and colleagues demonstrated in the first randomized controlled trial that there is better pain control at five years in patients who underwent surgery (34-52%) compared to those who received endoscopic treatment (15-46%).[22] Currently, there is no consistency in the different guidelines regarding the timing and choice of CP treatment.

The main objective of this study is to know the results obtained in the performance of a Puestow procedure for the surgical management of CP, in 19 years of experience in a high-volume center in Mexico City.

MATERIAL AND METHODS

All patients who underwent a Puestow type surgical procedure for the treatment of CP at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" between 2000 and 2019 were included. For the selection of subjects, a list of patients who had undergone pancreatic duct to small bowel bypass surgery with open or laparoscopic approach, according to the ICD-10 procedure code, was requested to the Statistics Department.

A review of the physical and electronic files was carried out and filtered data that met the inclusion criteria in an electronic database, which included the proposed variables were collected. A descriptive and comparative statistical analysis was performed depending on the type of variable. For the continuous variables of age, weight, body mass index (BMI), smoking rate, episodes of acute pancreatitis (AP), pancreatic duct diameter and follow-up in years of the operated patients, the mean, median, standard deviation and 95% confidence intervals were calculated.

Frequency values and percentages for categorical variables such as male sex, type 2 diabetes mellitus (T2DM), alcohol consumption, smoking, AP, endocrine and exocrine pancreatic insufficiency, and imaging study results such as

transendoscopic ultrasound (USTE), magnetic resonance imaging (MRI) and computed axial tomography (CT) scan were obtained. Other categorical variables included preoperative and intraoperative findings such as pancreatic calcifications, presence of stones, pancreatic atrophy, as well as previous interventions such as endoscopy, pancreatic pseudocyst drainage, necrosectomy, and use of pancreatic enzymes.

Variables related to postoperative evolution were analyzed, such as the use of drains, development of pancreatic fistulas, days of hospitalization and complications according to the ACCORDION scale, and follow-up variables such as recurrence of pain, use of opioids, development of de novo pancreatic insufficiency, hospital readmissions and follow-up in years were also analyzed. In the bivariate Mann-Whitney U analysis, the IBM SPSS Statistics v24 program was used. A p-value of less than 0.05 was considered statistically significant.

All those patients who had been operated by the Puestow procedure for a cause other than chronic pancreatitis were excluded from the study, as well as those who were operated in combination with any other type of pancreatic resection surgical procedure. Patients who were not operated on at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" and who did not have a complete physical or electronic file for data collection were eliminated from the study database.

RESULTS

We found 45 patients operated on by a Puestow procedure, secondary to the diagnosis of CP. The mean age was 46 years. There were 24 (53%) men, 21 (47%) women, and the mean body mass index was 22.71 kg/m^2. Of the patients with CP, five had a diagnosis of T2DM (11.1%). Regarding episodes of acute pancreatitis prior to surgery, 37 (82.2%) had presented at least one episode, and the overall mean episodes was 5.2 *(Table 1)*.

Of the patients (19 of 45), 42.2% had a history of alcohol consumption or a history of alcoholism, and 42.2% had a history of smoking, with a mean smoking index of 22.7 *(Table 1)*. Regarding endoscopic procedures prior to surgery, at least 15 patients (33.3%) underwent some type of intervention for the treatment of CP. Fourteen cases (31.1%) were detected with endocrine insufficiency, characterized by T2DM following the diagnosis of CP, while 19

Table 3: Bivariate analysis of postoperative pain recurrence.

Parameters	Recurrence of pain (N = 18) n (%)	No recurrence of pain (N = 27) n (%)	p
Age (years)	49.39 ± 11.96	44.48 ± 16.02	0.274
Male	12 (66.7)	12 (44.4)	0.143
Body weight (kg)	63.59 ± 10.63	60.65 ± 13.35	0.439
Previous acute pancreatitis	16 (88.9)	21 (77.8)	0.350
History of smoking	9 (50.0)	10 (37.0)	0.388
History of alcoholism	10 (55.6)	9 (33.3)	0.139
History of endoscopic surgery	6 (33.3)	9 (33.3)	0.999
Atrophic pancreas*	7 (38.9)	8 (29.6)	0.600
Hard pancreas	6 (33.3)	8 (29.6)	0.999
Post-surgical pancreatic insufficiency	11 (61.1)	9 (33.3)	0.066

Data are presented as median (p25-p75). Bivariate Mann-Whitney U analysis. * Intraoperative findings. Study data.

Table 4: Bivariate analysis of postoperative de novo pancreatic insufficiency.

Parameters	*De novo* pancreatic insufficiency (N = 20) n (%)	Non *de novo* pancreatic insufficiency (N = 25) n (%)	p
Previous acute pancreatitis	17 (85)	20 (80)	0.67
Atrophic pancreas*	6 (30)	9 (36)	0.71
Hard pancreas	8 (40)	6 (24)	0.90
Pancreatic duct diameter	3 (3-10)	4 (3-12)	0.47
Stone extraction	7 (35)	13 (52)	0.26

Data are presented as median (p25 -p75). Bivariate Mann-Whitney U analysis. * Intraoperative findings. Study data.

patients (40%) reported diarrhea; however, only nine (20%) had a diagnosis of exocrine insufficiency.

In the imaging studies, 32 (71.1%) patients with calcifications were considered as pathognomonic findings of CP, most of them located in the head of the pancreas (n = 16.50%), 12 (37.5%) within multiple localizations and the rest presented a modal distribution in the neck (n = 1, 3.1%), body (n = 2, 6.2%) and uncinate process (n = 1, 3.1%), respectively. The mean duct diameter reported was 8.03 mm *(Table 1)*.

In 15 (33.3%) patients, the presence of lithiasis was reported, located in the head (n = 11, 73%), neck (n = 1, 7%) and in multiple parts of the pancreas (n = 3, 20%). Fourteen (31%) of the subjects presented atrophy of the pancreatic gland *(Table 1)*. The most frequent indications for performing a Puestow procedure reported included pain in 21 patients (46.7%), repeated episodes of AP in 17 (37.8%) cases, three (6.7%) because of a disconnected duct and two (4.4%) for pancreatic insufficiency. Among the intraoperative findings, the pancreas was described as having a hard consistency in 14 patients (31%). The average diameter of the pancreatic duct reported was 8.19 mm and in 20 (44.4%) patients stones were extracted from the duct. Pancreatic atrophy was described in 16 cases (35%) *(Table 2)*.

The average hospital stay was seven days, no pancreatic fistulas were reported, and no patient required intensive care. All patients (100%) underwent some type of drainage during surgery. Regarding complications, 14 (31%) patients in total were characterized according to the ACCORDION surgical complication severity classification system as mild in eight (58%) patients, moderate in three (21%) and severe in three (21%) *(Table 2)*.

In the follow-up of the patients, 18 (40%) had recurrence of pain; due to this, five (11%) patients reported regular use of opioids despite the surgical procedure. On the other hand, 20 (44%) patients presented de novo pancreatic insufficiency, among which eight (18%) developed endocrine symptoms such as serum glucose alterations and 17 (38%) presented exocrine insufficiency manifesting diarrhea or steatorrhea. Secondary to these symptoms, 33 (73%) required pancreatic enzymes administration *(Table 2)*. The hospital readmission rate was 9% (n = 4). The mean follow-up of patients was 4.4 years.

In the bivariate analysis against recurrence of pain, age showed a p-value = 0.274, male sex a p = 0.143 and weight a p = 0.439 *(Table 3)*. Regarding patient history, the relationship with a history of alcoholism was p = 0.139 and smoking was p = 0.388, as well as in those with a history of acute pancreatitis and endoscopic procedures, the p-value was 0.350

and 0.999, respectively. The development of de novo pancreatic insufficiency after surgery showed a p = 0.67 against the history of acute pancreatitis, while according to the intraoperative findings, the presence of atrophy shoed a p = 0.71, a hard consistency of the pancreas with a p = 0.90, diameter of the duct p = 0.47 and finally compared to the extraction of stones a p = 0.26 *(Table 4)*. However, no significant values were obtained in the bivariate analysis.

DISCUSSION

Chronic pancreatitis (CP) is a complex disease that involves a physical, emotional, and financial burden for the patient, physicians, and the health care system. Our retrospective series included 45 patients who underwent a Puestow procedure as a surgical treatment described in CP. This review analyzed the results obtained over 19 years of experience, and despite being a retrospective analysis, there is no other current series described in Mexico that analyzes the experience in relation to this type of procedure. Different surgical techniques of drainage, resection or combined techniques have been published;[23-25] however, the Puestow procedure seems to offer lower morbidity and mortality rates by sparing pancreatic tissue and preserving functional organs such as the duodenum.

Alcohol consumption and smoking have been strongly identified as factors capable of altering the genetic-environmental relationship of patients, playing an important risk role in the evolution and development of CP. It is known that people with a history of alcoholic pancreatitis have a 12.5% risk of developing CP, but to date only in animal models attempts have been made to understand the pathophysiological and genetic mechanisms that predispose to the development of CP, including the SAPE model described above.[8] An important finding in our series was that 42.2% of patients had a history of smoking and/or alcohol consumption. However, it was not possible to directly relate these factors to the development of CP.

The choice of patient to undergo a Puestow procedure as part of the treatment of CP should consider the anatomic context, with a dilated pancreatic duct (> 5 mm) and absence of an inflammatory mass of the pancreatic head or bile duct obstruction.[11,18] The pathognomonic radiological findings of CP and the intraoperative findings in our series are in agreement with what has been suggested in other studies, since the mean diameter of the pancreatic duct between both findings was 8.11 mm, added to the presence of calcifications in the gland and stones in the pancreatic duct.

Another important aspect to highlight was the absence of pancreatic fistulas as a postoperative complication, and when analyzing that the consistency of the gland was hard in all the operative notes evaluated, it is suggested that this variable may play an important predictive role in the development of pancreatic fistulas; however, randomized studies are needed to validate this hypothesis.

Risk factors for developing pancreatic fistulae have been described with significant results in patients undergoing pancreatoduodenectomy. Zunxiang et al, based on the International Study Group on Pancreatic Surgery (ISGPS) definition, described that 39.1% of patients with soft pancreas developed grade B or C fistulae, versus patients who had a hard pancreas ($p < 0.0001$).[26]

Success rates for short-term pain relief after a Puestow procedure have been reported in 80-85% of patients and in the long term in 70-80% during five to 10 years of follow-up.[9,27] However, higher rates of pain recurrence (50%) have been described in those patients with a pancreatic duct diameter < 7 mm.[5]

In one of the largest series included in the review by Gouma DJ and his colleagues,[19] and described by Sakorafas GH and colleagues,[28] on the results obtained at the Mayo Clinic in the surgical treatment of CP, in 120 patients who underwent lateral pancreato-jejunal-anastomosis, the group described that the pain relief rate was 81% with a follow-up of up to eight years. In our study, 60% had no recurrence of pain, with a mean pain recurrence time of up to 102 weeks and an average follow-up of 4.4 years after surgery.

In the bivariate analysis of the recurrence of this symptom against demographic variables such as age, sex and body weight, as well as

against the history of smoking, alcoholism and the performance of endoscopic procedures prior to surgery, no statistically significant differences were seen that could prove the relationship of these variables as predictors of recurrence of postsurgical pain after a Puestow procedure. However, as evidenced in our results, 46.7% were taken to surgery under the indication of pain, followed by the history of repeated acute pancreatitis (37.8%), so this means that there may be a bias in the description of pain as a presurgical indication, due to the subjectivity of this symptom that is part of the clinical manifestations during any episode of acute pancreatitis.

The development of pancreatic insufficiency, manifested by T2DM and/or de novo diarrhea/steatorrhea in the postoperative course of a decompressive procedure such as Puestow's, are lower compared to that reported with other resection procedures, and in relation to our results it was like that reported in the series of Sakorafas and his group[28] although at a lower rate (diabetes 18 vs. 33% and steatorrhea 38 vs. 40%, respectively). However, there were no statistically significant results when we compared the development of de novo pancreatic insufficiency versus the intraoperative findings of the pancreas that could predispose to the development of this complication.

CONCLUSIONS

It is clear then that two of the goals in the treatment of CP are pain relief and improvement in the quality of life of patients. If medical treatment fails to mitigate pain, current literature suggests that surgical treatment has shown better results compared to medical-endoscopic therapies. These types of surgeries, such as the Puestow procedure and others that include pancreatic resection, are performed with low morbidity and mortality in high volume centers such as the Instituto Nacional de Nutrición y Ciencias Médicas "Salvador Zubirán" (National Institute of Nutrition and Medical Sciences "Salvador Zubirán").

At present, there is not an ideal surgical procedure for patients with CP, and the type of intervention chosen should reflect the balance between the success of the procedure and the inherent risks. Although pain relief was not achieved in 40% of the cases, which is comparable to that reported in other series, the success achieved should be considered in the context of the preoperative status of the patients, mostly in those who have failed medical, radiological and/or endoscopic treatment, in addition to the fact that chronic pain is disabling and affects the quality of life of people diagnosed with CP.

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Results of radiofrequency ablation in the treatment of hepatocellular carcinoma in Veracruz, Mexico

Resultados de la ablación por radiofrecuencia en el tratamiento de carcinoma hepatocelular en Veracruz, México

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Keywords: Hepatocellular carcinoma, radiofrequency ablation, survival, body mass index.

Palabras clave: *Carcinoma hepatocelular, ablación por radiofrecuencia, supervivencia, índice de masa corporal.*

ABSTRACT

Introduction: Hepatocellular carcinoma is the most frequent malignant primary hepatic tumor. Only 15% of patients will undergo surgical resection or transplantation, so local ablation is an alternative treatment with advantages. **Objective:** To evaluate the efficacy of radiofrequency ablation in our population. **Material and methods:** Retrospective study of patients with hepatocellular carcinoma who underwent radiofrequency ablation. Sociodemographic variables, tumor, stage (Child-Pugh, OKUDA, BCLC, CLIP, MELD and ALBI), use of sorafenib and survival were investigated. **Results:** We analyzed 16 patients (mean age 71.25 years) with concomitant pathology in 87.5%. Cirrhosis was present in 62.5% of the patients, 56.3% were in Child-Pugh A class and 6.3% in B class. 62.5% were OKUDA I, 37.5% were in BCLC stage A, 56.3% in BCLC B and 6.3 % in BCLC C. 56.3% were staged as CLIP 0, MELD 8.44 ± 2.15 and ALBI -2.54 ± 0.42. Mean tumor size was 5.81 ± 2.81 cm and sorafenib was administered in 25%. Median survival was 37.7 months, one-year survival was 58.5% and five-year survival was 23.4%. Body mass index was associated with low survival (p = 0.031). **Conclusion:** Our study indicates that radiofrequency ablation is used in patients with hepatocellular carcinoma in various stages and sometimes in tumors larger than 5 cm, making survival lower to that seen in other studies.

