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CASE REPORT

Radiofrequency Ablation of the Pancreas. II: Intra-Operative Ablation of Non-Resectable Pancreatic Cancer. A Description of Technique and Initial Outcome

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ABSTRACT

Context There is little reported experience of radiofrequency ablation of pancreatic tumours. Our group has reported the development of a porcine pancreatic model of radiofrequency ablation of the pancreas. This brief report details the application of this technique to clinical practice.

Case report A 58-year-old man with metastatic pancreatic tumour underwent operative radiofrequency ablation. An operative approach was utilised to protect the stomach and transverse colon and also to prevent thermal injury to the inferior vena cava. In addition, the operative technique was combined with prophylactic hepaticojejuno-stomy and gastrojejunostomy to anticipate ablation-related biliary injury or duodenal stenosis. A post-ablation CT scan two weeks after the procedure confirmed radiological evidence of ablation. The patient remained well until his death, 3 months after surgery.

Conclusion This report demonstrates that operative radiofrequency ablation is feasible and was safely carried out in this case. More experience is required to assess the spectrum of complications and if there is true oncological efficacy.

INTRODUCTION

Radiofrequency energy is widely used for the ablation of solid parenchymal tumours [1, 2, 3], in particular liver tumours [4, 5]. In contrast to the liver, where tumour-bearing tissue is surrounded by normal hepatic parenchyma, the pancreas is surrounded by structures such as the stomach, duodenum and colon and concerns regarding the risks for causation of thermal injury to these structures have limited the use of radiofrequency for non-resectable pancreas tumours. We recently reported the development of an *ex-vivo* model of radiofrequency ablation of the porcine pancreas [6, 7] which has been further characterized in this issue. In our model, thermal injury was recognizable by conventional histologic methods and was also characterized by loss of tissue oxidative enzyme activity measured as loss of nicotinamide adenine dinucleotide (NADH) activity [6, 7].

Given that these precursor studies have demonstrated evidence of precise, control-lable ablation of non-tumour bearing porcine pancreas, the present report details the translation of this technique to clinical practice.

CASE REPORT

A 58 year-old Caucasian male presented to the General Surgical Service with epigastric pain radiating through to the back. His symptoms settled rapidly after admission and he was allowed home to await out-patient gastroscopy and ultrasound scan. Both these tests were normal but as he reported that he was continuing to lose weight he underwent

Figure 1. Preoperative CT scan showing a tumour in the head of the pancreas (shown by an arrow).

computed tomography (CT). The CT scan was reported as showing a 3 cm transverse diameter mass in the head of the pancreas with dilatation of the proximal main pancreatic and duct and two hypodense areas in the liver (Figure 1). He was referred urgently to the Hepatobiliary Service some four months after his index presentation. The patient had a full Karnofsky score [8] and had no co-morbidity of note.

On examination, he was jaundiced. Abdominal examination was normal. There was no evidence of ascites. Laboratory tests revealed an obstructive pattern and the carbohydrate antigen (CA 19-9) was 70 U/mL (laboratory reference range: 0-22 U/mL).

The patient underwent urgent endoscopic retrograde cholangiopancreatography (ERCP) which confirmed the presence of a distal (intra-pancreatic) bile duct stricture with proximal dilatation. There was concomitant dilatation of the main pancreatic duct. In view of the CT evidence of suspected hepatic metastatic disease a 7.5 Fr 6 cm metal stent (Luminexx, Endoscopic Biliary Stent, BARD, MA, USA) was placed endoscopically across the stricture.

In order to establish a tissue diagnosis and to gauge the extent of his disease, the patient underwent laparoscopy. Laparoscopy showed that there were small tumour deposits (about 2 cm in size) on the anterior surface of segments III and V (corresponding to the CT appearances). There was no other evidence of peritoneal dissemination and the extra-pancreatic tumour burden appeared to be of relatively small volume. The lesions in segment III and V were biopsied and histology confirmed poorly to moderately differentiated adenocarcinoma consistent with a pancreatic origin.

