CLINICAL CASE

Cystic carcinoma, a clinical case

Carcinoma del cístico, a propósito de un caso

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Abstract

Primary cystic duct carcinoma is a rare tumor and comprises 0.1% to 0.2% of carcinomas of the gastrointestinal tract. We present a case of a male with weight loss and jaundice. Evidence is shown by imaging of intrahepatic and extrahepatic duct dilatation conditioned by extrinsic bile duct compression. An endoscopic retrograde pancreatic cholangiography was performed confirming the compression, so a surgical exploration was performed showing a tumor of the cystic duct, a cholecystectomy with resection of regional lymph nodes, as well as a hepatic-jejunal anastomosis. The tumor is reported as cystic duct carcinoma without lymph node involvement.

Keywords: *Cystic. Carcinoma. Duct. Jaundice.*

Resumen

El carcinoma primario en el conducto cístico es un tumor raro y abarca del 0.1% al 0.2% de los carcinomas del tracto gastrointestinal. Presentamos el caso de un varón con pérdida de peso e ictericia, en el que se demuestra por imagen una dilatación de vías intrahepática y extrahepática condicionada por una compresión extrínseca del colédoco. Se realiza colangiografía pancreática retrógrada endoscópica que confirma la compresión, por lo que se lleva a cabo una exploración quirúrgica que evidencia una tumoración del conducto cístico. Se realiza colecistectomía con resección de ganglios linfáticos, además de anastomosis hepatoyeyunal. La tumoración se reporta como carcinoma del conducto cístico sin involucro ganglionar.

Palabras clave: *Cístico. Carcinoma. Conducto. Ictericia.*

Introduction

Extrahepatic bile ducts neoplastic pathology is rare among gastrointestinal neoplasms, with an incidence ranging from 2% to 3.6%[1]. Cystic duct primary carcinoma was first described in 1951 by Farrar[2] and, since then, 70 cases have been reported in the literature[1,3]. It is a very low-frequency tumor that accounts for 0.1% to 0.2% of gastrointestinal tract carcinomas. The traditional form to diagnose it was by meeting certain described criteria, which include growth restricted to the cystic duct, absence of a neoplastic process in the gallbladder, the liver or common bile duct, and histological evidence of carcinoma[1-3]. However, these

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Date of reception: 06-04-2020
Date of acceptance: 03-02-2021
DOI: 10.24875/CIRUE.M23000357

Cir Cir (Eng). 2021;89(4):529-533
Contents available at PubMed
www.cirugiaycirujanos.com

strict criteria generated problems in clinical practice, which is why several authors proposed new criteria that categorized the disease by metastatic extension. With this advancement, treatment began to be analyzed, which previously was only surgical, without leaving the possibility to evaluate other adjuvant therapies such as postsurgical radiotherapy[1,3-5]. Owing to the small number of cases described in the literature and the importance for these patients to be evaluated, we present the following case that we had as an experience at the University Hospital of the Autonomous University of Nuevo León, Mexico.

Clinical case

Forty-nine-year-old male with a history of chronic liver disease under study and recurrent renal lithiasis. His symptoms had started with a 5-kg weight loss within previous 2 months accompanied by poor general condition, jaundice and generalized pruritus. On initial approach, laboratory tests revealed leukocytosis, transaminase abnormalities and hyperbilirubinemia with predominance of direct bilirubin: leukocytes 16.9 K/U, aspartate aminotransferase 120 IU/L, alanine aminotransferase 140 IU/L, alkaline phosphatase 911 IU/L, total bilirubin (TB) 12.5 mg/dL, direct bilirubin 7.3 mg/dL, indirect bilirubin 5.2 mg/dL. Viral serology was positive for hepatitis C virus (HCV) and negative for human immunodeficiency virus; therefore, the origin of the patient liver disease was considered to be viral. An upper abdomen ultrasound reported heterogeneous liver with intrahepatic bile duct dilation, gallbladder with 2-mm wall, and 16-mm common bile duct visible up to the head of the pancreas, which was observed to be normal. To better characterize the bile ducts, a magnetic resonance imaging study was performed, in which the gallbladder was observed with hydropic changes, in addition to an obstruction of the distal common bile duct middle third and ectasia of the bile duct proximal to this point, with no evidence of lithiasis, tumor on the head of the pancreas or any neoplastic process that caused this common bile duct point of dilation (Fig. 1).