RESUMEN

Introducción: *El carcinoma hepatocelular es el tumor primario hepático maligno más frecuente. Sólo 15% de los pacientes será sometido a resección quirúrgica o trasplante, por lo que la ablación local es un tratamiento alternativo con ventajas.* ***Objetivo:*** *Evaluar la eficacia de la ablación por radiofrecuencia en nuestra población.* ***Material y métodos:*** *Estudio retrospectivo de pacientes con carcinoma hepatocelular sometidos a ablación por radiofrecuencia; se investigaron variables sociodemográficas, del tumor, estadio (Child-Pugh, OKUDA, BCLC, CLIP, MELD y ALBI), uso de sorafenib y supervivencia.* ***Resultados:*** *Se analizaron 16 pacientes (edad media 71.25 años) con patología concomitante en 87.5%. El 62.5% de los pacientes padeció cirrosis, 56.3% Child-Pugh A y 6.3% B. El 62.5% fueron OKUDA I, 37.5% estadio BCLC A, 56.3% BCLC B y 6.3 % BCLC C; 56.3% se estadificó CLIP 0, MELD 8.44 ± 2.15 y ALBI -2.54 ± 0.42. El tamaño tumoral fue 5.81 ± 2.81 cm y sorafenib en 25%. La supervivencia media fue 37.7 meses, supervivencia al año 58.5% y a cinco años 23.4%. El índice de masa corporal se asocia a baja supervivencia (p = 0.031).* ***Conclusión:*** *Nuestro estudio indica que la ablación por radiofrecuencia se usa en pacientes con carcinoma hepatocelular en estadios variados y en ocasiones en tumores mayores a 5 cm, haciendo que la supervivencia sea menor a otros estudios.*

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Abbreviations:
HCC = hepatocellular carcinoma.
RFA = radiofrequency ablation.
MWA = microwave ablation.
PEI = percutaneous ethanol injection.
LSA = laser ablation.
CRA = cryoablation.
HIFU = high intensity focused ultrasound.
INR = International Normalized Ratio.
ALT = alanine aminotransferase.
AST = aspartate aminotransferase.
ALP = alkaline phosphatase.
AFP = alpha fetoprotein.
CLIP = Italian Liver Cancer Program.
BCLC = stages of liver cancer in the Barcelona clinic.
MELD = model for end-stage liver disease.
ALBI = albumin-bilirubin index.
BMI = body mass index.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most frequent primary malignant liver tumor worldwide.[1] It is the fifth most common neoplasm in men and the eighth most common in women and it represents the third leading cause of cancer-related mortality in the male population.[2] Treatments for HCC include liver transplantation, surgical resection, and local ablation methods. Liver transplantation is limited, given the scarcity of donors.[3] Unfortunately, only 5-15% of newly diagnosed HCC patients will undergo potentially curative resection or liver transplantation. Surgical resection is not feasible if multifocal disease is present, if the hepatic functional reserve is insufficient, or if the proximity of the tumor to vascular or biliary structures precludes achieving sufficient margins.[4] In the last 20 years, local ablation has become an important alternative treatment for smaller HCC and in cases considered surgically unresectable. Many different modalities have been proposed and accepted for ablation procedures; these include radiofrequency ablation (RFA), microwave ablation (MWA), percutaneous ethanol injection (PEI), laser ablation (LSA), cryoablation (CRA), high-intensity focused ultrasound (HIFU) and combinations of all these.[3] RFA is used to treat small (< 5 cm) or recurrent primary tumors in patients with poor hepatic reserve (Child Pugh B and/or C), and non-significant coagulopathy. RFA has advantages such as being a minimally invasive method applied percutaneously, for repeated use in recurrent hepatocellular carcinoma, and causing minimal damage to the hepatic parenchyma, and a with low rate of major complications.[5] The aim of this study is to evaluate the efficacy of RFA in our study population.

MATERIAL AND METHODS

A retrospective study was conducted in which patients with a histopathological diagnosis of HCC undergoing RFA, with complete clinical records, during the period from January 1, 2013, to January 1, 2018, at the High Specialty Medical Unit of the *Hospital de Especialidades No. 14*, and at the *Hospital Regional de Alta Especialidad de Veracruz*, Mexico, were included, after having obtained the authorization by the Local Ethics and Research Committee.

Age, sex, body mass index (BMI), presence of concomitant disease (diabetes mellitus, arterial hypertension, viral hepatitis, and liver cirrhosis) and laboratory values at diagnosis were recorded, including hemoglobin level, platelet count, coagulation times, International Normalized Ratio (INR), and serum creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, total proteins, albumin, and alpha fetoprotein (AFP). Variables corresponding to ablation and related to the lesion (size) and the use of sorafenib were evaluated. Patients were classified according to Child-Pugh classification,[6] the Italian Liver Cancer Program (CLIP),[7] OKUDA scale,[8] the Barcelona Clinic Liver Cancer Stages (BCLC),[8] the model for end-stage liver disease (MELD)[9] and the albumin-bilirubin index (ALBI).[10] Patients with a final diagnosis other than HCC or without a complete or illegible clinical record were excluded. Survival was calculated from diagnosis until death or loss to follow-up.

Under ultrasound guide, the StarBurst SDE RFA Device (AngioDynamics, N.Y., USA), an electrode was inserted in the center of the tumor, which was designed to produce spherical ablations in small lesions with difficult access, applying a high frequency alternating current from the generator. The electrosurgical radiofrequency generator used was a 1500X

model, which supplies radiofrequency energy for partial or complete coagulation and soft tissue ablation, with a power of 250 watts combined with the saline infusion pump. The radiofrequency waves were administered for an average time of 10 minutes, and, after a pause, the procedure was repeated to ensure necrosis.

Statistical analysis: Mean, standard deviation and range were used to describe continuous variables, and frequencies and percentages for categorical variables. Survival was calculated using the Kaplan-Meier test and the Log-Rank test (Mantel-Cox) to compare survival between groups. The estimated mean survival was recorded in months. ROC curve was performed to determine the area under the curve and the cut-off points with sensitivity and specificity to predict those values that influence survival. Data were analyzed using the SPSS 25 software (SPSS, 2016, Chicago, USA). A p-value < 0.05 was considered statistically significant.

RESULTS

Sixteen patients were analyzed, of whom 10 (62.5%) were women and six (37.5%) men with a mean age of 71.25 ± 5.8 years (59-80 years), and a mean BMI of 25.54 ± 4.22 kg/m^2 (17.8-33.7). Seven (43.8%) had type 2 diabetes mellitus, four (25%) arterial hypertension, and six (37.6%) chronic viral hepatitis; of the latter, five (31.3%) were carriers of hepatitis C and one (6.3%) of hepatitis B. Ten patients (62.5%) had liver cirrhosis. Laboratory values are shown in *Table 1*. Based on the ablation approach, 12 (75%) were open, two (12.5%) laparoscopic and two (12.5%) percutaneous. The mean tumor lesion size was 5.81 ± 2.81 cm (3-13), of which 10 (62.5%) had a lesion smaller than 5 cm and six (37.5%) had a lesion larger than 5 cm. Nine patients (56.3%) were classified as Child-Pugh A and one (6.3%) a Child-Pugh B class. *Table 2* shows the staging of patients according to OKUDA, BCLC, CLIP, MELD and ALBI. Four patients (25%) received sorafenib treatment and 12 (75%) did not. Complications associated with RFA occurred in three cases (18.75%) including two (12.5%) with transient liver failure and one (6.25%) with pneumonia. The mean estimated survival (Kaplan-Meier) was 37.7 ± 10.2 months (95% CI, 17.68-57.84) and the estimated median survival was 24 months. Actuarial survival of all patients at 1 year was 58.5% and at 5 years was 23.4%.

Factors associated with survival. Deceased patients had a lower BMI (23.3 ± 3.5 kg/m^2) compared to living patients (27.7 ± 3.7 kg/m^2) ($p = 0.031$ by Student's t test). None of the other variables recorded had a significant difference in patient survival as shown in *Table 3*. ROC curve

Table 1: Laboratory results at the time of diagnosis of hepatocellular carcinoma.

Parameter	
Hemoglobin g/dl	12.04 ± 1.4 [10.8-14.3]
Platelets mm^3 10x^9	126.22 ± 58.97 [61.0-236.0]
Prothrombin time	13.47 ± 2.32 [10-18.90]
International Normalized Ratio	1.12 ± 14 [0.95-1.45]
Creatinine mg/dl	0.99 ± 0.22 [0.70-1.50]
ALT IU/l	45.88 ± 15.89 [31-78]
AST IU/l	46.88 ± 9.15 [29-60]
Alkaline phosphatase UI/l	163.71 ± 52.81 [114-266]
Total bilirubin mg/dl	0.83 ± 3.00 [0.26-1.40]
Total protein mg/dl	13.50 ± 2.34 [10-18.90]
Albumin g/dl	3.86 ± 41.00 [2.80-4.30]
Alpha fetoprotein	4,026.71 ± 14,132.07 [2.50-56,838.84]
Model for end-stage liver disease	8.44 ± 2.15 [6-13]
Albumin-to-bilirubin ratio	-2.54 ± 0.42 [-3.14 to -1.51]

Table 2: Staging of patients submitted to radiofrequency.

Stadium	n (%)
OKUDA	
I	10 (62.5)
II	6 (37.5)
BCLC	
A	6 (37.5)
B	9 (56.3)
C	1 (6.3)
CLIP	
0	9 (56.3)
1	5 (31.3)
2	2 (12.5)
MELD	
< 10	11 (68.75)
> 10	5 (31.25)
ALBI	
Grade 1	9 (56.3)
Grade 2	7 (43.8)

OKUDA I: none positive, II: one or two positive, ALBI grade 1: ≤ -2.60, grade 2: -2.60 to ≤ -1.39. BCLC = liver cancer in Barcelona clinic, CLIP = Italian liver cancer program, MELD = model for end-stage liver disease, ALBI = albumin-bilirubin index.

analysis of BMI was performed, finding an area under the curve of 0.79 (95%, CI 0.56-1.0) (p = 0.046) with a cutoff point of 22.06 (sensitivity 100%, specificity 38%). However, there was no difference in survival estimated by the Kaplan-Meier method (Log-Rank) when applying the cutoff point < 22.06 kg/m^2 with a mean of 16.0 ± 10.53 months (0.0-36.6) and > 22.06 kg/m^2 with a mean of 47.4 ± 12.2 months (23.5-71.3). In this case, the p-value was 0.20.

DISCUSSION

The results of our study indicate that patients who underwent RFA have lower survival at one and five years, compared to other publications that applied the same treatment. However, we found that almost 40% of the lesions were larger than 5 cm and most of the patients were at more advanced stages than those recommended by the BCLC for RFA. There are studies with superior survival to our results when patients present lesions smaller than 5 cm. Lencioni and collaborators[11] evaluated cirrhotic patients (Child-Pugh A and/or B class), early stage of HCC (BCLC A, lesions smaller than 5 cm) submitted to RFA, obtaining a survival of 97% at one year and 41% at five years, with a median of 49 months.[11] Kim and his group,[12] in patients who underwent RFA, obtained 59.7% survival at five years, with significant predictors for lower survival being the patient age, Child-Pugh in class B and the presence of extrahepatic recurrence. In turn, Lee and associates[13] evaluated 162 patients with more than three tumors with a maximum diameter of 5 cm, finding a five-year survival of 67.9%, where the most significant predictors of lower survival rate were Child-Pugh class B, elevated AFP levels and the presence of portal hypertension. Even though these studies recorded higher survival rates than ours, there are others in which survival is like ours with lesions larger than 5 cm and patients in intermediate stages of BCLC. Among these studies are that of Nouso and collaborators[14] which included 91 patients in intermediate stages of BCLC (B1, B2 and B3) and in which survival of 73.8% at three years and 57.3% at five years was achieved. Also, the study of Dai W and associates,[14] which involved 63 patients who underwent RFA with a mean lesion size of 6.0 cm (5.2-8.0), obtaining a survival rate at one, three and five years of 93.3, 70.5 and 20.9%, respectively, with a median survival of 39.8 months. And finally, the study of Yin X and associates[15] that analyzed 49 cases with tumor size between 3-7 cm and survival rate at one year of 75.8% and at five years of 15.4%. The use of RFA in intermediate stages and lesions larger than 5 cm with five-year survival rates like ours (around 20%) may justify the use of this resource in our population, which has been reported since 2006.[16]

There are studies that support that BMI has a significant impact on the prognosis of patients with HCC. Qinggan Li and associates[17] analyzed 379 patients, where those with a BMI less than 23 kg/m^2 had a survival of 353.9 days (316.9-391.0) and with a BMI greater than 23 kg/m^2 they found a survival rate of 571.8 days (532.3-611.4). Likewise, Xiyu Liu and

associates[18] evaluated 136 patients, obtaining higher survival rates in patients with a BMI less than 25 kg/m^2 of 95% at one year and 16% at five years than in those with BMI greater than 25 kg/m^2 (p = 0.048). Our study found an estimated median survival of 1,410 days (47 months) in patients with BMI greater than 22.06 kg/m^2; furthermore, these patients did achieve survival records greater than five years. Unfortunately, we were unable to confirm this association as a risk factor by statistical analysis (ROC curve/Cox regression), possibly because of our sample size. Our study points out that the use of sorafenib after RFA influences a longer survival rate than in those patients who did not receive it. This agrees with the series by Feng et al[19] that included 64 patients with single therapy (RFA) and 64 with combined therapy (RFA + sorafenib), finding a median survival rate of 118.6 weeks and 161.8 weeks, respectively; and with the study by Quanyou and associates[20] that analyzed 50 patients with single therapy and 40 with combined therapy, finding a tumor-free survival rate of 8.4 and 12.3 months, respectively, with a median follow-up of 35 months.

Table 3: Survival estimates by the Kaplan-Meier method.

Variable	Mean ± SD, months	95% CI	Survival at one year (%)	Five-year survival (%)	p-value
Body mass index	16.00 ± 10.53	0-36.65	34.17	NR	0.2
< 22.06	47.43 ± 12.2	23.51-71.35	64.70	48.55	
> 22.06					
Type 2 diabetes mellitus					
No	44.50 ± 15.66	13.79-75.2	66.45	44.40	0.73
Yes	23.31 ± 5.7	12.13-34.49	53.33	NR	
Arterial hypertension					
No	41.94 ± 13.7	15.08-68.80	83.30	27.78	0.28
Yes	14.31 ± 3.22	8-20.63	56.14	NR	
Viral hepatitis					
No	37.93 ± 13.00	12.43-63.42	66.66	35.56	0.91
Yes	26.16 ± 7.69	11.08-41.24	66.67	NR	
Liver cirrhosis					
No	15.66 ± 4.04	7.74-23.59	67.50	33.75	0.82
Yes	33.83 ± 10.07	14.09-53.57	66.10	NR	
Lesion size					
< 5 cm	21.75 ± 6.08	9.83-33.66	53.57	NR	0.25
> 5 cm	51.42 ± 14.03	23.92-78.92	71.43	53.57	
OKUDA					
I	40.42 ± 11.82	17.25-63.59	72.92	27.34	0.43
II	14.16 ± 4.05	6.21-22.12	50.00	NR	
Alpha fetoprotein					
< 200	34.37 ± 11.2	12.40-56.34	60.61	22.73	0.68
> 200	14.25 ± 4.95	4.53-23.96	50.00	NR	
Sorafenib					
No	20.00 ± 3.68	12.78-27.21	66.45	NR	0.93
Yes	38.04 ± 12.45	13.63-62.44	58.74	29.37	

OKUDA I no positive criteria, II one or two positive, SD = standard deviation, NR = not recorded.

There is very little information on the use of RFA in patients with HCC in our country. Mondragón-Sánchez and collaborators[21] published the use of RFA in a variety of liver tumors, the majority being HCC (n = 18) with a mean lesion size of 5.5 cm, a one-year survival rate of around 20% and an estimated mean of 18 months. Subsequently, Ladrón de Guevara and associates[22] published on the use of RFA in two patients with HCC with a one-year survival of 40 months and an estimated mean survival of eight months. Recently, Cisneros Garza and associates[23] reported the use of RFA in 13 patients, six in stage A, seven in stage B and one in stage C class without specifically reporting their survival. The results of our study evidenced a better survival rate both in the estimated mean time and the percentage of survival at one year without being able to compare it at five years, since it was not reported. For this reason we assume that this is the Mexican study of RFA for HCC with the highest mean follow-up published to date.

CONCLUSIONS

RFA in Veracruz, Mexico, is used in patients with HCC at various stages and in tumor lesions of various dimensions, with mixed results, depending on the characteristics to be studied. The results of RFA in Veracruz, Mexico, may be the largest follow-up of this therapeutic modality in our country. Given the size of the sample, it is not possible to establish risk factors that may significantly influence this therapy.

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ORIGINAL ARTICLE

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Irritable bowel syndrome following laparoscopic cholecystectomy. A prospective cohort study

Síndrome de intestino irritable posterior a colecistectomía laparoscópica. Estudio de cohorte prospectivo

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Keywords:
Cholecystectomy, laparoscopy, diarrhea, irritable bowel syndrome.

