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Intraductal ablation by radiofrequency for inoperable biliopancreatic neoplasms with jaundice: experience at a regional hospital

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ABSTRACT
The current treatment of choice for inoperable and/or unresectable biliopancreatic neoplasms complicated by jaundice is the placement of metal biliary stents. The most common complication is obstruction due to tumor growth. The application of radiofrequency ablation (RFA) is a new minimally invasive technique for the thermal ablation of the tumor tissue that causes biliary stenosis. Experience with RFA is scarce and there are few retrospective studies of clinical cases with a limited number of patients. Thus, there is little information on technical difficulty, safety and short-medium term monitoring. We present three cases, one cholangiocarcinoma and two pancreatic adenocarcinomas, with jaundice due to biliary stenosis. RFA was used with an ELRA catheter during endoscopic retrograde cholangiopancreatography (ERCP). The patients were monitored for ten months in order to assess the difficulty of treatment, efficacy and immediate and medium-term complications.

Key words: Radiofrequency. Biliary stenosis. ERCP (endoscopic retrograde cholangiopancreatography).

INTRODUCTION
The placement of a biliary stent is the current treatment of choice for an unresectable malignant biliary stenosis (1). Unfortunately, jaundice reappears within 4-6 months due to biliary obstruction caused by detritus (biliary sludge) or proximal, distal or intraprosthetic tumor growth. This complication interferes with both the quality of life due to the need for hospitalization and increased morbidity due to cholangitis. Furthermore, the use of chemotherapy is complicated and limited by increased bilirubin levels.
Endoluminal radiofrequency ablation (RFA) applied during endoscopic retrograde cholangiopancreatography (ERCP) is a minimally invasive technique for the thermal ablation of the tumor mass occluding the bile duct (2). Experience with this technique has been reported in the literature. This includes retrospectively reported clinical cases and a single prospective study (IGNITE-1) of 18 patients, which concluded that the technique was feasible and safe and the permeability of the stent was maintained (3). We present our experience with three patients at the Hospital Francesc de Borja in Gandia (Valencia, Spain). These cases had malignant neoplasms that caused stenosis of the bile duct. RFA with the VIVA combo™ RF System (Taewoong Medical) and an ELRA™ (STARmed, Goyang-si, Gyeonggi-do, Seoul, South Korea) bipolar RF electrode were used for the bile duct, with an exposure length of 18 mm and a 175 cm long and 7 Fr diameter catheter.

**CASE REPORT 1**

The case was an 83-year-old ex-smoker male with type 2 diabetes mellitus (DM), high blood pressure (HBP) and an aortic valve disease bioprosthetic valve that was fitted in 2009. He also had a recurrent cardioembolic stroke that was treated with acenocoumarol. He was admitted for magnetic resonance imaging (MRI) due to painless jaundice in October 2016. This identified a dilation of the intrahepatic bile duct up to the level of the hepatic hilum, with an obstructive filling defect in the common hepatic duct. A mass in the vesicular bed in the hilar liver parenchyma was also identified, which was heterogeneous, hypovascular and measured 4 cm. Blood tests showed total bilirubin (TB) 11.91 mg/dl, direct bilirubin 10.64 mg/dl, AST 78 U/l, ALT 103 U/l, GGT 496 U/l and AP 421 U/l. An ERCP identified the distal bile duct of around 7 mm with an abrupt stop from the middle third to almost the intrahepatic confluence, suggestive of Bismuth IV cholangiocarcinoma. The intrahepatic bile duct was very dilated and a 10 x 80 mm WallFlex™ fully covered metal stent was fitted. A new ERCP was performed in December 2017, after ruling out surgical treatment. The metal stent was removed and ELRA™ radiofrequency was applied to the stenosis. This consisted of four pulses of two min each at 75 degrees, one pulse on each branch of the biliary bifurcation and two on the common hepatic. Two 12 cm x 8.5 Fr stents were
placed with a good biliary drainage. Bilirubin levels decreased to 0.99 mg/dl after the procedure. After 72 hours, the patient complained of chest pain with elevated troponin and the echocardiography was normal. A cardiac MRI was ruled out. He was subsequently admitted in March 2017 with ascites secondary to peritoneal carcinomatosis and a poor general condition (TB 2.88 mg/dl). He was also admitted again in May 2017 due to fever, jaundice, TB of 7 mg/dl and septic shock and subsequently died.

CASE REPORT 2

The case was a 60-year-old female with Barrett’s esophagus, HBP and obesity. A Toupet fundoplication and cholecystectomy were performed in 2015 and she was admitted in November 2016 due to painless jaundice. Laboratory tests showed TB 9.83 mg/dl, direct bilirubin 8.99 mg/dl, AST 43 U/l, ALT 79 U/l, GGT 295 U/l, AP 358 U/l and CA 19-9 44 U/ml. A thoraco-abdominal-pelvic CT scan identified a suspicious pancreatic neoformation in the corpocephalic transition, with infiltration of extrahepatic portal vein and the gastroduodenal artery. The ERCP identified a malignant stenosis from the middle of the common bile duct to almost the confluence of about 3 cm, with dilation of the pre-stenotic common hepatic duct. The intrahepatic bile duct was very dilated and endoscopic sphincterotomy was performed and a 9 cm x 8.5 Fr plastic stent was placed. A subsequent endoscopic ultrasound was performed that identified gastroduodenal artery involvement without involvement of the hepatic artery. The cytology was adenocarcinoma. In light of the borderline adenocarcinoma, neoadjuvant chemotherapy and subsequent surgical assessment was decided upon. The patient started FOLFIRINOX therapy in January 2017, with moderate digestive and hematological toxicity tolerance. A CT scan was performed and radical radio chemotherapy was proposed as there was no response and no possibility of a R0-resection. An ERCP was performed in July 2017 and RF was applied at 75 degrees for two minutes, without complications, and a 10 Fr x 9 cm plastic stent (not metal) was placed to avoid modifying the radiotherapy parameters. A CT scan three months later showed the biliary tree unchanged, the biliary stent in normal position, improvement in the stenosis of the portal vein and a modest increase in the size of the
A WallFlex™ uncovered metal stent was placed. There have not been any biliary complications to date, with a TB of 0.27 mg/dl ten months after RF.