The findings, disease stage and treatment options were discussed with the patient. It was explained that in the presence of advanced disease, standard care would comprise referral for chemotherapy. The option of radiofrequency ablation was discussed as part of a research protocol. After full informed consent and specifically with the knowledge of the lack of information on clinical safety profile and the lack of evidence of beneficial outcome, the patient elected to undergo operative radiofrequency ablation.

At operation, a transverse right subcostal incision was made. Full laparotomy confirmed the presence of a relatively small tumour in the head of the pancreas. There were several small surface deposits of tumour on the liver as noted on laparoscopy. There was no other evidence of trans-peritoneal dissemination.

The hepatic flexure of the colon was mobilised and retracted downwards. An incision was made on the peritoneum on the lateral aspect of second part of duodenum and the duodenum was mobilised using Kocher's manoeuvre to expose the infrahepatic inferior venacava and the right border of the aorta. The Kocher manoeuvre extended from the lateral border of the bile duct to the level of the superior mesenteric vessels crossing the duodenum. The mobilisation was not extended into the infra-colic compartment.

The lesser sac was opened by incising the leaf of peritoneum between greater curvature of the stomach and transverse colon keeping the plane of dissection out with the gastroepiploic arcade. The tumour in the head of pancreas was now controllable bi-manually and was physically isolated from the cava, stomach and transverse colon (Figure 2). Radiofrequency ablation (RITA systems Mountain View, CA, USA) of the pancreatic

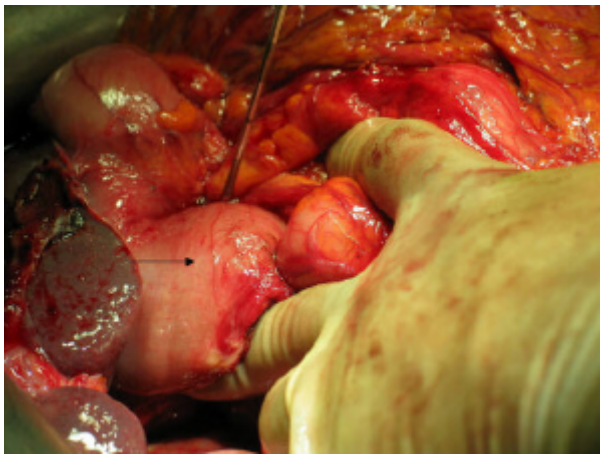

Figure 2. Intraoperative radiofrequency ablation of the pancreas. Note the Kocherised duodenum (arrow) and bimanually stabilised tumour with probe in situ. Inferior venacava is protected by the left middle finger behind the duodenum. Stomach and colon (protected by left index finger) are mobilised away from the ablation point.

tumour was then carried out under bi-manual control. A multi-array probe (Starburst XL, Rita Systems Inc., Mountain View, CA, USA) bearing seven individual probe-tip thermal sensors was used for radiofrequency ablation. Three passes of the probe at 90°C for 10 minutes each were made to the central portion of the head, the superior portion of the head and the para-duodenal portion. For each new ablation, the probe was removed and re-passed. No occlusion of the superior mesenteric vein/portal vein was employed during ablation. There was no external or luminal duodenal cooling during the procedure.

The small surface lesions in the liver were treated by surgical excision. Biliary bypass was then performed in a standard fashion: cholecystectomy was undertaken and the common hepatic duct transected. The jejunum was divided 25 cm distal to the duodeno-jejunal flexure and the proximal jejunal limb used to create an antecolic isoperistaltic side-side gastrojejunostomy. The distal (Roux) limb was brought up and a retrocolic end-side hepaticojejunostomy fashioned with interrupted 3-0 'polydioxanone synthetic' absorbable suture (Ethicon, Edinburgh, Scotland). The cut distal bile duct was closed above the dorsal border of the pancreas. Intestinal continuity was restored by a jejunojejunostomy. Although ablation for 10 minutes was associated with biliary thermal injury in some of our animal studies, this was not an issue in the present study as biliary drainage was secured by hepaticojejunostomy.