Palabras clave:
Colecistectomía, laparoscopia, diarrea, síndrome de intestino irritable.

ABSTRACT

Introduction: Laparoscopic cholecystectomy is one of the most frequently performed digestive surgical procedures in the world. Irritable bowel syndrome has been reported to occur more frequently in patients submitted to cholecystectomy, especially the diarrhea-predominant subtype. **Objectives:** To evaluate the presence of irritable bowel syndrome before and after laparoscopic cholecystectomy. **Material and methods:** A prospective cohort study, with control group. Irritable bowel syndrome was defined according to ROMA IV criteria, and was followed up at one, three, six, and 12 months postoperatively in search of symptomatology. The statistical analysis was performed with Fisher's exact one-way test. **Results:** Out of 166 patients, six presented an irritable bowel syndrome beyond six months postoperatively. In the control group there was two new cases at the end of follow-up. There were eight cases of post-cholecystectomy syndrome. **Conclusions:** It was not possible to establish a relationship different from chance between patients who underwent laparoscopic cholecystectomy and the presence of irritable bowel syndrome in any of its variants.

RESUMEN

Introducción: *La colecistectomía laparoscópica es uno de los procedimientos quirúrgicos digestivos que se realiza con más frecuencia en el mundo. Se ha descrito que el síndrome de intestino irritable se presenta con mayor frecuencia en pacientes sometidos a colecistectomía, sobre todo el subtipo con predominio de diarrea.* ***Objetivos:*** *Evaluar la presencia de síndrome de intestino irritable antes y después de una colecistectomía laparoscópica.* ***Material y métodos:*** *Estudio de cohorte prospectivo, con grupo de control. Se definió síndrome de intestino irritable de acuerdo con los criterios de ROMA IV, y se dio seguimiento al mes, tres, seis y 12 meses postoperatorios en busca de sintomatología. El análisis estadístico se realizó con prueba exacta de Fisher unidireccional.* ***Resultados:*** *De 166 pacientes, seis presentaron síndrome de intestino irritable más allá de los seis meses postoperatorios; en el grupo de control hubo dos casos nuevos al término del seguimiento. Se presentaron ocho casos de síndrome post-colecistectomía.* ***Conclusiones:*** *No se puede establecer una relación diferente al azar entre pacientes intervenidos de colecistectomía laparoscópica y la presencia de síndrome de intestino irritable en cualquiera de sus variantes.*

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Abbreviations:

BLD	=	bladder lithiasis disease
LC	=	laparoscopic cholecystectomy
IBS	=	irritable bowel syndrome
IBS-D	=	irritable bowel syndrome-subtype diarrhea
IBS-C	=	irritable bowel syndrome-constipation subtype
IBS-M	=	irritable bowel syndrome-mixed subtype
PCS	=	post-cholecystectomy syndrome

INTRODUCTION

Bladder lithiasis disease (BLD) is highly prevalent in the western population.[1] Laparoscopic cholecystectomy (LC) is one of the most performed digestive surgical procedures worldwide; in the United States it

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exceeds 750,000 procedures per year.[2] Irritable bowel syndrome (IBS) is a common functional digestive disorder in general practice and in gastroenterology characterized by abdominal discomfort and pain and abnormal bowel habits, among other nonspecific symptoms.[3] Ryle noted that multiple abdominal surgical procedures are notably more common in patients with this syndrome, such as hysterectomy, appendectomy and cholecystectomy.[4] The multicenter collaborative study by Corazziari et al (MICOL) concluded that patients with IBS are more prone to cholecystectomy than the general population.[5] A retrospective study by the Amieva-Balmori team,[6] evaluated the presence of IBS and its subtypes according to the ROME IV criteria in a group of patients with a history of cholecystectomy, finding that irritable bowel syndrome subtype diarrhea (IBS-D) occurred more frequently in patients submitted to cholecystectomy patients. There are abdominal pain/discomfort[7] in a non-negligible number of patients after cholecystectomy, and diarrhea stands out; however, there are no prospective studies that demonstrate this association, which is why we conducted the present prospective cohort study.

MATERIAL AND METHODS

This was a comparative, prospective, dynamic cohort, controlled study conducted at the Hospital Regional de Monterrey of the *Instituto para la Salud y Seguridad Social de los Trabajadores del Estado* (ISSSTE) in patients surgically intervened during 2017 and followed up during 2018. The study was approved by the ethics and research committee of hospital (folio 042, October 2016). According to probability sampling (10% difference in proportions, 5% adjusted for losses), 171 study subjects were included. Patients were not informed about the follow-up objective and were not given postoperative dietary recommendations different from those usually given for a healthy diet, with the aim of decreasing the Hawthorne effect. Patients with GBD diagnosis scheduled for CL and not having gastrointestinal alarm data suggesting other more serious disorders were randomly included (through a simple table of numbers). Patients with diagnosis of digestive malignancies, liver cirrhosis, upper or lower GI bleeding, chronic renal failure, uncontrolled diabetes, or psychiatric conditions that prevented a reliable direct questioning were excluded. Cases with IBS prior to surgery were also excluded from the analysis if they had been converted to open surgery and had presented any of the previously described situations during the intraoperative, immediate postoperative, and follow-up periods. The follow-up in search of IBS according to ROMA IV criteria *(Table 1)* was performed at one, three, six and 12 postoperative months. The investigator who performed the initial assessment was different from the surgeon, as well as the investigator of the subsequent follow-up. At the same time, an age- and sex-matched control group was included, randomly obtained from the general medical practice of two of the investigators, who were followed up in person and by telephone during the same periods of time, in search of symptoms compatible with IBS according to ROMA IV. This was done for both groups in these periods.[8] Data were collected in an electronic data sheet,

Table 1: ROME IV diagnostic criteria.

	Signs		
Abdominal pain,* at least one day a week (3-months minimum)	Related to defecation	Associated with a change in the frequency of stool	Associated with a change in the shape of the stool (Bristol scale)

* The presence of abdominal pain in addition to one or more of the signs shown is a necessary condition for diagnosis.
Modified from: Sebastián-Domingo JJ.[8]

Table 2: Initial distribution of the groups to be followed, homogeneously distributed by age, sex, and prevalence of irritable bowel syndrome. N = 336.

	Patients scheduled for laparoscopic cholecystectomy N = 168	Control patients N = 168	Homogeneity (p-value)
Age (average) years	46.4	45.2 ± 10.0	p ≤ 0.01
Sex			
Female	105	105	p ≤ 0.01
Male	63	63	
IBS (initial)			
IBS-D	2	1	p ≤ 0.01
IBS-C	0	0	
IBS-M	0	1	
Remaining healthy patients	166	166	

IBS = irritable bowel syndrome, IBS-D = irritable bowel syndrome subtype diarrhea, IBS-C = irritable bowel syndrome subtype constipation, IBS-M = irritable bowel syndrome subtype mixed.

from the patient's clinical history that included all the questionnaires both preoperatively and at follow-up. The data obtained were tabulated to calculate the relative risk, absolute increase in risk, and one-way Fisher's exact test, taking as significant a *p*-value < 0.05.

RESULTS

Of a total of 171 patients with GBD sent to surgery during the study period, two were eliminated due to loss to follow-up, and one more due to the finding of gallbladder cancer, and for the statistical analysis, two with IBS prior two surgery were also eliminated (total losses: five cases, 2.92%). Of the total number of patients (166) who underwent surgery, 91.57% (152) were elective; 8.43% (14) were admitted through the emergency department for early LC for acute cholecystitis. The mean surgical time was 92 ± 51 minutes and there were no cases of open-surgery conversion *(Table 2)*. At initial assessment, two cases of diarrhea subtype IBS were found in the group of cases that were to undergo LC; six more cases of diarrhea subtype IBS occurred during follow-up in the surgically operated group, with persistent symptoms even 12 months postoperatively (specifically IBS-D) *(Table 3)*. It should be noted that eight patients presented symptoms (including diarrhea) from the first postoperative days compatible with post-cholecystectomy syndrome (PCS), which subsided within the first four postoperative weeks, and were different from those who presented IBS. In the control group, two cases were initially found, one diarrhea subtype and one mixed subtype; and during the follow-up period, two new cases were found, equally distributed. The statistical analysis showed a relative risk of 3.00 (0.61-14.54), the absolute risk increase (ARI) was 2.41 for IBS-D, with a *p*-value = 0.0875 (not statistically significant). Considering patients who presented with diarrhea, within the spectrum of symptoms of PCS, compared to the open population, their relative risk (RR) was 4 (0.86-18.55), the absolute risk increase was 4.05, with a *p*-value = 0.032 (statistically significant), with 28.5 as the number needed for harm (NNH). Although the RR seems to be high, it was not statistically significant, and that association seems to be given by chance (other variables). For post-cholecystectomy syndrome, the RR was four times higher; and the NNH leads us to conclude

that up to one in 28 patients undergoing LC may develop this syndrome, which will be transient, and a limited number of patients will develop chronic diarrhea apparently without a direct and complete relationship to the lack of gallbladder. There are other variables that should be studied.

DISCUSSION

The evidence[5,6] derived from retrospective studies suggests that patients who develop IBS, mainly the diarrhea subtype (IBS-D), have a history of cholecystectomy,[9] with no difference between conventional or laparoscopic. In the classic surgical literature,[10,11] has mentioned the existence of diarrhea derived from the surgical procedure itself as a possible complication, even chronic, and hence the recommendations of restricting fatty foods in the diet after the surgical procedure, information that has passed from generation to generation in surgical teaching, although without substantial evidence. We consider that there is no solid evidence to support this practice, as demonstrated in this work. An epidemiological study reported a higher frequency of IBS in patients who underwent hysterectomy and cholecystectomy;[12] and another study performed at the Mayo Clinic concludes that patients with cholecystectomy have a 2.2 higher risk of developing and irritable bowel syndrome.[13] Manríquez and collaborators, in a study of 100 patients (non-probabilistic sample), found that 15% presented postoperative diarrhea and 8% had chronic diarrhea, and in the rest of their population it subsided within the first 28 days.[14] We obtained similar data in our group, but with a probabilistic sample. The theory that supports the current conclusions is the result of some experiments in which the retention of some radiolabeled bile acids was evaluated in patients with IBS, which correlate with the severity of symptoms, especially in the mixed alternating and diarrhea-predominant varieties.[15] Post-

Table 3: New cases of irritable bowel syndrome presented at follow-up. N = 166.

	Months			
	1	3	6	12
Patients undergoing laparoscopic cholecystectomy				
Postcholecystectomy syndrome	8*	0	0	0
IBS-D	0	6	6	6‡
IBS-C	0	0	0	0
IBS-M	0	0	0	0
	Remaining healthy = 160			Total = 6
Control patients				
IBS-D	0	0	1	1‡
IBS-C	0	0	0	0
IBS-M	0	1	1	1‡
Total	Remaining healthy = 164			Total = 2

* For post cholecystectomy syndrome, a separate analysis is performed; cases of this syndrome presented rapidly and were self-limited also quickly.
‡ The patients who presented irritable bowel syndrome were different from those who presented post cholecystectomy syndrome. Patients with a previous diagnosis of irritable bowel syndrome were not included in the analysis. For descriptive purposes, they continued with the same symptoms after laparoscopic cholecystectomy.
IBS = irritable bowel syndrome, IBS-D = irritable bowel syndrome subtype diarrhea, IBS-C = irritable bowel syndrome subtype constipation, IBS-M = irritable bowel syndrome subtype mixed.

cholecystectomy syndrome has also been described,[7] which should be differentiated from IBS-D by morning predilection of symptoms, intolerance to fatty foods, nausea, vomiting, aerophagia, aero-coly and, in some cases, fecal urgency[16] that is clearly relieved by evacuation. The physiopathology of this syndrome was excellently described by Jaramillo and Otero.[17] They stated that malabsorption of bile acids or their contribution increases the concentrations of these bile acids in the colon, which modifies the displacement of water and electrolytes, causing osmotic diarrhea, which could be due to a poorly diagnosed chronic cause, especially in patients with cholecystectomy cases[18] and its possible treatment with bile acid sequestrants.[19] However, the evidence from clinical studies not specifically designed has failed to demonstrate causality;[6,7,20,21] therefore, there must be other variables besides bile acids in the pathophysiology of chronic diarrhea. Reviews on IBS continue to place a history of cholecystectomy in a statistically significant association with IBS according to ROMA criteria.[22-24]

CONCLUSIONS

Our team concluded that there is no a randomly different association between laparoscopic cholecystectomy and the development of symptoms of abdominal pain and chronic intermittent diarrhea compatible with the diagnosis of IBS-D.

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Loose peritoneal bodies

Cuerpos peritoneales libres o ratones peritoneales

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Keywords:
Free peritoneal bodies, epiploic appendages, omental appendages, peritoneal mice.

Palabras clave:
Cuerpos peritoneales libres, apéndices epiploicos, apéndices omentales, ratones peritoneales.

ABSTRACT

Free peritoneal bodies are benign formations usually discovered incidentally during surgery or autopsies. It is extremely rare to find free foreign bodies in the peritoneal cavity. There is limited information on the incidence of free peritoneal bodies worldwide. It is only known that they are more frequent in the male sex with a male to female ratio 18:4 and that they mostly occur between 50 and 70 years of age mainly due to their low incidence and the fact that they are mostly asymptomatic. The most accepted etiologic theory proposes that they originate from twisted and infarcted epiploic appendages that detach from the colon serosa and gradually evolve into fibrosis and calcification. We present the clinical case of an 81-year-old patient with acute appendicitis in whom, as an incidental finding during exploratory laparotomy, three free peritoneal bodies were discovered. It was an incidental, unexpected finding, discovered during laparotomy, unrelated to acute appendicitis.

RESUMEN

Los cuerpos peritoneales libres son formaciones benignas generalmente descubiertas de manera incidental durante una cirugía o en una autopsia. Es extremadamente raro encontrar cuerpos extraños libres en la cavidad peritoneal. Existe información limitada sobre la incidencia de cuerpos peritoneales libres en todo el mundo, sólo se sabe que son más frecuentes en el sexo masculino con una relación hombre-mujer 18:4 y que en su mayoría se presentan entre los 50 y 70 años debido principalmente a su baja incidencia y a que en su mayoría cursan asintomáticos. La teoría etiológica más aceptada propone que se originan a partir de apéndices epiploicos torcidos e infartados que se desprenden de la serosa del colon y gradualmente sufren fibrosis y se calcifican. Presentamos el caso clínico de un paciente de 81 años con apendicitis aguda en quien, como hallazgo incidental durante la laparotomía exploradora, se descubrieron tres cuerpos peritoneales libres. Fue un hallazgo incidental, inesperado, descubierto durante la laparotomía, sin relación alguna con la apendicitis aguda.

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INTRODUCTION

Free peritoneal bodies are calcic-fibrotic formations generally found incidentally in the abdominal cavity, without being attached to or dependent on any abdominal organ and without their own blood supply (hence their terminology "free").[1] There are several theories about their etiology, the most accepted being that they originate from epiploic appendages, which after undergoing a chronic process of ischemia become detached to the peritoneal cavity, with subsequent accumulation of superimposed layers of albumin and fibrotic tissue.[1,2]

There is limited information on the incidence of free peritoneal bodies worldwide, mainly because they are very infrequent and mostly correspond to asymptomatic lesions that go unnoticed. It is even rarer to find giant peritoneal bodies (greater than 5 cm in diameter)[2] or multiple bodies, as in the case of the patient presented below. In the eight articles reviewed, eight cases of single peritoneal bodies between 3 and 9.5 cm in diameter are reported. Five of these eight reported free peritoneal bodies were larger than 5 cm (giants), all patients described were male between 50 and 72 years of age. In one of the articles reviewed,[3] a comparative table

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of 25 cases in total is presented. The oldest from 1951 and the most recent from 2016. These free peritoneal bodies were found in four females (two months, 33, 33, and 69 years) and 21 males (aged 47 to 79 years); 23 were single-body cases and two multiple-body cases (a 63-year-old male with two free peritoneal bodies measuring 5.8 × 4.5 × 3.7 cm and 5.2 × 4.5 × 3.7 cm; and another 79-year-old male, with two bodies measuring 7.0 × 6.0 cm and 7.0 × 6.0 cm).

