Case Report

The effects of endobiliary radiofrequency ablation in two patients with pancreatic cancer: Gross and microscopic findings

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A B S T R A C T

Endoscopic palliation of malignant biliary obstruction through the placement of plastic or self-expandable metal stents (SEMS) is the standard treatment for unresectable disease. Endobiliary radiofrequency ablation (RFA) is a therapeutic modality that has been recently used as a primary therapy to restore biliary patency in unresectable biliary malignancies and to treat occluded uncovered biliary SEMS because of tumor ingrowth. Preliminary animal studies have shown the tissue effects of RFA; however, the correlation of histopathologic findings in humans has not been reported. In this paper, we present two patients with a surgically resectable malignant distal biliary obstruction that was secondary to pancreatic adenocarcinoma. After they underwent biliary decompression, endobiliary RFA was performed. This was immediately followed by the placement of an uncovered biliary SEMS. Both patients subsequently underwent pancreatectoduodenectomy. A histopathologic review showed a circumferential zone of necrosis of 1.0–1.5 mm in depth. When compared to published animal data, the zone of necrosis was demonstrably reduced. These discrepant findings are likely multifactorial (e.g., heat-sink phenomenon, differences in study protocol, and comparison of dissimilar tissues). Based on our preliminary histopathologic findings, further studies may be necessary to definitively determine the depth of penetration within the human bile duct during endobiliary RFA.

Keywords: Biliary cancer, Pancreatic adenocarcinoma, Radiofrequency ablation, Stent

Introduction

Endoscopic palliation of malignant biliary obstruction is the primary treatment for patients with surgically unresectable disease. The placement of plastic or self-expandable metal stents (SEMS) provides decompression of malignant biliary obstruction from extrabiliary cholangiocarcinoma or pancreatic adenocarcinoma.1–4 Uncovered SEMS lose their patency over a period of 3–6 months, primarily because of tumor ingrowth or overgrowth.5 Photodynamic therapy (PDT) for hilar cholangiocarcinoma—with or without biliary SEMS—demonstrably reduces cholestasis, improves quality of life, and increases survival rates.6–8 However, PDT is limited by availability, photosensitivity, procedural cost, and the need for repeated treatment sessions.

Endobiliary radiofrequency ablation (RFA) has recently become a therapeutic option for treating malignant biliary obstruction. Endobiliary RFA delivers a temperature-dependent and time-dependent energy deposition into bile duct tumors, and thereby induces thermal injury and subsequent localized necrosis.3 Early reports suggest RFA can be used as the primary therapy for unresectable biliary malignancies and used to restore the patency of uncovered biliary SEMS occluded by tumor ingrowth.9,10 In a recent study, Steel et al11 found that endobiliary RFA, followed by SEMS placement in patients with malignant biliary obstruction (16 cases of pancreatic adenocarcinoma and 6 cases of cholangiocarcinoma), resulted in 90% stent patency at 30 days and continued stent patency at 90 days. Radiofrequency ablation of malignant biliary obstruction prior to SEMS insertion may delay the occlusion of uncovered SEMS by tumor ingrowth.

Reports have been published of in vivo and ex vivo porcine models to assess endobiliary RFA.12,13 However, the correlation with human histopathologic findings has not been reported. In this paper, we describe the first gross and microscopic findings in the human bile duct after radiofrequency ablation.

Case report

Two patients underwent endobiliary RFA, followed by pancreatectoduodenectomy at the Imperial College London (London, United Kingdom), for pancreatic adenocarcinoma that had caused malignant biliary obstruction. Patient 1 was a 76-year-old man with compensated hepatitis B cirrhosis and systemic arterial hypertension who presented with recent weight loss and jaundice (his...
bilirubin level was 13.5 mg/dL) over a 6 week period. Patient 2 was a 74-year-old man who also presented with recent weight loss and jaundice (his bilirubin level was 26.9 mg/dL) over the previous 8 weeks. In both patients, computed tomography (CT) revealed an obstructing pancreatic head mass.

Endoscopic retrograde cholangiopancreatography (ERCP) using a standard video duodenoscope (Olympus TJF-160VR; Olympus America, Center Valley, PA, USA) confirmed a distal common bile duct (CBD) stricture in both patients. After placing a 10 Fr 7-cm biliary stent for initial decompression, an endoscopic ultrasound (EUS) and repeat ERCP were performed at 2 weeks in Patient 1 and at 5 weeks in Patient 2. The EUS demonstrated resectable lesions. Fine-needle aspiration confirmed adenocarcinoma in both patients. Repeat ERCP with RFA (Habib EndoHPB catheter; EMcision UK, London, United Kingdom) was performed to provide optimal biliary drainage and potentially mitigate tumor ingrowth and overgrowth in the event that surgical intervention was delayed. Energy was delivered by a RFA generator (1500 RF generator; RITA Medical Systems, Fremont, CA, USA), which delivered electrical energy at 400 kHz at 10 W for 120 seconds. Sequential applications were applied throughout the length of the stricture with a 1-minute rest period between applications. Immediately after RFA, an uncovered biliary SEMS (Wallflex RX; Boston Scientific, Natick, MA, USA)—10 mm in diameter and 80 mm in length—was placed. Both patients underwent successful pancreaticoduodenectomy 20 days later (Patient 1) and 32 days later (Patient 2).