**CASE REPORT 3**

The case was a 60-year-old male with no known drug allergies and ex-smoker for the past 15 years. He also had type 2 DM with a poor metabolic control and HBP. He was admitted in February 2017 due to constitutional syndrome and mild conjunctival jaundice (TB 0.99 mg/dl). Laboratory tests showed AST 110 U/l, ALT 231 U/l and C-reactive protein (CRP) 218.39 mg/l. A thoraco-abdominal CT identified a neoplasm in the pancreatic head that was in contact with the portal vein at the junction of the mesenteric vein, with no plane of separation. An ERCP identified a stenosis that was suggestive of malignancy of around 20 mm at the level of the middle bile duct. A 10 Fr x 7 cm plastic stent with correct drainage of the bile duct was placed. An MRI cholangio identified dilation of the extrahepatic bile duct and the common bile duct was 18 mm in size. A stenosis of around 12 mm in length was identified, with parietal ring enhancement after intravenous gadolinium administration. Several millimetric focal hepatic lesions in the RHL were found, the largest was around 20 mm, as well as subcapsular lesions in the VI/VII segments, which were suggestive of metastasis. An endoscopic ultrasound identified a 32 mm x 29 mm pancreatic head injury with retrograde dilation of the main pancreatic duct. The lesion did not make contact with the superior mesenteric artery or the celiac trunk. However, it did have a portomesenteric axis with no plane of separation, although there were no clear signs of infiltration. A puncture using a 25 G needle with aspiration (adenocarcinoma) was performed.

In light of the pancreatic ADC stage IV diagnosis, first-line treatment with gemcitabine/Abrazane was started in April 2017. ERCP was performed in July 2017 and the plastic stent was removed. During the procedure, 2 cm of the pre-papillary bile duct of 7 mm caliber appeared with 3-4 mm of a filiform stenosis of around 3 cm. The common hepatic was dilated to around 12 mm, with a normal intrahepatic duct. RFA was applied with an ELRA™ catheter at 75 degrees for two minutes to the stenotic area.
and there were no incidents. A 10 x 60 mm WallFlex™ Boston uncovered metal stent was placed with good biliary drainage. There were no biliary clinical or laboratory test abnormalities (TB 0.26 mg/dl) ten months after post-RFA monitoring.

DISCUSSION
The current paradigm of the palliative treatment of choice for unresectable malignant biliary stenosis is the placement of a permanent metal biliary stent. However, there was no treatment to control local intraprosthetic tumor growth. The experience to date with RFA has been anecdotal, with reports of retrospective clinical cases and a single prospective phase 2 study with 18 patients and only three months of surveillance (3).

We present our experience in a regional hospital with three clinical cases, two with a pancreatic neoplasia and one with Bismuth IV cholangiocarcinoma. All cases were unresectable and candidates for palliative treatment. None of the patients had immediate complications (< 48 h) and only one had chest pain with a significant elevation of troponin 72 hours after the procedure. There was no possibility to assess whether it was secondary to the application of RFA or due to stress derived from the ERCP itself and sedation with propofol IV.

During monitoring, one of the patients died five months after the procedure due to progression of the disease. Two patients remained asymptomatic and had normal TB ten months after the radiofrequency treatment. With regard to technical difficulty, no differences were found in terms of the level of difficulty, although there was a difference in the duration, as thermal ablation (7-10 W) had to be applied for at least two minutes, depending on the extension and impedance. It was not necessary to enlarge the sphincterotomy to insert the catheter and dilation of the bile duct was not used in any of the cases. According to the literature (4,5), a covered metal stent is placed in patients with malignant distal biliary stenosis. An uncovered metal stent or 10 Fr plastic stents are placed in patients with hilar neoplasia, depending on the biliary lumen and location.

Preliminarily data suggest that the application of intraductal biliary RFA in patients with non-resectable/inoperable neoplasia that causes bile duct stenosis apparently
does not increase technical difficulty. However, it does extend the duration of the examination. Thus, our experience suggests that it is feasible and safe due to the absence of immediate complications. However, more cases and long-term monitoring are pending. This previously non-existent treatment option provides patients with metal biliary stents that improve the quality of life and prevent repeated admissions due to obstructive jaundice and/or cholangitis.

REFERENCES
Table 1. Total survival (months) during 10 months

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<tr>
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<th>Survival, months</th>
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<tr>
<td>Case 1</td>
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<td>Case 2</td>
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<td>Case 3</td>
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BB0: total bilirubin at diagnosis; BB1: total bilirubin a month after ERCP with radiofrequency; BB5: total bilirubin five months after ERCP with radiofrequency; GGT0: GGT at diagnosis; GGT1: GGT a month after ERCP with radiofrequency; GGT5: GGT five months after ERCP with radiofrequency A; ALP0: alkaline phosphatase at diagnosis; ALP1: alkaline phosphatase a month after ERCP with radiofrequency; ALP5: alkaline phosphatase five months after ERCP with radiofrequency.
Fig. 1. Caso clínico 1. Sonda ARF ELRA™ en conducto hepático común.
Fig. 2. Caso clínico 2. Estenosis maligna colédoco medio.