PRESENTATION OF THE CLINICAL CASE

An 81 years-old male presented with a 72-hour abdominal pain evolution, predominantly at the level of the right iliac fossa (RIF), associated with an episode of bacteremia, hyporexia, nausea, vomiting and liquid stools. The abdomen was tender on palpation of the RIF with positive signs of appendix inflammation; hyperactive peristalsis was hard on auscultation and there was evidence of a peritoneal irritation syndrome. His lab tests showed leukocytosis of 11.2 × 10^3 uL with neutrophilia of 86.9%. An abdominal-pelvic tomography scan with intravenous contrast medium *(Figure 1)* showed the cecal appendix with data of an acute inflammatory process. Open appendectomy was performed by McBurney incision. Upon entering the abdominal cavity, three free peritoneal bodies were found incidentally, which were sent for histopathological study,

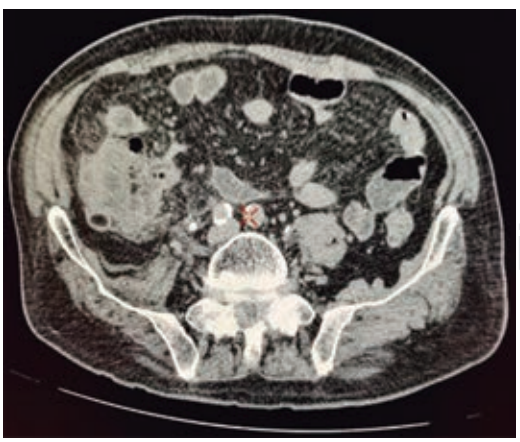

Figure 1: *Abdominal tomography scan with IV contrast.*

Figure 2: *Free objects found in abdominal cavity and cecal appendix.*

together with the resected cecal appendix *(Figure 2)*.

Macroscopic pathological analysis reported three ovoid neoformations of 17 × 15 × 10 mm, 16 × 10 × 10 mm, and 14 × 10 × 10 mm each, with a smooth, yellow, firm surface *(Figure 3)*. When cut they are solid, with a 4-mm whitish gray peripheral thick zone and a yellowish central zone of firm consistency *(Figure 4)*.

Microscopic description consists of epiploic appendices with dense connective tissue at the periphery, with dystrophic calcification and areas of fat necrosis, without other alterations or histological changes of malignant neoplastic type. Final diagnosis was of an acute fibrinopurulent appendicitis *(Figure 5)*.

DISCUSSION

Mobile or free abdominal-pelvic masses are extremely rare and usually tend to be located in the pelvic area due to the effect of gravity.[2] Within the differential diagnosis of mobile masses, the existence of free peritoneal bodies should always be kept in mind.[3] Free peritoneal bodies, also called by some authors "peritoneal mice" or "peritoneal crumbs",[3] are calcium-fibrotic formations found free in the peritoneal cavity. Since they are mostly asymptomatic, on many occasions they represent incidental findings during surgeries or autopsies.[1] In the case of our patient, they were also asymptomatic since they did not confirm additional pathology to the appendicular

condition. Only on some occasions, depending on the size and location, can they produce non-specific symptoms characterized by lower abdominal pain/discomfort, constipation, intestinal obstruction, or urinary symptoms such as polyuria or acute urinary retention.[4] There is very little epidemiological data published on these neoformations; however, it seems that they are more frequent in males with a male-female ratio of 18:4, which coincides with the patient we present, and that they mostly occur between 50 and 70 years of age, although there are reports of their presence as young as two months of age.[3] The few reports in the literature are mostly about single giant bodies larger than 5 cm in diameter,[2-8] unlike the case we present in which we discovered not one, but three different peritoneal bodies, but smaller than those reported in the literature. In our hospital (HMG Coyoacán), no similar cases have been reported since 2016 to date.

Different theories have been proposed on the origin of these free peritoneal bodies, but their exact etiology is still unknown. Possible origins include epiploic appendages, omentum, self-amputated adnexa, or pancreatic adipose tissue. The most accepted theory is that they originate from epiploic appendages.[3] The first to describe the epiploic appendages was Andre Vesalius and subsequently several anatomical studies were carried out to describe other anatomical aspects of them. The first to report a series of cases of free epiploic appendages was Harrigan in 1917.[5] The theory on the sequential changes leading to their formation was presented by Virchow in 1863, where it was proposed a gradual and progressive increase of fatty tissue within an epiploic appendix, usually in the context of obesity, leading to obliteration

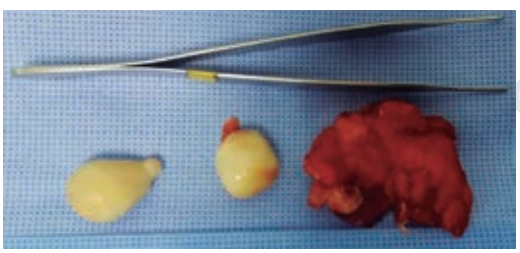

Figure 3: *Cecal appendix and ovoid objects found in abdominal cavity.*

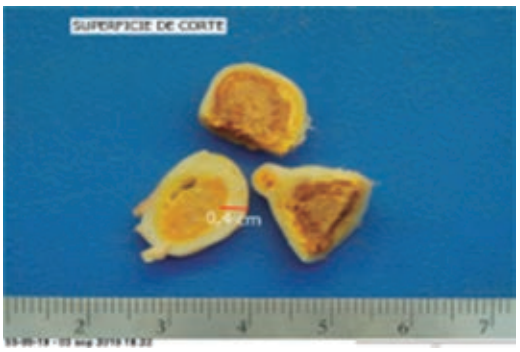

Figure 4: *Macroscopic aspect at cut surface.*

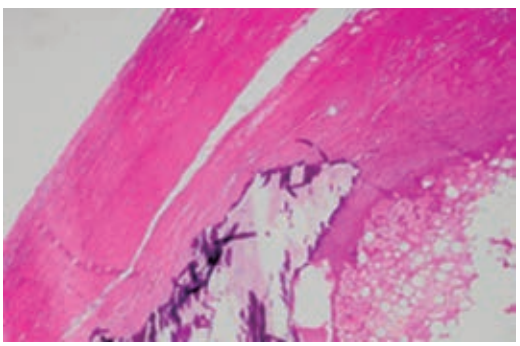

Figure 5: *Fibrous wall seen under the microscope.*

and obstruction of the blood vessels of the pedicle; then a process of torsion, strangulation, and necrosis of the epiploic appendix occurs until its amputation.[2] Later, in 1933, Patterson proposed that ischemia is the predominant etiological factor in its pathophysiology and that it is the cause that leads to infarction of the epiploic appendix. It is the dominant etiologic factor in the pathophysiology meaning that this ischemia leads to infarction and amputation.[4] Once the epiploic appendix is free floating in the abdominal cavity, it undergoes a process of saponification and calcification.[6] Over the years, the peritoneal reaction on this free body and the deposition around it of peritoneal fluid (exudative serum fluid rich in proteins, mainly albumin) produces the progressive increase in its size by addition of peripheral fibrous layers.[2,4] This theory was proven in 1968 by Donado and Kerr, who took peri-uterine fat from guinea pigs and placed it in the peritoneal cavity of these animals, generating typical free peritoneal bodies that became larger over

time.[7] Once formed, establishing a correct preoperative diagnosis is difficult, and on many occasions, they are mistaken for neoplasms and resected unnecessarily. These peritoneal free bodies are rare and asymptomatic lesions, but sometimes they can be detected by imaging studies. In computed tomography scans they are seen as masses, usually single, round or oval, well defined, with central calcification, and surrounded by peripheral soft tissue. In MRIs they are seen as well circumscribed masses, hypointense in T1 and T2, but with an area of central hyperintensity in T1. By lacking vascular supply, they are not seen with any imaging modality on contrast media administration.[1] If serial imaging studies are performed or taken in different positions, either supine or prone, and compared, the mobility of the mass can be seen as showing variable locations within the abdominal cavity.[1,7] A proper differential diagnosis should be made with benign diseases, such as leiomyomas, rhabdomyomas, teratomas, and fibromas; malignant diseases including colorectal cancer, ovarian cancer, lymphomas, metastases; urinary, biliary or appendicular calculi; dermoid cysts, tuberculous granulomas, lymph node calcification, foreign bodies, and hydatid cysts, among others.[3,7] If detected incidentally in surgery, which occurred in our case, the free peritoneal bodies floating inside the peritoneal cavity are seen, and they look like a white, hard, shiny concretion giving the appearance of a boiled egg.[1,8] Surgical excision with subsequent histologic examination can definitively confirm the diagnosis based on morphologic features. Such pathologic findings consist of a central core of calcified necrotic fat, laminated by layers of hyalinized acellular fibrous tissue at the periphery,[1,2] as was the case of the bodies found in our patient. If an adequate preoperative diagnosis is achieved, free peritoneal bodies usually do not require treatment and are managed only with surveillance.[2] It is essential that physicians know this entity and its features in imaging studies, as well as its differential diagnoses, in order to make the correct diagnosis with a high index of suspicion and avoid unnecessary interventions, since these are benign neoformations that can be managed with surveillance.

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Experience in the management of common bile duct cyst in a general surgery service. Report of four cases

Experiencia en el manejo del quiste de colédoco en un servicio de cirugía general. Reporte de cuatro casos

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Keywords:
Cyst, common bile duct, adult.

Palabras clave:
Quiste, colédoco, adulto.

ABSTRACT

Choledochal cysts are dilatations of the biliary tract that occur mainly in females during childhood. In adulthood a high index of suspicion is required, especially in rural hospitals where there is no technology to diagnose them. Management can be by endoscopic or surgical approach, depending on the classification of the cyst. It is well determined that the older the patient is at the time of diagnosis, the greater the chances of malignant transformation, with up to 30% reported. In this report four female patients between 14 and 43 years of age were included. Three of them were not diagnosed as choledochal cyst of first intention; instead, they were diagnosed as hepatic cyst, acute cholecystitis, and biliary tract stenosis. The main symptom was abdominal pain, and only one of the patients showed jaundice and a palpable abdominal mass. Three of the patients presented a type I cyst and the other a type IV A cyst. All of them underwent open surgery with resection of the cyst and Roux-en-Y hepatic-jejunal-anastomosis. There were no postoperative complications. The histopathological study was negative for malignancy in all cases.

RESUMEN

Los quistes de colédoco son dilataciones de la vía biliar que se presentan principalmente en el sexo femenino durante la infancia, en la etapa adulta se requiere un alto índice de sospecha, sobre todo en hospitales rurales donde no existe la tecnología para diagnosticarlos. El manejo puede ser por abordaje endoscópico o quirúrgico, dependiendo de la clasificación del quiste. Está bien determinado que, a mayor edad durante el diagnóstico, las posibilidades de transformación maligna también son mayores, reportándose hasta en 30%. Se incluyeron cuatro pacientes mujeres entre 14 y 43 años. A tres no se les realizó el diagnóstico de quiste de colédoco de primera intención, siendo diagnosticadas como quiste hepático, colecistitis aguda y estenosis de la vía biliar. El síntoma principal fue dolor abdominal, sólo una de ellas mostró ictericia y masa palpable. Tres presentaron quiste tipo I y la otra tipo IV A. A todas se les realizó cirugía abierta con resección del quiste y hepatoyeyunoanastomosis en Y de Roux. No hubo complicaciones postoperatorias. El estudio histopatológico fue negativo a malignidad en todos los casos.

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INTRODUCTION

Choledochal cysts (CC) are congenital cystic dilatations of the biliary tree. The incidence is 1:100,000 to 1:150,000 in populations of Western countries. They mainly affect women and although sometimes they are diagnosed in childhood, up to 20% of patients are adults when the diagnosis is done.

The risk of developing cholangiocarcinoma in choledochal cysts increases with age, and they occur more frequently in types I (68%) and IV (21%),[1,2] which supports their complete removal when diagnosed. Several theories have been proposed to explain the pathogenesis of common bile duct cysts. The current and most accepted is the anomalous union of the pancreatic and biliary ducts outside the

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duodenal wall, forming a single channel, which can reach a length between 10 and 45 mm. This anomaly causes reflux of pancreatic secretions into the biliary tree and because the pressure of the pancreatic duct is greater than the pressure of the biliary duct, it results in activation of pancreatic enzymes, alteration of the biliary composition, local inflammation, and damage to the biliary epithelium, causing weakness and dilatation of the biliary duct wall.[3,4]

The most used classification is that made by Todani and collaborators, who classify the common bile duct cyst in five types:[3]

Type I: saccular or cystic dilatation of the extrahepatic bile duct.

Type II: common bile duct diverticulum.

Type III: dilatation of the intraduodenal portion of the common bile duct (choledococele).

Type IV A: multiple intrahepatic and extrahepatic cysts.

Type IV B: multiple extrahepatic cysts.

Type V: intrahepatic cysts (Caroli's disease).

Less than half of patients present with the typical clinical triad of abdominal pain, jaundice, and an abdominal mass. In more than half of the cases the symptoms are nonspecific.[3,4] Since incomplete excision of the cyst can lead to recurrence, symptoms and malignant transformation within the remnant tissue, current surgery involves removal of the entire cyst (including the gallbladder) and restoration of biliary-enteric continuity.[5]

PRESENTATION OF CLINICAL CASES

Case report 1: a 14-year-old female with four-year evolution of colicky pain in the right hypochondrium. Four months prior to her admission she presented more frequent episodes, adding jaundice, coluria, acholia, nausea, and vomiting. She was admitted with jaundice, pain on palpation in the right hypochondrium and epigastrium, and an abdominal mass measuring approximately 15 × 15 cm. Liver function tests showed mixed hyperbilirubinemia (total bilirubin: 7.1 mg/dl, direct bilirubin: 3.7 mg/dl, increased alkaline phosphatase: 651 U/l). The ultrasonography scan revealed calculous cholecystitis and choledocholithiasis versus common bile duct cyst. The computed tomography (CT) scan showed a calculous cholecystitis and cystic dilatation of the bile duct *(Figure 1)*. The cholangial-resonance imaging showed a 72 mm choledochal cyst with intrahepatic bile duct dilatation *(Figure 2)*. Elective surgery was performed where a gallbladder with lithiasis and a type I choledochal cyst according to Todani's classification attached to duodenum measuring 17 × 10 × 10 cm was found *(Figure 3)*.