The post-operative course was complicated by a brief episode of polyuria (without impairment of renal function) but was otherwise unremarkable. A CT scan of the pancreas taken two weeks after ablation is seen in Figure 3. It showed a well-defined homogenous low-density area thought to represent ablated tumour. He received post-operative chemotherapy in the form of gemcitabine and remained well until the time of his death 3 months after surgery.

ETHICS

This study was approved by the Local Research Ethics Committee as the index case of a programme for evaluation of radiofrequency ablation for non-resectable pancreatic tumours.

DISCUSSION

There is little reported experience of radiofrequency ablation in human pancreatic cancer [9]. The available reports utilised probes from earlier generation equipment and

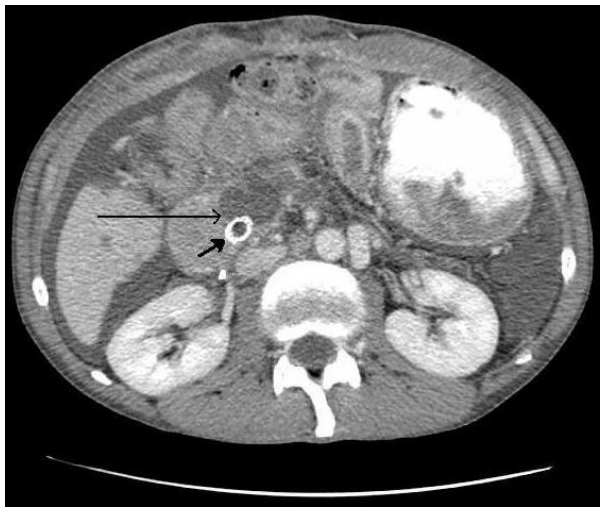

Figure 3. Postoperative CT scan showing a well defined homogenous low density area suggesting ablated tumour (long arrow). Note metal stent in situ (short arrow) and presence of ascites.

as a consequence did not have well defined optimal ablation parameters. There is also a critical lack of information on the safety of the technique in terms of injury to peripancreatic structures. Injury to structures such as the duodenum during radiofrequency ablation in the setting of a non-resectable pancreatic tumour may be associated with a lethal outcome. The technique described here represents an extension of an on-going programme of evaluation of radiofrequency ablation of the pancreas. In an *ex-vivo*, non-tumour bearing setting in the porcine pancreas we have reported the development of a technique that permits controlled ablation of pancreatic parenchyma associated with loss of tissue oxidative enzyme activity whilst sparing the duodenum and portal vein. Logically, the programme of research would continue in a live animal model but there is no large animal model of pancreas cancer and inter-species variations in the precise anatomical relationships between the duodenum and the pancreas [10] suggest that important lessons can only be learnt from evaluation of the technique in man.

Although radiofrequency energy is well-established for the treatment of other solid-organ tumours, adaptation of the technique for the ablation of pancreatic tumours needs attention to details of technique. The aim of this report is to share our initial experience and to generate discussion on the issues relating to the technique.

First, the ablation is carried out surgically. Although many reports now attest to the safety of the percutaneous approach for ablation of liver tumours, the presence of important adjacent viscera anterior, posterior and inferior to the head of the pancreas raise the risks of the percutaneous approach. Further, in our *ex-vivo* studies we demonstrated that ablation of the head of the pancreas is associated with ablation of the distal intra-pancreatic bile duct. Although in the present case there was a metal endobiliary stent in situ to serve as a conduit, the issue of the potential significance of biliary injury was avoided by a concomitant hepaticojejuno stomy. Similarly, the potential late sequelae of duodenal occlusion as a result of fibrosis were addressed by concomitant gastrojejuno-stomy.