Gross examination of the resected specimens revealed a patent CBD with a zone of necrosis at the RFA treatment area (Fig. 1). A histologic review of Patient 1 demonstrated a circumferential area of necrosis that was limited to the mucosa (Fig. 2A). It was 1 mm thick (Fig. 2B). A dense mixed inflammatory infiltrate surrounded the zone of necrosis.

The resected specimen from Patient 2 revealed focal tumor infiltration into the CBD wall and within the partially necrotic and inflammatory zone surrounding the dilated and denuded CBD. This necrotic inflammatory zone surrounding the CBD measured up to 1.5 mm in thickness.

**Discussion**

The initial results of endobiliary RFA show its safety and efficacy as a treatment for malignant biliary obstruction.\(^1\) This technique evolved from similar percutaneous and intraoperative techniques used for treating primary and secondary hepatic cancers.\(^14\,\,15\) The commercially available Habib EndoHPB catheter (EMcision UK) is an 8 Fr (2.6 mm) 1.8 m long bipolar radiofrequency (RF) catheter that passes over a 0.035 inch guidewire and across malignant strictures during ERCP or percutaneous transhepatic cholangiography. The distal tip of the catheter has two stainless steel ring electrodes that deliver controlled RF energy through contacted tissues.\(^1\) The delivered energy results in rapid ionic motion, thereby generating heat around the probe and within surrounding tissues, and eventually culminating in coagulative necrosis.\(^1\)

Experimental studies using porcine models have evaluated the gross and histopathologic changes immediately following endobiliary RFA. Zacharoulis et al\(^1\,\,13\) and Itoi et al\(^1\,\,12\) demonstrated a positive correlation between the amount of RF energy delivered and the extent of thermal injury. However, Zacharoulis et al\(^13\) utilized an in vivo healthy porcine model. The researchers noted that 6–7 W delivered over 50–60 seconds induced full thickness coagulation of the bile duct wall without injuring surrounding structures. Itoi et al\(^12\) positioned the RFA catheter directly into a freshly resected porcine liver parenchyma, and attempted to mimic malignant biliary obstruction. Maximal energy of 20 W delivered over a 120-second application time yielded 11.3 ± 1.2 mm of penetration and 29.0 ± 1.0 mm of spread, compared to 4.3 ± 0.6 mm of penetration and 11.0 ± 1.0 mm of spread by using the minimal settings (i.e., 5 W for 60 seconds). The zone of necrosis was microscopically equivalent to the grossly measured area of ablation. Based on experimental and initial clinical data, the settings of 7–10 W delivered over 120 seconds are believed to be adequate baseline RFA settings;\(^1\) however, characteristics such as tumor size, bile duct wall thickness, and the anatomic relationship to surrounding structures need to be considered.

Our patients were treated with endobiliary RFA set at 10 W for 120 seconds. Both patients subsequently underwent pancreaticoduodenectomy, which included resection of the RFA-treated area. The histological circumferential zone of necrosis was 1 mm (Patient 1) and 1.5 mm (Patient 2). These results are notably discrepant in comparison to the 10.3 ± 0.6 mm of penetration noted when identical settings were used in the ex vivo porcine model.\(^1\) The conflicting findings can likely be explained by a combination of the heat-sink phenomenon, differences in study protocols, and the comparison of dissimilar tissues. Blood flow within tissue surrounding the human CBD—including the portal vein and hepatic artery—provides a cooling or heat-sink effect that could account for the minimal necrosis observed in our patients. Both patients underwent SEMS placement immediately after undergoing RFA. The histologic evaluation was moreover performed at least 20 days (Patient 1) and 32 days (Patient 2) after the index RFA procedure. Radial expansion of the SEMS may have compressed necrotic tissue, causing a modest zone of necrosis in comparison to the zone of necrosis in the ex vivo findings. The ex vivo liver histologic evaluation occurred immediately after RFA, whereas in our patients it was delayed, thereby allowing for tissue healing within the bile duct and/or sloughing of necrotic intraductal debris. Tissue differences may account for the discrepant findings. The RFA catheter was placed directly into the porcine liver parenchyma during the ex vivo study and into an otherwise normal porcine CBD in the in vivo study. These tissues are not identical to that of our patients. The response to RFA is likely to be different when comparing porcine versus human tissue and healthy versus
cancerous tissue. It is impossible to discern whether applying RFA produced ablation beyond the tumor margin in our patients. This case report is the first description of the human bile duct after endobiliary RFA. Further human studies are needed to determine optimal RFA settings in patients with malignant biliary obstruction.

Conflicts of interest

Ryan Law: No conflicts of interest. Madhava Pai: No conflicts of interest. Todd H. Baron: No conflicts of interest. Nagy Habib: Stockholder and board member for EMcision Ltd. UK.

References