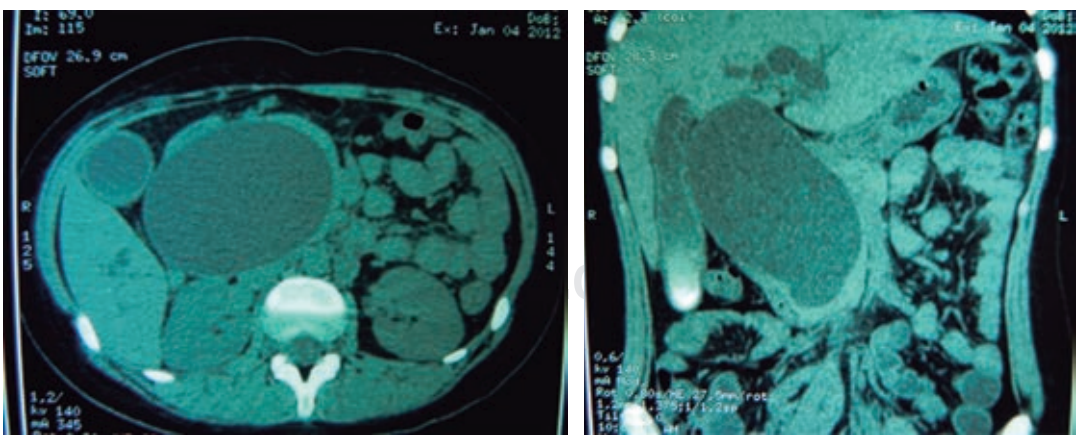

Figure 1: *Axial tomography scan showing a cystic image of the common bile duct, with thickening of the gallbladder wall and presence of stones in the gallbladder.*

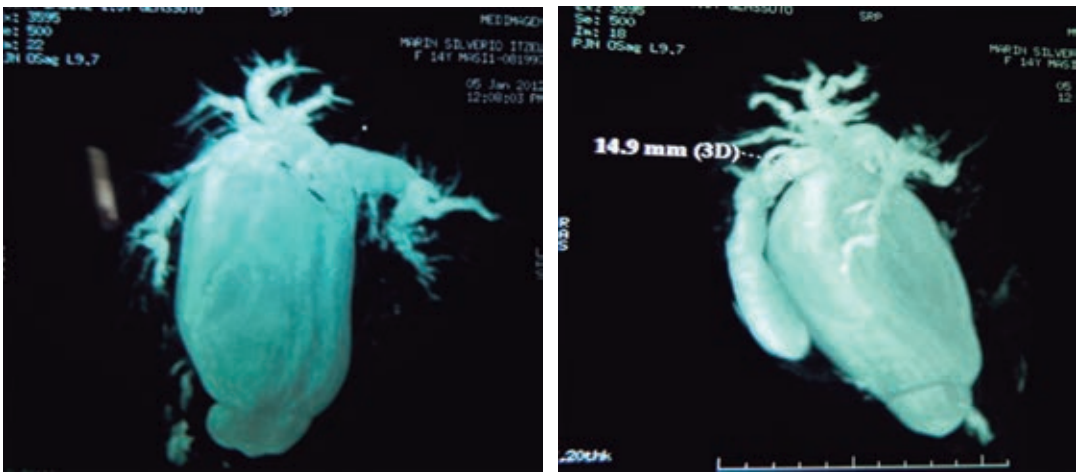

Figure 2: *MRI cholangiopancreatography showing a giant common bile duct cyst type I.*

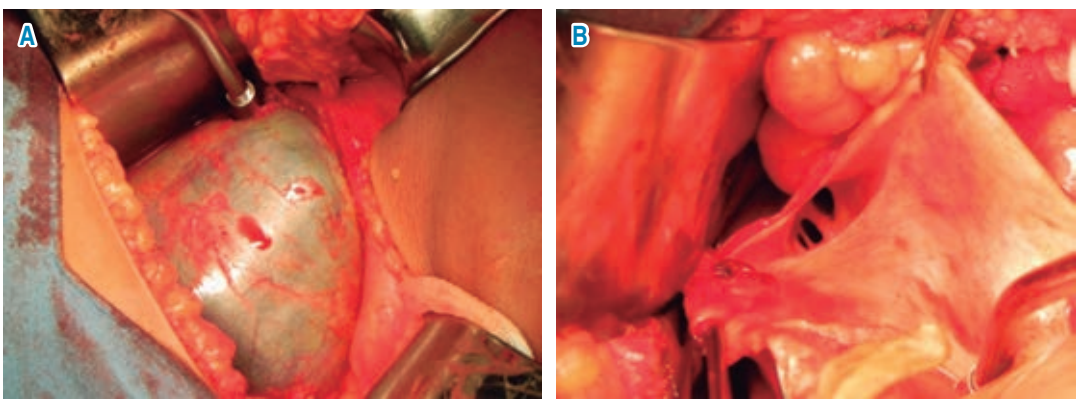

Figure 3: A) *Image of a common bile duct cyst once the adhesions were released.* ***B)*** *After the cyst is opened, the hepatic ducts and the cystic orifice are identified.*

Case report 2: a 43-year-old woman presented with colicky pain in the right hypochondrium, without accompanying symptoms; she attended a rural hospital, where she underwent open cholecystectomy during which an increase in the diameter of the common bile duct was observed. It was decided to perform a choledochotomy with T-tube placement. In the outpatient clinic, a T-tube cholangiography was requested, which showed a common bile duct cyst, so she was referred to our hospital. She was admitted without jaundice and an open Kerr type tube with biliary output. Liver function tests were within normal parameters and only shoed hypoalbuminemia. Surgery was performed with findings of a common bile duct cyst measuring 15 × 8 × 7 cm attached to the duodenum, stomach, pancreas, portal vein and vena cava. A right and left hepatic duct with a diameter of 1 cm was found.

Clinical case 3: a 15-year-old female, with a history of right hypochondrium pain and fever. The ultrasonography scan revealed a hepatic abscess. She underwent exploratory laparotomy where a giant tension common bile duct cyst with necrosis and adhesions to the gallbladder was found. Choledochotomy, aspiration and primary closure with placement of a Penrose drainage was performed. On the second postoperative day, 400 cm^3 of bile came out through the drainage and, by ultrasound,

free liquid in the cavity was seen, for which reason she underwent a new laparotomy. In this second surgery drainage, cholecystectomy, and placement of a Kerr probe in the cyst bag were performed. She was referred to our hospital, where she was maintained with medical treatment and later sent to outpatient care. A T-tube cholangiography revealed a cystic pocket compatible with a common bile duct cyst. A scheduled surgery was performed, and a common bile duct cyst of approximately 8 × 5 cm with a T-tube inside and multiple adhesions was detected *(Figure 4)*.

Case report 4: a 43-year-old woman presented with two-year evolution of colicky pain in the right hypochondrium. Two months prior to her referral to our hospital she presented with increasing pain intensity, accompanied by nausea, vomiting and fever. An endoscopic retrograde cholangiopancreatography (ERCP) was performed, which reported common bile duct dilatation measuring 25 mm of the intrahepatic and extrahepatic bile duct. A sphincterotomy and stent placement were performed. The cytology brushing was negative for malignancy. She was sent to our hospital, where a cholangial-resonance imaging was performed, which showed fusiform dilatation of the main biliary tract, and two more smaller dilatations in the right and left hepatic duct. A diagnosis of type IV A choledochal cyst was made. Liver function tests showed a serum alkaline phosphatase level of 595 U/l, an aspartate aminotransferase (TGO) level of 139 U/l, and alanine aminotransferase (TGP) level of 181 U/l and a total bilirubin level of 1.2 mg/dl.

All patients underwent cyst resection and Roux-en-Y choledochal-duodenal-anastomosis, and two of them also underwent cholecystectomy. They were discharged without complications *(Table 1)*.

DISCUSSION

The choledochal cyst (CC), although rare, is a well-described clinical entity, affecting women more frequently. Even though choledochal cysts are diagnosed in infancy or childhood, up to 20% of patients are adults when the diagnosis is made. The risk of a choledochal cyst transforming into a cholangiocarcinoma increases with age and occurs more frequently in types I (68%) and IV (21%),[1,2] which justifies its complete removal when diagnosed. The most accepted theory is the anomalous union of the pancreatic and biliary ducts outside the duodenal wall, forming a single duct, which can reach a length between 10-45 mm.[6] The most frequent symptoms are right upper abdominal pain and jaundice. Fever may also

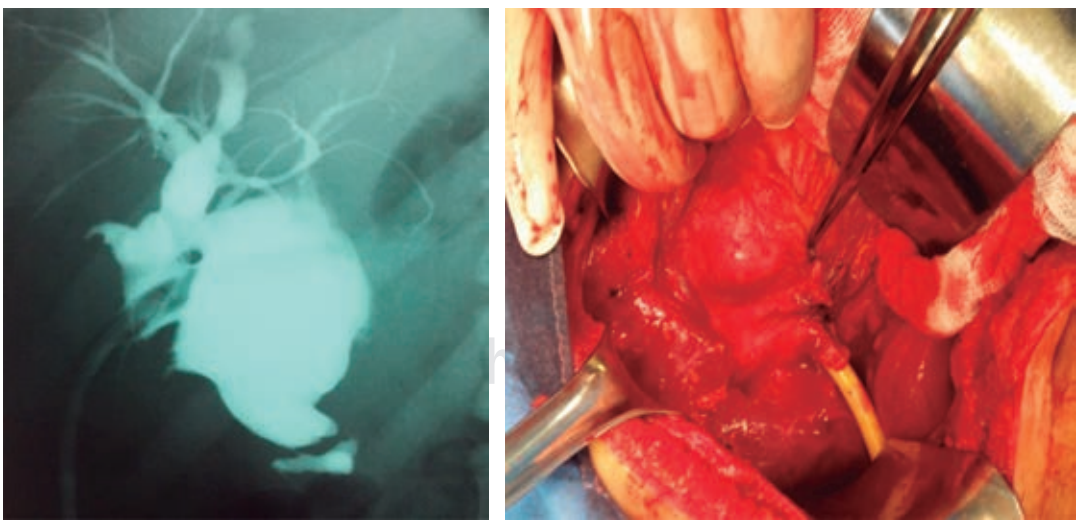

Figure 4: *Cholangiography with a Kerr probe demonstrating the presence of a common bile duct cyst; intraoperative findings exhibiting abundant adhesions and the probe being inserted into the cyst cavity.*

Table 1: Clinical and paraclinical features and surgical findings of patients with common bile duct cyst.

	Case 1	Case 2	Case 3	Case 4
Sex	Female	Female	Female	Female
Age (years)	14	43	15	43
Pain	Yes	Yes	Yes	Yes
Jaundice	Yes	No	No	No
Abdominal palpable mass	Yes	No	No	No
Classic clinical triad	Yes	No	No	No
Fever	No	No	Yes	Yes
LFT abnormalities	Yes	No	No	No
Ultrasound	Vesicular lithiasis Probable common bile duct cyst	Lithiasis cholecystitis	Hepatic abscess	Bile duct dilatation
Diagnosis	Cholangial-resonance	Cholangiography with a Kerr probe	Cholangiography with a Kerr probe	Cholangial-resonance
Type of cyst	Todani I	Todani I	Todani I	Todani IV A
Surgery	ERYHJA	ERYHJA	ERYHJA	ERYHJA
Hospital stay (days)	6	6	6	6
Complications	No	No	No	No
Histopathological	Benign	Benign	Benign	Benign

LFT = liver function tests; ERYHJA = excision and Roux-en-Y hepato-jejunal-anastomosis.

be detected when associated with cholangitis. On physical examination, an abdominal mass may be palpated in the right upper quadrant.[6,7] In our patients, all of them started with pain and two of them (50%) had fever as a symptom of cholangitis. The classic triad of abdominal pain, jaundice and an abdominal mass is present in less than 15% of adult cases. We saw it in only one patient. A study of 20 patients revealed that 100% were female, 19 (95%) had a type I choledochal cyst, while one had a choledochal cyst type IV. The main symptom was abdominal pain in 15 women (75%) and the other five (25%) had jaundice and/or cholangitis, which coincides with the findings seen in our patients. The diagnostic suspicion was made by ultrasonography scan in 50% of the cases and 18 (90%) were diagnosed by magnetic resonance cholangiopancreatography (MRCP).[8] In our study we observed that with ultrasonography scan, being an operator-dependent study, only one patient had a choledochal cyst suspected, and the diagnosis was attained by means of a Kerr probe cholangiography and two of them by MRCP. Two patients were operated on under suspicion of another diagnosis. The Todani classification is widely adopted for the classification of choledochal cysts and the choice of surgical management. The concept of complete excision is the ideal treatment. In proximal cyst removal the procedure must be performed carefully to protect the portal vein and hepatic artery. In distal cysts, the cyst usually extends into the pancreas, so excision may be difficult due to surrounding adhesion to the pancreas. Sometimes complete excision is not possible due to postoperative risk, pancreatic leakage, bleeding, and peritoneal infection.[9,10] However, the unresected intrapancreatic choledochal cyst gives rise to the formation of a dead space within the pancreas. Reflux of intestinal secretions results in activation of pancreatic enzymes in the remaining cyst, which can lead to infection, stone formation, and increased risk of malignancy.[11] Type I choledochal cyst, which has no obvious

relation to the pancreatic duct, intrapancreatic cyst or apparently normal bile duct, shall be completely excised and the stump is sutured. In our study, three patients were carriers of type I choledochal cysts, so total resection of the cyst was performed, taking special care in the intrapancreatic portion and in the dissection of the portal adhesions. In type IV choledochal cysts according to Todani's classification with extrahepatic and intrahepatic cysts, the extrahepatic cyst must be completely excised. If the intrahepatic cyst is limited, a partial hepatectomy with biliary-enteric reconstruction is performed.[12] In Mexico, Martínez-Ordaz carried out a study that analyzed 23 patients in 17 years that were operated on. Of these, 70% were women, 87% presented with pain and only four of them had the classic clinical triad; 74% had a type I choledochal cyst. Patients with type I and IV A cysts underwent resection of the cyst and Roux-en-Y choledochal-jejunal-anastomosis by open surgery. Three patients were reoperated for biliary leakage. There were no deaths.[13]

The laparoscopic approach is gradually replacing open surgical treatment of choledochal cysts in pediatric patients.[14] In contrast, laparoscopically choledochal cyst excision in adults is technically difficult and associated with a high rate of complications and conversion into open surgery; however, some authors have reported results like those obtained in children. In a study of 20 patients, Hirdaya found that laparoscopic excision could be completed in 16 cases (80%), while the other four (20%) required conversion to the open approach. The main reason for conversion was technical difficulty due to the initial learning curve, the presence of adhesions, and inflammation of the cyst and/or duct wall. There were no deaths.[8] In a study of 110 patients, where half were under 16 years of age, Palanisamy et. al. observed that type I cysts were the most common (71.82%) with an average size of 4.67 ± 1.59 cm. They were operated under laparoscopic approach. They compared the results obtained in the group of children versus adults and demonstrated that minimally invasive surgery had better results in pediatric patients with a lower conversion to open approach rate, a shorter hospital stay and a lower rate of complications. The reported hospital mortality after laparoscopic choledochal cyst excision is 1.8% and that of open choledochal cysts excision is 3 to 4%.[15] Altered anatomy, presence of adhesion and lack of palpatory sensation during the laparoscopic excision make it technically difficult and increase the risk of injury. In our hospital unit the patients had a good postoperative evolution, with no morbidity or mortality. In our population there is still no experience in the laparoscopic approach due to the low number of patients with choledochal cysts.

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Biliary ileus resolved by laparoscopy

Íleo biliar resuelto por laparoscopia

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Keywords:
Biliary ileus, laparoscopy, cholelithiasis.

Palabras clave:
Íleo biliar, laparoscopia, colelitiasis.

ABSTRACT

Introduction: Biliary ileus is a mechanical obstruction of the gastrointestinal tract caused by impaction of one or more gallbladder stones into the intestinal lumen through a bilio-enteric fistula. **Case report:** A 59-year-old woman with multiple comorbidities came to the emergency room with intestinal obstruction; imaging studies identified pneumobilia and intestinal loops distension, so it was decided to take her to the operating room for a probable biliary ileus and perform diagnostic laparoscopy, after which a 3.5 cm diameter lithium was found nestled in the terminal ileum. **Conclusion:** Biliary ileus is a rare complication of cholelithiasis. Treatment integrates rehydration and surgery to correct the cause of intestinal obstruction.