In view of these findings, the patient underwent an endoscopic retrograde cholangiopancreatography (ERCP), which showed the ampulla of Vater, which was cannulated; there was an area of extrinsic stenosis in the common bile duct with no evidence of intraluminal neoplastic process; the cannula was passed, but it was not possible to enter the intrahepatic biliary tract and neither was passing to the cystic duct.

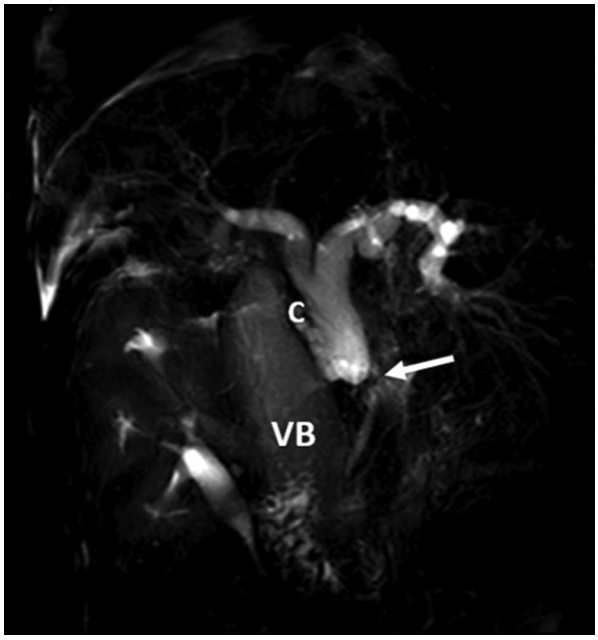

Figure 1. *Bile duct magnetic resonance reconstruction. The arrow indicates the point of common bile duct dilation transition, which coincides with the point where the cystic duct (C) connects to the common bile duct. VB: gallbladder.*

A sample was taken for cytology and the procedure was completed with a sphincterotomy. Despite the ERCP, the patient continued with hyperbilirubinemia at the expense of direct bilirubin. Bile fluid cytology reported protein, biliary and cellular material without abnormalities.

To complement the workup procedure, an endoscopic ultrasound was performed, in which the head of the pancreas was inspected without relevant findings, and a markedly dilated extrapancreatic common bile duct (12 mm), with scarce mud within, was observed, with no frank identification of any tumor activity, and intrapancreatic common bile duct of normal caliber (3 mm). Regional lymphadenopathy of apparent reactive nature was observed at hepatic hilum region (Fig. 2).

In view of these findings, a contrasted computed tomography (CT) scan of the chest and abdomen was performed, which reported common bile duct dilation of up to 2 cm accompanied by intrahepatic duct dilation, as well as hydropic gallbladder, with no evidence of distant lesions suspicious of malignancy in the liver, lungs or bone tissue.

Performing a surgical exploration was decided, in which the liver was found to have generalized cirrhotic characteristics, the gallbladder was visualized and the thickened cystic duct was identified, which was

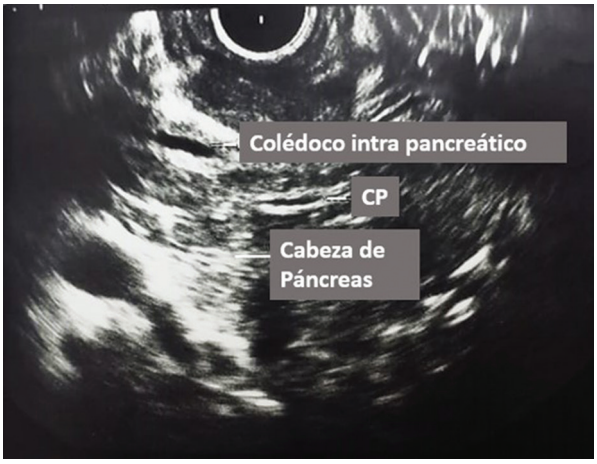

Figure 2. *Endoscopic ultrasound showing common bile duct dilation (12 mm) with no evidence of neoplastic process in the head of the pancreas, in addition to a normal pancreatic duct. Colédoco intra pancreático: intra-pancreatic common bile duct; CP: pancreatic duct; Cabeza de Páncreas: head of the pancreas.*