Second, from an oncological perspective there is little information on whether ablation of pancreatic tumours has any beneficial effect on survival. In reality, this lack of information affects practice in two areas: patients with operable pancreatic cancer must undergo standard care in the form of resection and laparotomy must not be undertaken in the majority of individuals with known metastatic disease simply in order to undertake ablation. It is accepted that the present case falls into the latter category. Reasons for undertaking laparotomy for application of radiofrequency ablation in this individual were his relatively young age, lack of co-morbidity, fully-informed desire to pursue all known and novel interventions. It is anticipated that the future patient in whom radiofrequency ablation may be utilised is the individual with a tumour which is found to be unresectable at laparotomy because of locally advanced disease. In this setting, given that laparotomy has already been undertaken to assess the resectability, operative radiofrequency ablation of the pancreas may become an option in much the same way as radiofrequency ablation of the liver can be used as an adjunct. Further, from the oncologic perspective, it must be acknowledged that as the mode of death in many patients with pancreatic cancer is either related to loco-regional or systemic tumour progression, the effect of a local treatment on tumour course is unknown. It is tempting to speculate that ablation may be used to downstage the tumour but there is no evidence to date to support its use in such a fashion.

In summary, this report describes the detailed technique of operative radiofrequency ablation of a non-resectable cancer of the head of the pancreas with concomitant biliary and gastric bypass. The initial favourable outcome is worthy of wider dissemination within the pancreatic surgical community but

further development of the technique must be carefully regulated and under rigorous and ethically scrupulous supervision.

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References

1. Venbrux AC, Montague BJ, Murphy KPJ, Bobonis LA, Washington SB, Soltes AP, Frassica FJ. Image-guided percutaneous radiofrequency ablation for osteoid osteomas. J Vasc Interv Radiol 2003; 14:375-80. [PMID 12631644]

2. Anzai Y, Lufkin R, DeSalles A, Hamilton DR, Farahani K, Black KL. Preliminary experience with MR guided thermal ablation of brain tumours. AJNR Am J Neuroradiol 1995; 16:39-48. [PMID 7900601]

3. Rosenthal DI, Springfield DS, Gebhardt MC, Rosenberg AE, Mankin HJ. Osteoid osteoma: percutaneous radio-frequency ablation. Radiology 1995; 197:451-4. [PMID 7480692]

4. Decadt B, Siriwardena AK. Radiofrequency ablation of liver tumours: systematic review. Lancet Oncol 2004; 5:550-60. [PMID 15337485]

5. Lam CM, Ng KKC, Poon RTP, Ai V, Yuen J, Fan ST. Impact of radiofrequency ablation on the management of patients with hepatocellular carcinoma in a specialized centre. Br J Surg 2004; 91:334-8. [PMID 14991635]

6. Date RS, Biggins J, Paterson I, Denton J, Mcmahon RF, Siriwardena AK. Development and validation of an experimental model for the assessment of radiofrequency ablation of pancreatic parenchyma. Pancreas 2005; 30:266-71. [PMID 15782106]

7. Date RS, McMahon RF, Siriwardena AK Radiofrequency ablation of the pancreas. I: Definition of optimal thermal kinetic parameters and the effect of simulated portal venous circulation in an ex-vivo porcine model. JOP. J Pancreas (Online) 2005; 6:581-7.

8. National Institute for Clinical Excellence. Technology Appraisal Guidance No. 25. 2001/16 NICE issues Guidance on Gemcitabine for Pancreatic Cancer. London, United Kingdom: May 2001.

9. Matsui Y, Nakagawa A, Kamiyama Y, Yamamoto K, Kubo N, Nakase Y. Selective thermocoagulation of unresectable pancreatic cancers by using radiofrequency capacitive heating. Pancreas 2000; 20:14-20. [PMID 10630378]

10. Schantz LD, Laber-Laird K, Bingel S. Pigs: applied anatomy of the gastrointestinal tract. In: Jensen SL, Gregersen H, eds. Essentials of Experimental Surgery: Gastroenterology. New York, NY, USA: Harwood Academic Publishers, 1996:2611-9. [ISBN 3-7186-5496-2]