RESUMEN

Introducción: *El íleo biliar es una obstrucción mecánica del tracto gastrointestinal y está causada por la impactación de uno o más litos de la vesícula biliar dentro de la luz intestinal a través de una fístula bilioentérica.* ***Caso clínico:*** *Mujer de 59 años con múltiples comorbilidades. Acude a urgencias por cuadro de obstrucción intestinal; mediante imagen se identifica pneumobilia y distensión de asas intestinales, por lo que se decidió ingresar a quirófano por un probable íleo biliar y realizar laparoscopia diagnóstica, tras lo cual se encontró un lito de 3.5 cm de diámetro enclavado en el íleon terminal.* ***Conclusión:*** *El íleo biliar es una complicación rara de la colelitiasis. El tratamiento integra la rehidratación y cirugía para corregir la causa de la obstrucción intestinal.*

INTRODUCTION

Biliary ileus (BI) is defined as a mechanical intestinal obstruction secondary to the presence of a gallstone in the intestinal lumen.[1] It is a rare and potentially serious complication of cholelithiasis, accounting for 1-4% of all intestinal obstructions in adults. The most frequent cause is the impaction of a stone in the ileum after passing through a bilioenteric fistula, usually cholecystic-duodenal (68-95%).[2] This occurs when there are recurrent episodes of acute cholecystitis that produce inflammation and adhesions between the gallbladder and the digestive tract.[3] In most cases, the obstruction occurs in the terminal ileum (60%), followed by the proximal ileum (25%) and, more rarely, in the jejunum (9%), sigmoid colon (4%) or duodenum (2%).[4] It mostly occurs in patients over 65 years of age where it can reach up to 25% of small bowel obstructions;[5] it is more prevalent in women, with a female to male ratio of 3.6:1. The mortality rate associated with biliary ileus ranges from 12 to 27%, and the morbidity rate reaches 50%, due to the advanced age of patients, associated pathologies (usually severe), late hospital admission and delayed therapeutic treatment.[6]

CLINICAL CASE

This is the case of a 59-year-old female patient with a history of a stroke event five years ago, type 2 diabetes under control with oral hypoglycemic agents (metformin 850 mg every 12 hours and glibenclamide 5 mg every 24 hours), hiatal hernia and ischemic heart disease under control. She also took acetylsalicylic acid 100 mg orally every 24 hours and atorvastatin

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40 mg orally every 24 hours. Her condition began with nausea and vomiting of brown gastrointestinal contents, which leaded to intolerance to the oral route accompanied by pain in the epigastrium zone and referred in intensity of 7/10. She self-medicated with antispasmodics and nonsteroidal anti-inflammatory drugs (NSAIDs), with partial improvement; 48 hours after the onset of symptoms, the intensity of pain increased and she presented abdominal distension, as well as inability to pass gases through the rectum. On admission to the emergency department, the patient was found to be dehydrated, with distended abdomen, painful on superficial palpation and metallic noises on auscultation. A gastric tube was placed, and the aspirated liquid was fecaloid in appearance. Biochemically she had acute renal failure, hydro electrolyte imbalance and metabolic acidosis lab results. Radiographically, there were dilated small bowel loops, pneumobilia *(Figure 1)* and evidence of intestinal occlusion. In view of this, a laparoscopic surgical exploration was decided which showed dilatation of small bowel loops up to a segment of ileum, located 150 cm from the ileocecal valve, where a protrusion was observed that marked the end of the intestinal dilatation and that corresponded to a 3.5 cm interlocked biliary stone. An enterotomy with stone extraction were performed. The closure was in one plane, with continuous suture with 2-0 Prolene *(Figure 2)*. During the intraoperative period, the patient had hemodynamic instability, so it was necessary to start support with norepinephrine (16 mg in 250 ml of 0.9% saline solution) at a rate of 8 ml/h, dose that was decreased until completely discontinued after 48 hours. Subsequently, she evolved favorably, being discharged on the fifth day while maintaining hemodynamic stability, tolerating the oral route and with no data of systemic inflammatory response. Currently, one year after surgery, she continues to be seen as an outpatient with no complications related to the surgical event.

Figure 1: *Plain abdominal X-ray showing dilated small bowel loops. The arrow shows pneumobilia.*

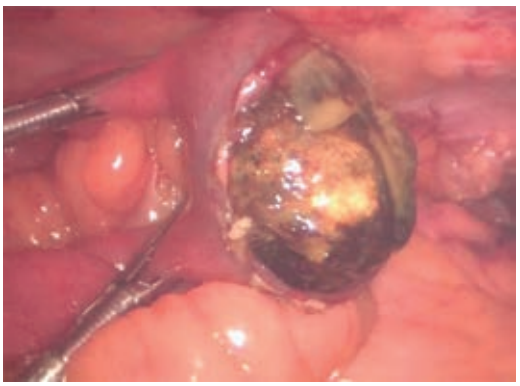

Figure 2: *The enterotomy and the stone coming out of the lumen of the small bowel are seen.*

DISCUSSION

Biliary ileus represents 0.5% of cholelithiasis complications and it is a rare and potentially serious event. It occurs more frequently in elderly women. It accounts for 1-4% of all intestinal obstructions in adults over 65 years of age implying a high risk of complications, with a mortality of 12-27%.[7] It is a pathology that is not usually diagnosed prematurely, due to the similarity of symptoms with more common acute abdominal conditions, and the diagnosis is usually done by intraoperatively. Our case is a 59-year-old woman with associated comorbidities. These findings correspond to those published by Sánchez-Pérez and collaborators,[2] who studied a group of patients

with a diagnosis of intestinal obstruction; of which, 10 cases were caused by biliary ileus; eight were women and the mean age of presentation was 61.9 years. This causes patients to present to the emergency department in poor condition. They usually present with acute renal failure due to dehydration and acid-base imbalance. In our case, the patient presented to the hospital with 48 hours of evolution without tolerance to the oral route, during which time she did not have an adequate food and liquid intake. This conditioned the patient to present acute renal failure due to dehydration and metabolic acidosis together with data of a systemic inflammatory response, findings that this type of patients usually have.[2]

For a biliary ileus to occur, there must be a bilioenteric fistula, mostly cholecysto-duodenal (68-95%), which appears as secondary to recurrent episodes of acute cholecystitis that produce inflammation and adhesions between the gallbladder and the digestive tract. The stone must have a diameter ≥ 2-2.5 cm to cause obstruction.[8] Approximately, only 50% of patients presenting with biliary ileus are aware of having cholelithiasis, being reluctant to elective surgery. The rest of the patients report a history of non-specific abdominal pain, treated as dyspepsia or functional disorders of the colon, and the diagnosis is made intraoperatively as in this case. Our patient was unaware of the history of cholelithiasis and reported abdominal pain in upper quadrants with the ingestion of gastric irritant foods, rich in cholecystokinetic food, which was controlled with antacids, proton pump inhibitors and antispasmodics, so she never sought medical attention. This pattern has been occurring repeated approximately every three weeks for "his entire adult life".

Radiographic findings in a simple abdominal projection include: pneumobilia, evidence of intestinal obstruction, an image suggestive of a stone in intestinal loops, and changes in the location of the stone as was visualized in a previous radiograph.[9-13] The use of computed tomography scan is an important diagnostic support since it has a diagnostic sensitivity, specificity, and accuracy of 93, 100 and 99%, respectively, as has been reported.[13] Initial treatment requires IV solution administration, as these patients usually present with dehydration. The laparoscopic surgical approach offers more advantages compared to open surgery; recovery requires less time. However, it represents a technical challenge, especially when the intestinal loops are edematous and dilated.[14] In our case, we preferred the laparoscopic approach over the open approach because of the advantages that minimally invasive surgery offers. The patient did not present complications related to the surgical event. There is controversy regarding the management of bilioenteric fistula. On the one hand, only enterotomy, removal of the stone and primary closure is preferred, and on the other, in addition to the above, dismantling of the fistula and cholecystectomy are performed.[8] It has been reported that elderly patients with multiple comorbidities represent a real challenge, since there is a considerable increase in leakage, both intestinal and biliary, when performing all the procedures described in a single surgery.[15] In our case, we decided to perform only enterotomy, removal of the stone and primary closure due to the patient's condition at the time of admission to the operating room and due to the intraoperative hemodynamic instability. We made the decision to resolve the emergency.

As reported by Halabi WJ et al, 5% of patients who underwent enterolithotomy as the only treatment will develop biliary symptoms and 10% will require another emergency operation. In the presence of residual stones, the estimated prevalence of recurrence is 5 to 17% and more than half of these recurrences will be within six months of initial presentation.[15] Because of this, if the gallbladder is preserved at the first surgery, deferred cholecystectomy should be performed.

In his article, Salvador Eloy García-Valenzuela and his colleagues present a couple of cases with biliary ileus resolved, one by laparoscopy and the other by conventional open surgery. They point out that they were different scenarios, had different comorbidity factors and different surgical procedures were performed, but the patients evolved satisfactorily, and they concluded that both surgical procedures are valid, and the choice is made by the surgeon, considering the

nutritional factors, the comorbidities of each patient and his/her own experience.[16] Therefore, the decision to submit our patient to laparoscopic procedure was based on the wide experience in laparoscopy of our team, being a successful procedure and demonstrating that this condition can be solved by this approach.

CONCLUSION

Biliary ileus is a rare pathology that mainly affects elderly people, predominantly women. Enterolithotomy with removal of the ileum is the most frequently performed procedure due to its low incidence of complications.

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Mid-gastrointestinal tract bleeding secondary to gastrointestinal stromal tumor

Sangrado de tubo digestivo medio secundario a tumor del estroma gastrointestinal

René Zavala-Gutiérrez*

Keywords:
Gastrointestinal stromal tumors, surgical treatment.

Palabras clave:
Tumores del estroma gastrointestinal, tratamiento quirúrgico.

ABSTRACT

Introduction: Gastrointestinal stromal tumors are mesenchymal tumors of the gastrointestinal tract that express specific receptors, such as c-kit tyrosine kinase. They represent less than 1% of gastrointestinal neoplasms, most are in the stomach (60-70%) and small intestine (30%). They usually present with non-specific symptomatology, most frequently bleeding and/or intestinal obstruction. **Case presentation:** A case of gastrointestinal stromal tumor with ileal gastrointestinal tract bleeding in a 56-year-old woman is presented. **Conclusion:** Its vague symptomatology makes it a diagnostic challenge. Being a rare pathology, diagnostic suspicion is important to provide adequate treatment.

RESUMEN

Introducción: *Los tumores del estroma gastrointestinal son tumores mesenquimales del tracto gastrointestinal que expresan receptores específicos, como la tirosina cinasa c-kit. Representan menos de 1% de las neoplasias gastrointestinales, la mayoría se localiza en estómago (60-70%) e intestino delgado (30%). Por lo general, presenta sintomatología inespecífica, más frecuentemente sangrado y/o obstrucción intestinal.* ***Presentación del caso:*** *Presentamos un caso de tumor de estroma gastrointestinal con sangrado de tubo digestivo de íleon, en una mujer de 56 años.* ***Conclusión:*** *Su vaga sintomatología lo convierte en un reto diagnóstico. Siendo una patología rara, la sospecha diagnóstica es importante para proporcionar un tratamiento adecuado.*

INTRODUCTION

Gastrointestinal stromal tumors (GIST) are defined as mesenchymal tumors of the gastrointestinal tract that express specific receptors, such as c-kit tyrosine kinase (CD117).[1] GISTs have an indolent growth pattern resulting in medium-sized tumors with a mean diameter of 8 cm at diagnosis.[2] GISTs account for less than 1% of gastrointestinal neoplasms and 20% of small bowel neoplasms, with an incidence of 10-20 million people.[3] The annual incidence in the United States is approximately 4,500 cases per year.[4] Most are in the stomach (60-70%), small intestine (30%), colon and esophagus (5%), but can arise in any part of the gastrointestinal tract, from the esophagus to the anus.[3]

Recently, many epidemiological centers reported in their data a high occurrence of GIST associated with another malignant neoplasm.[5] The most frequent association is stomach and colorectal neoplasms. Reports indicate a frequency that ranges from 2.95 to 33%.[6]

GISTs originate from interstitial cells of Cajal or their precursor stem cells. Studies based on the expression of the proto-oncogene c-kit support the hypothesis of a common carcinogen in their etiology.[7]

The most common presentation is gastrointestinal bleeding with or without obstruction. It manifests as vague abdominal symptoms or without specific clinical

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manifestation 69% of the time. They are usually incidental findings by endoscopy, surgery, or imaging studies in 21% of cases and 10% are found in autopsies.[4]

A case of small bowel GIST is presented here in a patient who manifested intestinal bleeding and partial obstruction, and in whom a surgical resection with free margins was performed. This condition most frequently presents as intestinal obstruction and may also show intestinal bleeding due to erosion caused by the tumor; however, the symptomatology is usually vague.

Bleeding is the result of erosion in the gastrointestinal tract. Other symptoms result from the mass effect of the tumor, causing discomfort, nausea, vomiting, and early satiety.

Endoscopy frequently fails to detect submucosal and extraluminal GISTs and biopsy specimens are often negative. Fine needle aspiration guided by ultrasound or tomography has been developed as a method for obtaining tumor cells and has allowed preoperative diagnosis of GIST by histological examination with immunohistochemistry.[8]

Diagnosis can be challenging and involves the use of endoscopy, ultrasound, CT scan, or MRI.

Computed tomography (CT) scan is recommended in these patients to differentiate the cause of obstruction, which can help in deciding management. The CT scan is a class II recommendation by the East Workshop for the management of small bowel obstruction.[9]

New masses detected clinically or radiologically in patients with a history of GIST should be sampled by biopsy for exclusion of a non-malignant GIST.[10]

Treatment consists of surgical wedge resection without lymphadenectomy, which represents the cure for patients with a localized primary tumor.[11] Since gastric GIST rarely metastasize to lymph nodes, they do not require lymphadenectomy.[12] To achieve an adequate resection, a free margin of 1 to 2 cm is recommended.[13]

Laparoscopic wedge resection could be considered as the procedure of choice and a valid alternative to conventional open surgery for resection of small 2 GISTs < 2 cm.[8] The development of endoscopic stapling devices and the evidence of laparoscopic resection of a GIST is an effective approach with minimal morbidity and no reported mortality.

With the advancement of minimally invasive surgery, laparoscopic resection of gastric GISTs ≤ 5 cm has been reported in several studies to be feasible and safe. Open gastrectomy was usually adopted for larger GIST tumors in the stomach.[1]

Laparoscopic surgery should be considered in cases of intestinal obstruction and cancer. The results are appropriate in the short and long term, like those of open surgery. Laparoscopic surgery has a shorter hospital stay, less bleeding and less requirement of pain medication.[14]

The introduction of imatinib mesylate opens a new perspective in the treatment of GISTs. It is especially used as a neoadjuvant in cases with inoperable stages and to achieve negative resection margins. Imatinib is a competitive tyrosine kinase inhibitor (KIT), which has been shown to be effective in controlling GIST growth.

Currently, the factors that condition a worse prognosis in gastrointestinal stromal tumors are a size > 5 cm and a mitotic index of 5 mitoses per field.[4,15]

CLINICAL CASE

A 56-year-old woman provided her consent to the presentation of her case. She a history of three months of evolution, with abdominal pain, small amount of bowel movements with melena, loss of appetite and weight loss, accompanied by headache, asthenia, and adynamic. She was admitted to the emergency department after fainting. The patient has a surgical history of left oophorectomy, laparoscopic cholecystectomy, previous hospitalizations for lower gastrointestinal tract bleeding and mild anemia; she was recently treated for chronic gastritis. The patient had received blood transfusions for post cesarean hemorrhage 17 years ago. She takes no medications and denies any allergies.

On physical examination she had pallor of skin and mucosa, a soft non-tender and depressible and distended abdomen, with good peristaltic sounds. Rectal examination

showed no bleeding. She had a severe anemia with a hemoglobin level of 2.6 g/dl, hematocrit 9.1%, and a blood platelet count of 382 × 10^3/µl. Therefore, a blood transfusion as administered.

An abdominal ultrasonography (USG) scan was performed, reporting an image of a tumor in the right iliac fossa measuring 10.5 × 5.5 × 9.9 cm. The colonoscopy study showed no evidence of tumor in the rectum and colon, and an apparent extrinsic compression at the ileocecal valve orifice *(Figure 1)*.

A computed axial tomography (CT) scan showed a stenosing and infiltrative tumor of the ileum walls with a narrow lumen and distended bowel loops *(Figures 2 and 3)*.

During the exploratory laparotomy, a 10 × 10 cm terminal ileum-dependent tumor with partial obstruction of the intestinal lumen was located. Subsequently, resection and open ileostomy were performed, and ceftriaxone 1 g and metronidazole 500 mg were administered post-surgery during her hospital stay. During the surgical procedure the stump was closed with 3-0 Vicryl sutures and the surgical specimen was sent to pathology *(Figure 4)*.