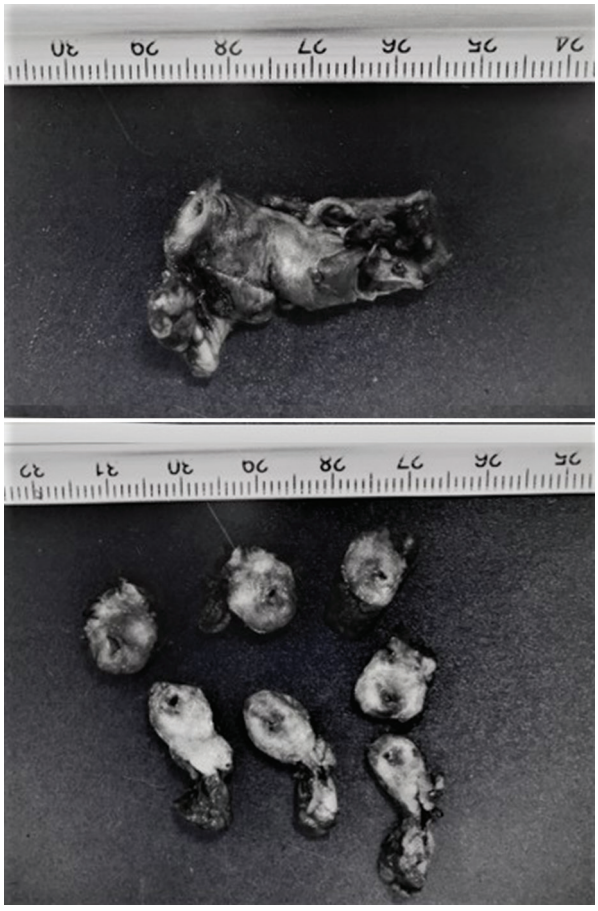

Figure 3. *Sectioned cystic duct surgical specimen in which the neoplastic process is observed. Thickening of the duct and decreased size of its lumen can be observed.*

secondary to a tumor of the structure without infiltration towards the common bile duct, hepatic ducts or vascular structures on gross examination. Cholecystectomy with common bile duct resection in proximity of the cystic tumor was performed, as well as regional lymph nodes resection for histopathological examination. For bile duct reconstruction, a hepato-jejunal anastomosis was performed at 60 cm from the angle of Treitz, with the surgical procedure being carried out uneventfully. Figure 3 shows the tumor found in the cystic duct.

On immediate postoperative period (24 hours), TB decreased to 8.4 mg/dL with direct bilirubin of 5.1 mg/dL, with TB normal values (0.9 mg/dL) being obtained 72 hours after surgery, and the patient was therefore discharged with no eventualities.

Histopathological analysis of a 11.6 x 4 x 0.6-cm gallbladder was reported, with data consistent with chronic cholecystitis and no evidence of neoplastic cells in the gallbladder, in addition to identifying the cystic duct with 2.5 x 1 x 0.9-cm dimensions, with wall thickness of 0.4 cm and lumen of 0.1 cm, with histological section showing neoplastic cells consistent with with cystic duct carcinoma at its middle third with infiltration to the wall, as well as lymphatic, perineural and periductal and fatty tissue infiltration without lymph node infiltration, and resection borders negative for malignancy.

This patient was classified as carrier of a clinical stage IIIA cystic duct carcinoma, and was kept under oncological surveillance for the next 12 months by means of control CT scans, with no evidence of residual disease.

A new CT scan was performed during oncological surveillance at the end of the second year post-surgery, with multiple lymphadenopathies being identified at the level of the hepatic hilum, para-aortic, aortocaval and celiac trunk. In view of regional relapse suspicion, chemotherapy with gemcitabine (1,000 mg/m^2) and cisplatin (42 mg) every 21 days was started; at fourth chemotherapy cycle, gemcitabine was replaced by capecitabine due to the development of toxicity.

Currently, during his third postsurgical year, the patient has remained stable, functional, with disease at first line of treatment.

Discussion

Primary cystic carcinoma has a male preponderance, and mean age at presentation is 65 years (range: 38-79 years)[6-9]. It has not been associated with vesicular lithiasic disease, since it is found only in

25% of all cases[1,8,10,11], and neither has it been associated with the presence of HCV[12], which is why we consider that, in our patient, it was a coincidence rather than an etiological association, although, despite being an exceptional case, these associations are not described in the literature due to the low frequency of this condition. Its clinical presentation is not specific, highly similar to that of bile duct lithiasis, but its main symptoms are abdominal pain and jaundice. In a series of 33 cases, 81% were reported to present with right upper quadrant abdominal pain, 41% with an associated abdominal mass, and only in 4 of all 33 cases was there obstructive jaundice[6]. Very few patients are preoperatively diagnosed by imaging studies[2,13-15]; in most cases, the tumor is discovered by laparotomy or on histopathological examination of the specimen, as it occurred in our case.

Various systems have been developed for cystic duct carcinoma staging, but no diagnostic protocol has been established that is applicable to all cases. The Farrar criteria are strict and do not cover advanced disease, because, according to them, once lymph node invasion is present, it becomes a "non-cystic duct carcinoma"[2,4]. Therefore, new diagnostic classifications define cystic duct carcinoma as a tumor with location centered on the cystic duct with capacity to invade lymph nodes and neighboring structures, a denomination that is more practical for most cases at advanced stages (Table 1). The incidence of lymph node metastases is 40%, which has been reported to be low in comparison with that of extrahepatic bile ducts (50%) or gallbladder cancer (80%)[7,16,17].

Early development of symptoms due to cystic duct obstruction, its slow growth and late metastases favor a better prognosis in patients with cystic carcinoma[3,4,9,16-19]. Perineural invasion is one of the most significant prognostic risk factors, with a frequency of 85-93%[1,11,12,20]. Our patient had perineural and angiolymphatic invasion.

The recommended treatment is radical surgery, which comprises cholecystectomy and bile duct excision with regional lymphadenectomy. Postsurgical adjuvant radiation therapy may be considered in cases of advanced disease, particularly in those with positive surgical margins. Mean survival is 27.2 months, while that of gallbladder carcinoma is only 5.8 months, and that of other extrahepatic bile ducts, 3-11 months; in our patient, we have exceeded this mean survival, with 32 months of survival currently having being reached.

Table 1. Farrar criteria and new criteria for cystic duct carcinoma diagnosis

Farrar criteria	New criteria
– Tumor growth strictly restricted to cystic duct	– Tumor growth may go beyond the cystic duct
– Absence of neoplastic process in gallbladder or liver ducts	– Tumor primary site is defined by the site of greatest thickness (tumor geometric center), with the cystic duct being the anatomical site of this process
– Histological evidence of carcinoma	– Presence of carcinoma cells on histopathological examination

Conclusions

The nature of this ailment was biased for a long time due to strict diagnostic criteria, which left out cases of advanced disease; however, with the new diagnostic criteria, more cases can be included and, therefore, increase the significance of prospective studies, with postsurgical therapy for advanced disease being emphasized, as well as long-term follow-up of patients with localized disease. In this case, incidental diagnosis was established due to the higher frequency of cases with cholangiocarcinoma we treat in our center; however, it is of great importance for this disease to be considered as one of the possible differential diagnoses in patients with obstructive jaundice and cancer characteristics.

Acknowledgements

The authors thank each one of their patients, who are a new story to tell and enable knowledge advancement. And to the work team and patients of our teaching hospital, who are the raison d'être of our work.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures that were followed adhered to the ethical standards of the responsible committee for experimentation on human subjects and were in agreement with the World Medical Association and the Declaration of Helsinki.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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