The pathology study reported segmental resection of the ileum, with a gastrointestinal stromal tumor (GIST) measuring 13 cm, with more than 5 mitoses in 50 HPF. The surgical borders were free of tumor and a follicular reactive hyperplasia of lymph nodes was seen.

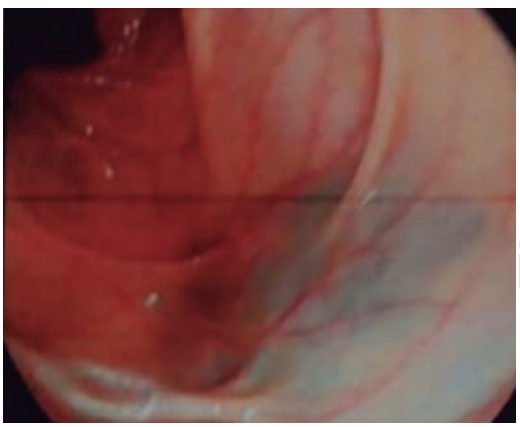

Figure 1: *Ileocecal valve orifice with apparent extrinsic compression.*

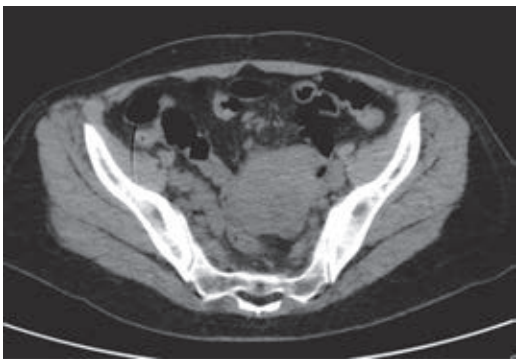

Figure 2: *A simple CT scan slice showing an abdominal tumor.*

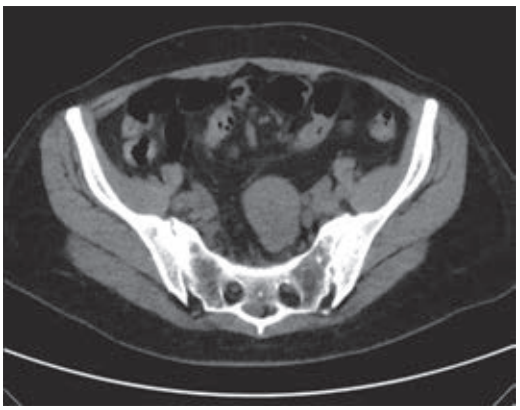

Figure 3: *A simple CT scan slice showing dilatation of small bowel loops, with air levels, suggestive of intestinal obstruction.*

The patient recovered and was discharged on her third postoperative day.

RESULT

The patient did not have any complications after surgery and was asymptomatic and stable at the time of her discharge. She was then sent for further management by the medical oncology department for follow-up.

DISCUSSION

This patient presented with a partial obstruction and vague symptomatology. About 70% of GISTs are symptomatic at the time of diagnosis.

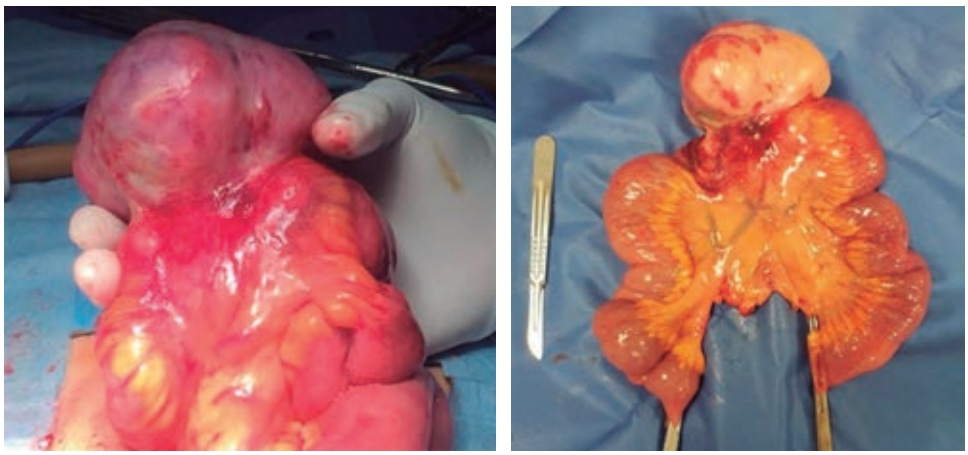

Figure 4: *A 10 × 10 cm gastrointestinal stromal tumor of ileum.*

A small percentage require emergency surgery. In this case, the patient presented a partial obstruction and chronic bleeding, requiring improvement of her general conditions with transfusions. She presented with an intestinal obstruction. These tumors may have different characteristics such as a continuous growth of the lesion causing direct occlusion of the bowel, as in this case, and rarely intussusception which has been reported only in a few cases in the literature.[16]

CT scan was used for diagnosis, which is imaging study of choice since it permits differentiation of possible causes of obstruction.

Curative treatment was possible, since complete resection was performed, avoiding tumor rupture and with negative macroscopic margins.

Although laparoscopic resection would have been preferable due to its low morbidity and mortality, the patient had a good evolution.

Tumor size represents a negative prognostic factor, and resection with free margins is curative, being predictors of good prognosis for the patient.[17]

CONCLUSION

GIST is a rare pathology. However, it may require emergency medical management. In patients with symptoms of bleeding and/or obstruction, the presence of GIST should be suspected when tumors are found during imaging studies.

It is very useful to perform a CT scan, as it happened in this case, to establish the diagnosis. Resection of the pathology specimen with adequate free margins was performed by open surgery.

In cases of localized tumors where complete resection is possible, the laparoscopic technique is preferable due to its low morbidity and mortality.

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Testicular tuberculosis

Tuberculosis testicular

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Keywords: Testicular tuberculosis, HIV-AIDS, Mexico.

Palabras clave: *Tuberculosis testicular, VIH-SIDA, México.*

ABSTRACT

Introduction: Testicular tuberculosis is a rare pathology condition that requires a high diagnostic suspicion. Its poor clinical correlation, low frequency and high association with HIV-AIDS make its prognosis poor, regardless of the age of onset. **Case report:** A 33-year-old male with testicular tuberculosis diagnosed because of symptoms of intestinal occlusion. **Conclusion:** Testicular tuberculosis is an extremely rare entity with non-specific manifestations whose diagnosis requires high suspicion.

RESUMEN

Introducción: *La tuberculosis testicular es una patología de rara aparición y requiere de una alta sospecha diagnóstica. Su poca correlación clínica, escasa frecuencia y alta asociación con el VIH-sida hacen que su pronóstico sea malo, independientemente de la edad de aparición.* ***Caso clínico:*** *Masculino de 33 años con tuberculosis testicular diagnosticado a consecuencia de síntomas de oclusión intestinal.* ***Conclusión:*** *La tuberculosis testicular es una entidad sumamente rara, con manifestaciones poco específicas cuyo diagnóstico requiere de alta sospecha.*

INTRODUCTION

Genitourinary tuberculosis (TB) accounts for 14% of extrapulmonary cases being the epididymis the site where it can be found. Associated with AIDS (acquired immunodeficiency syndrome), the risk of suffering it is 500 times higher than in general population.[1] Intestinal TB has been detected in up to 70% of AIDS patients.[2]

CLINICAL CASE

We present the case of 33-year-old male with multiple risky sexual partners. He was treated by a private physician, who performed an ultrasound and clinically corroborated the diagnosis of orchi-epididymitis, for which he received antibiotic treatment with no improvement. Three weeks later he sought a second opinion; a new ultrasonography scan was performed, and the diagnosis of orchi-epididymitis was confirmed, so he was treated again with antibiotics without remission of symptoms. One month later he experienced left testicular enlargement (approximately 10 × 8 cm), weight loss, asthenia and adynamic, so while seeking a third opinion, he went to a public hospital where he underwent a left orchiectomy on suspicion of seminoma, being discharged after 48 hours. That same day he presented constant pain, inability to pass gases and to evacuate, progressive abdominal distention, nausea and vomiting of gastro-alimentary content, so he requested a fourth opinion and underwent a laparoscopy procedure for intestinal occlusion. Multiple implants were found throughout the small intestine as well as retroperitoneal lymph node growth that caused intestinal occlusion at the level of the Treitz angle. A derivative gastrostomy and

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jejunostomy for feeding were performed, and lymph node biopsies were taken. His evolution was torpid, and he died on the third postoperative day. Two days after his death, a histopathological report of both surgeries was received, which concluded testicular tuberculosis *(Figures 1 and 2)* and a report of the ELISA test for HIV was received, which was positive.

DISCUSSION

Genital tuberculosis affects patients under 50 years of age in 75% of cases, in a 2:1 ratio in favor of male sex.[1] In our case, the patient was a 33-year-old male. Due to its incidence, rapid progression, and aggressiveness, it is a potentially fatal pathology, as it was for the patient presented in this case.

Its presentation is more frequent in HIV-positive patients; however, there have been published cases such as the one of Cruz-Garciavilla[3] in which tuberculosis manifested in HIV-negative patients.

World medical literature mentions that the usual symptomatology consists of increasing and painless pollakiuria that does not respond to usual antibiotic treatment,[1] which may explain why our patient persisted with fever and pain despite the administration of antibiotics and specialty treatments aimed at the symptomatology he showed.

Intestinal tuberculosis, according to the world literature, is predominantly found in the ileocecal region, involved in 75-90% of patients, followed by the colon and jejunum,[4] which is related to the surgical findings in our patient as well as to the pathology report indicating TB activity in the lymph node region of this area.

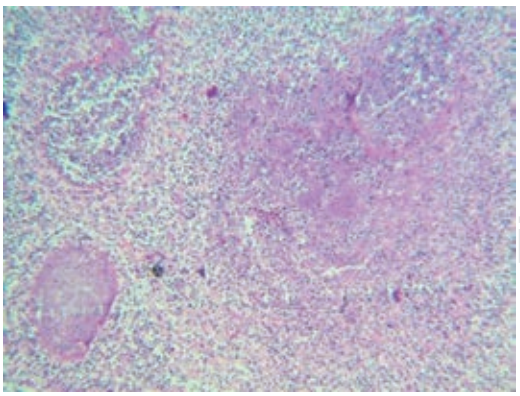

Figure 1: *Seminiferous tubules with caseous necrosis and peripheral granuloma.*

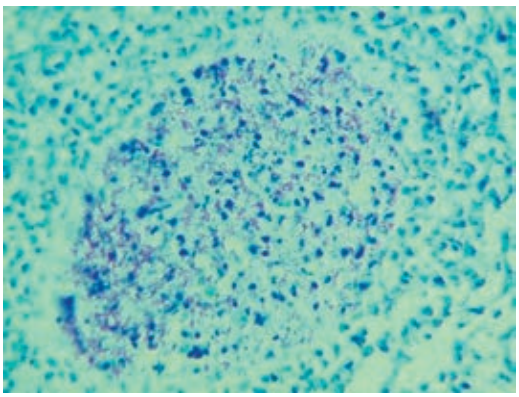

Figure 2: *Granuloma with positive Ziehl-Nielsen (ZN) staining tuberculosis bacilli.*

Symptoms are non-specific and vague, have a mean duration of two months, and 50 to 70% of patients have a history of symptoms over six months.[4] Its clinical diagnosis requires a high index of suspicion, since it can simulate other pathological processes of the testicle or intestinal pathologies that present with obstructive symptoms, which is largely related to the fact that the patient had about four to five months with symptoms prior to its definitive diagnosis.

Abdominal tuberculosis is most frequently located in the mesenteric lymph nodes or in the small bowel.[5] Initially, in our patient the possibility of having an intestinal occlusion was questioned due to more frequent pathologies of the digestive tract or adhesions. In the intraoperative period, lymph node biopsies were taken, both mesenteric and retroperitoneal, which confirmed to be the reason for the intestinal occlusion, and together with the patient's testicular history plus the confirmation by histopathology provided the accurate diagnosis of the patient with testicular and intestinal TB.

Patients with peritoneal tuberculosis, in addition to ascites, show constitutional

symptoms such as fever and weight loss.[5] Although our patient did not have ascites, he had a significant weight loss with consumption signs as well as febrile symptoms that did not respond to pharmacological treatment, part of which made diagnosis difficult due to the ambiguity of the symptoms that led the medical staff to think of an oncologic pathology.

Dr. Vinka Calás Hechavarria and collaborators present a case of a 34-year-old HIV-positive patient, who had fever for approximately two months and was diagnosed with genitourinary TB.[6] This case clearly represents the average age of onset of the most severe symptoms of genitourinary tuberculosis, which coincide with the case presented by us.

Urinary tuberculosis is a disease of young adults (60% of patients are between 20 and 40 years of age) and is more frequent in men.[7] Our patient, who was 33 years-old, was within the average age range in which the disease manifests itself as well as the sex with the highest incidence.

Genital tuberculosis in the male manifests as epididymitis or orchi-epididymitis with testicular swelling, usually painless.[8] The above is related to the clinical evolution of our patient as well as to the fact that the clinical focus was initially misdirected towards one of these two pathologies, which are epidemiologically more frequent than the testicular TB our patient had.

Ultrasonography of the epididymis affected by TB provides a heterogeneous appearance that depends on the stage of the inflammatory process in which caseous necrosis, granulomas or fibrosis may predominate.[9] In our case, it is noteworthy that in the first two medical visits the ultrasonography scans performed were normal.

María Teresa Milanés-Virelles and her collaborators present the case of a 32-year-old male patient who underwent an exploratory laparotomy where the presence of a citrine-yellow ascitic fluid and crowded and blocky loops covered by multiple vesicular lesions the size of a pimple were seen. Biopsy confirmed peritoneal tuberculosis; the Ziehl-Nielsen staining was positive.[10] This case is consistent with the age, surgical findings and pathology report of the case we present, which is striking because of the important correlation in both cases, being a sample of the non-specific clinical features, that testicular TB can present.

CONCLUSION

Testicular tuberculosis is an extremely rare entity, with non-specific manifestations. The diagnosis requires a high suspicion index and the close relationship it has with HIV can give us an orientation towards the diagnosis. The short-term prognosis can be good if diagnosed early, although this rarely occurs due to its low suspicion and rapid progression.

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Ethical considerations and responsibility

Protection of humans and animals: The authors declare that no experiments on humans or animals have been performed for this research.

Data confidentiality: The authors declare that they have followed their center's protocols on the publication of patient data.

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The antifragile surgeon

El cirujano antifrágil

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ABSTRACT

In this article I discuss how, under uncertainty, our inferences can be optimistic without a firm basis and how induction creates a false confidence that prevents the anticipation of catastrophic events. I explain the qualities 'fragility', 'robustness' and 'antifragility' in biological and human systems. Finally, I discuss the surgeon's professional antifragility strategies to minimize harm and continue with his/her work.

RESUMEN

En este artículo discuto cómo, en la incertidumbre, nuestras inferencias pueden ser optimistas sin una base firme y cómo la inducción crea una falsa confianza que impide la anticipación de eventos catastróficos. Explica las cualidades 'fragilidad', 'robustez' y 'antifragilidad' en sistemas biológicos y humanos. Finalmente, discuto las estrategias de antifragilidad profesional del cirujano para minimizar el daño y continuar con su trabajo.

"Wind extinguishes a candle and energizes fire. Likewise with randomness, uncertainty, chaos: you want to use them, not hide from them. You want to be the fire and wish for the wind."
Nassim Taleb[1]

INDUCTION: DERIVING THEORIES FROM OBSERVATIONS

We have the idea that scientific knowledge is derived from observations or experiments. However, it is not as easy as one might suppose to establish a scientific fact. It is first necessary to determine whether a set of observations is sound, whether the standards of proof are sufficient and whether they are accepted by the scientific community.

In the face of uncertainty, we find ourselves in the situation of the chicken or the egg, which observations will form a predictive theory or whether a theory –as a set of hypotheses– can be derived from observations that can then be generalized. At times, the researcher and the physician find themselves in this awkward situation.

What kind of orderly arguments allow us to go from observations to facts that we expect to deduce logically from them? Some arguments, taken as premises, are simple. For example, the syllogism (1) All men are mortal, (2) Socrates is a man, therefore (3) Socrates is mortal. The premises (1) and (2) are true, and the conclusion (3) is also true.

But real life does not have the logic of a syllogism. Consider (1) Some poetry books are boring, (2) this is a poetry book therefore (3) this book is boring. The conclusion (3) does not necessarily follow from (1) and (2), even if they are true.

The problem arises when the quantifier item 'some' is interpreted as 'all'. To the question why we believe that the Sun will rise tomorrow we can answer «because it rises *every day*». We could even add «*always*». We have that firm belief because the Sun has always risen in the past, and we infer that it will because we have observed the regularity of that phenomenon. We do not doubt that the Newtonian laws of motion will also be operative tomorrow, and we do not doubt it because they have worked so far.

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'All' and 'always' are *universal* quantifiers that we apply intuitively to *cases*, without considering that there may be exceptional cases. For example, an asteroid of about 10 kilometers in diameter hitting the Earth at more than 90,000 kilometers per hour, spewing millions of tons of ash into the atmosphere, returning as incandescent rain, and then obscuring it until it prevents sunlight from reaching the surface, thus creating a night that extinguishes most life. The catastrophe happened 65 million years ago in Yucatan. Improbable and impossible are not synonyms.

Experience seems to show that the repetition of a regular succession of events would be the *cause* of such events, when that repetition only causes our *expectation* that they will happen one or many more times. This association of ideas produces in us a habit consisting of creating general laws known as «inductive inferences»; that is, by a mechanism of induction we make, based on past experiences, conclusions for the future.

The first reference known as «the problem of induction» refers to David Hume in his *Treatise on Human Nature* (1739) and then in the *Inquiry Concerning Human Understanding* (1748). Induction creates an effect of confidence that makes us ignore the possibility of extraordinary events, especially when encouraging observations are numerous.

But with observations that are based on our sensory perception we can only make limited predictions. When it comes to biological phenomena, such as this pandemic, cause-effect relationships do not have the immediacy of physical phenomena. Moreover, the idea of pandemic and its consequences is, to say the least, very unpleasant. That is why a layman can still refuse to believe that it exists.

It is the case that I will call *The Inductivist Turkey*. In Bertrand Russell's original example,[2] it is a chicken that makes the mistake, but Taleb's turkey is more fun. The turkey knows that every day man feeds him, so he infers two conclusions that acquire belief status; (1) *based on evidence* (sounds familiar?), it infers that man will *always* feed him; (2) based on his *inductive thinking*, it infers that man loves him.

The induction appears to be correct until the day when, at the peak of its confidence, its prediction fails. On Christmas Eve he will correct his belief *in extremis*, just before the man twists his neck.

The Turkey went from many true observations to a false conclusion (induction). Experience leads us to believe that the Sun will rise tomorrow, but we are in no better position of certainty than the turkey (or the chicken).

Thus, our expectations persist despite being misleading. Our beliefs about the future are supported by past cases whose validity have not been examined closely by us. We will then have to refine our future expectations based on past regularities, asking ourselves whether there is a reasonable basis for giving them some weight, or question their validity. This is what happens with the large number of articles published in the face of urgency without proper peer review.

The mistake is a daily one. We confuse, like the turkey, the absence of evidence since there is nothing aggressive in the behavior of the farmer because he is always smiling, with evidence of absence on the intention to fatten him up for Christmas. That intention may well have been the cause of the farmer's smile, misinterpreted by the turkey. Inductive thinking can neither be proven nor invalidated by our previous experiences. Nor do we have any reason to believe in the so-called «regularity of nature». With some frequency we have incomplete data, with no evidence of its present truth or future validity.

FRAGILITY, STRENGTH, AND ANTIFRAGILITY

Whoever has seen a multitude of white swans could argue that according to his data it is *likely* that all swans are white. If a black swan appears, it means that it *can happen,* even though it is improbable that black swans exist. But improbable and impossible are not synonymous. The neck-twisting event was for the farmer a white swan, another baked stuffed turkey Christmas, but it was a black swan for the turkey, who mistook improbable for impossible. By the way, not all turkeys are black.

Black swans are large-scale events with massive unintended consequences. They

are improbable events of extreme impact, predictable only in retrospect, when the pieces of the catastrophe fit together *after the fact*.

Complex economic and social processes, such as devaluations, street protests and politicians' statements, have the volatility of randomness.[3] Zoonoses also have the volatility of randomness. These processes may *appear to be* stable for a long time, without extreme variations, like currency quotes and politicians' statements. But when subjected to large variations they can become chaotic, such as stock market crashes, epidemics or, even more so, this pandemic.

This pandemic is a black swan. For years the health system resisted with precarious stability despite, among other things, budget cuts, lack of supplies, shortage of doctors and the increasing demand of patients who for economic reasons increasingly resorted to public health services, along with the increasingly difficult conditions imposed by insurers and the high costs of private services.

Before Black-Swank-CoV-2, the robustness of Mexico's healthcare system was overrated. That reminds me of the song about the white elephant that was swinging on a spider's web. As he saw that it was resisting, he went to call another elephant... ... And as it resisted, throughout different administrations it was left to its resilience, the ability to withstand tensions and return to the previous state. Indefinitely.

Since it was resistant, it was not thought that erosion would end up collapsing it in the event of a catastrophic event. The possibility of such an event was dismissed. Its complex consequences include, among others, a spike in contagions, increased mortality, loss of jobs, increased extreme poverty and pressure on interdependent social systems.

But it is also an illusion to think that planning and budgets alone solve emerging problems. They do not. The incidence of future events cannot be measured since they have not happened. Risk cannot be measured either; it can only be estimated.

The fragility of the system could have been measured by comparing the gradual increase in the demand for services against the availability and capacity of care centers. Shortcomings could have been remedied.

However, a robust healthcare system would not have been sufficient to avoid the tipping point of a large random event and contain its effects. Resilient hospitals are once again having problems due to a lack not only of ventilators and trained personnel, but also of drugs to treat the sick.[4,5] In the face of an extreme random event, robust and resilient are not enough.

BIOLOGICAL ANTIFRAGILITY

Since robustness is not possible at all, complex systems require, for their preservation, mechanisms that can continuously self-regenerate. In this way they can become *antifragile*.

In nature there is no complacency but rather *redundancy*, a property of living systems against risk. The body has two kidneys, two lungs, alternating cerebral circulation (the polygon of Willis), hepatic sinusoids, and so forth. The various «layers of redundancy» are a fundamental property of natural systems. Redundancy «may seem like a waste if nothing unusual happens. Except that, usually, something unusual happens».[6]

The biological systems and processes of living beings are exposed to the challenges of an ever-changing environment. To adapt, they create variants that give them antifragility. This is how they evolve. One example is proteins with flexible regions, which can undergo functional alterations in response to environmental stress. In this way, they achieve «improvised repairs», or self-maintenance through simple repairs.[7]

This is how biological structures become difficult to inactivate or destroy. Although in any case, when their processes reach the point of no return, their fate is sealed. Either they harden for a while (becoming robust) or they remain the same (fragile) and degrade. As examples, in a few months, cancer cells defeat chemotherapies; in a few days of insufficient treatment bacteria become resistant to antimicrobial drugs.[7]

The emergence of new conditions requires adaptation, such as those bacteria that have

adapted to use Nylon® from our industrial waste as a source of nitrogen and carbon.[8,9]

The SARS-CoV-1 coronavirus became antifragile during the 2003 epidemic by creating a new surface antigen from a genome that formed a common pattern.[10] Coronaviruses tend to recombine and mutate very frequently.

The antifragility of SARS-CoV-2 is not surprising. The virus itself is fragile; it is easily destroyed with soap and water, or with alcohol-gel in appropriate concentration. But the information encoded in it during mutations makes it antifragile; it can do more than react through mutations. It has «a built-in property [literally, the flexibility of its proteins and processes] that allows it to find solutions in the face of adversity».[7]

RESILIENCE AND ROBUSTNESS ARE NOT ENOUGH

On the contrary, human-designed systems seek economy, simplicity, and *elegance*, say the mathematicians. Nothing missing, nothing surplus, nothing redundant, nothing spare. Usually resilient or robust systems are not damaged by the volatility of disorder, until they reach the point where their capacities are overwhelmed.

Given the increase in hospitalizations, Mexico has had to call for interns in social service (students in their last year before graduation), whose only requirement is to present their letter of completion, the *Letter of Internship*, with the promise to offer them «*high quality* personal protective equipment and *intensive training* in the *comprehensive* management of patients with covid» (my *italics*), according to the call.[11] What experience can a medical undergraduate student have? What kind of care can they offer with this very brief «*intensive training*»?

There are two perspectives to be considered here; that of the State that summoned them and that of the students who accepted, with no little exaltation. As for the first perspective, let us recall the military use of child soldiers during World War II by Germany, Japan, Russia, Poland, and the United Kingdom. As the conflict progressed, more and more youngsters were recruited; they were 16, 15, 14 years old. In Mexico, recruitment quickly shifted from specialists to general practitioners to interns, to fill the shortage.

From the second perspective, an anonymous source told me that some of the interns enthusiastically enlisted to treat patients with COVID-19. In the effervescence of the rush, and before the vaccination program began, the impetus of these young, not yet medical doctors, could well be due to some extent to the *glamour*, poorly thought out, of the commonplace of the hero who is not afraid of anything.

This reminds me of the expeditions known as the Children's Crusade, which left Germany (Cologne) and France (Vendôme) for the Holy Land in 1212, probably around Easter or Pentecost (an interesting trigger for the action) in search of the Holy Cross. Some sources refer to «*eodem anno fuit iter stultorum puerorum*» («that same year was the way of the foolish children»).[12] Some authors are inclined to ascribe the movement to divine inspiration; others, who knew of its sad end, conceive it as the work of the devil.

Many perished of hunger and thirst without reaching their destination or were stripped by the Lombards. Of those who left by sea, some were shipwrecked, others were sold as slaves by pirates, and the maidens were raped. Few returned home and some managed to reach Rome. According to the medievalist historian Dana Munro, although the children wished, in their enthusiasm, to join the various outposts, «it is difficult to explain the acquiescence of their parents or the favorable opinion of learned clerics». Munro also mentions a quotation from Pope Innocent III, the exclamation «these children have put us to shame, for while we sleep, they hasten to recover the Holy Land».[12] These two analogies show how, in the face of a catastrophic event, a fragile system tries to reinforce itself with resources that are also fragile.

But let's go back to the present and do a thought experiment now. We know (we know about) the disease, but we don't know how our body will react. What kind of turkey induction would we apply to decide, in the face of *our* worsening symptoms? The availability of

beds? The best equipped hospital? The best managed or the closest? The reputation or the distance? The cost? The intensity or the speed of evolution of the clinical picture as a function of distance? The advice of a colleague? Or the wait and see approach?

In addition, we would need the luck that the nearest public hospital had some robustness, available beds, medicines and supplies, and an adequate staff. If it is a private institution, availability would be needed, but also that the insurance would fully cover the costs, which have ranged from $433,000.00 MXN ($21,936.00 USD) for hospitalization to one million pesos in case intensive care is required and up to 3.67 million ($185,917.00 USD) in case of intubation. «The case with the highest amount of compensation reported has had a cost of 25.52 million pesos ($1,292,806.00 USD)»[13] (exchange rates are as of December 2020). Incidentally, one of several terms for 'luck' in Latin is '*alea*', whence 'random'.

PROFESSIONAL ANTIFRAGILITY

The *illusion* of robustness has the effect of tranquility and routine; it comes from the *desire* to maintain stability. Illusion and desire are particularly strong as the surgeon grows older and relies on his experience of white swans.

The Inductivist Surgeon was calm, he had always done things this way and they had always worked out well, but the voice of his experience has put him at the mercy of the Mexican health systems, public and private. *The Inductivist Surgeon* cannot remain, however, on the moon. If there were a Sea of Tranquility on Earth, it would not cease to be a sea. The Pacific Ocean is anything but peaceful. Tranquility reduces the capacity to adapt and respond, produces complacent and dysfunctional individuals in the face of the «new» reality, which is not new but always changing.[14] Heraclitus already said that «the Sun is not new every day, but continually new».[15,16]

On the other hand, resilience and robustness can allow us to rise from the ashes, but only up to a certain limit. In mythologies, the indestructible exist, but not in real life. The surgeon cannot stop operating. As a psychotherapist, he cannot resign himself to giving virtual consultations. He must become antifragile; it depends on his art, the *ars chirurgia*.

The anti-fragile surgeon will have to forget the stable era since we no longer live in it. In addition to making up for the limitations of a fragile State, he/she will have to accept the adaptive measures of private institutions, which will not look after their welfare (they are not healthcare institutions, they are businesses). They will protect themselves to the detriment of the parts (the medical corps and other personnel) that cease to be functional (that fall ill or die); those that, from being assets (that have value, that generate profit) become liabilities (that mean expenses). A sick surgeon who cannot work, loses monetary value; for «*his*» hospital and his family he is a liability.

The first step towards antifragility is to cushion the fall; the emotional damage of loss aversion. What is lost is lost. This involves taming emotions that, like uncertainty, cannot be eliminated. I do not say it's easy, no one is immune and there are no recipes; emotions are part of rationality. But what is broken tends to remain broken, and fragility punishes just like a terminal illness.[17]

As a second step to avoid remaining at the mercy of the system, the surgeon will have to perform damage control and design survival strategies; relying on his ability to improvise, which has allowed him to resolve adverse trans-operative events in the past. It will be indispensable to *accumulate redundancy* of resources to continue operating, redundancy in equipment and backup structures, such as personal protective equipment (Tyvek®), masks (N95, KF94, FFP), face masks, gloves, and others; and to keep a list of reliable suppliers. In addition, virtual communication platforms and the corresponding computer equipment with several levels of data storage, external and in different sites or clouds are essential items today.

The surgeon is at a disadvantage when faced with the rising cost of materials and services on which he/she relies to provide service and generate his/her income. But what

is redundant when there is no need becomes indispensable when there is a shortage. What seemed to be liabilities become assets. It is better redundancy than lack, especially when the free market reduces stocks and manipulates prices to the detriment of its revenues, a large part of which it will now have to allocate to anti-fragility if it wants to remain operational.

The third step toward antifragility involves peer support structures and networks. This is where cooperation to share changing information comes into play. Information is an input. The isolated surgeon is fragile.

Not least important, is that the best asset is oneself, the robust and antifragile surgeon who invests in his own health, improving his/her quality of life, his/her self-knowledge, turning pandemic confinement into that honest and deep introspection for which he/she had no time before. That's where he/she will get the resistance.

To become antifragile, the surgeon will have to consider this pandemic as a very long trans-surgery. He/she will have to become an expert in strategies of changes and adjustments, of improvised repairs, and constant re-evaluations.

And even when the pandemic becomes endemic, we will have to keep in mind Albert Camus' *The Plague*, since there have already been several episodes of decreasing contagions during which people go out to celebrate as if nothing had happened, an emotionally understandable but rationally inadequate attitude. I would like to end by quoting the ending of his 1947 novel, which I think is still valid:

> «Listening, indeed, to the shouts of joy that went up from the city, Rieux [the doctor] remembered that this joy was always threatened. For he knew what this joyful crowd ignored and which can be read in books, that the plague bacillus never dies or disappears, that it can remain for decades asleep in furniture and clothing, that it waits patiently in rooms, cellars, suitcases, handkerchiefs and papers and that, perhaps the day would come when, to the misfortune and teaching of men, the plague would awaken its rats and send them to die in a blissful city.»[18]
> (My own translation.)

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