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CASE REPORT

USE OF ELECTROLYSIS FOR THE TREATMENT OF NON-RESECTABLE HEPATOCELLULAR CARCINOMA

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Abbreviations: CT, computed tomography; HCC, hepatocellular carcinoma.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common solid organ malignancy worldwide, responsible for approximately 1000 000 deaths annually.[1] Surgical resection is the modality that offers the best chance for a cure[2] but <20% of patients are considered suitable for surgery.[3] Multifocal disease, tumour size, vascular invasion and liver cirrhosis account for the low resectability rates.[4]

Several ablative techniques have been investigated to manage non-resectable liver tumours.[3] These involve either injection of an ablative agent or delivery of a thermal insult, but all have their limitations.[3] In contrast, electrolysis results in tissue ablation by a non-thermal process.[5] The delivery of a direct current (Coulombs; C) through tissue between an anode and cathode produces sodium hydroxide, hydrogen ions, hydrochloric acid and chlorine gas, and pH changes, which are cytotoxic.[6] The amount of Coulombs delivered (Amperes × s), is directly proportional to the volume of necrosis induced.[7] The electrolytic ablation of primary HCC has previously been described in China with promising results.[8,9] This is a report of the first known patient in the Western world to have a HCC treated by electrolysis.

CASE REPORT

A 68-year-old Vietnamese man with known liver cirrhosis was referred with an asymptomatic, 4 cm liver mass found on a surveillance computed tomography (CT) scan (Fig. 1a). The lesion straddled segment VIII and IV. His past history included chronic obstructive airways disease, non-insulin-dependent diabetes and hepatitis B (surface antigen positive). Liver function tests and α-fetoprotein (4 kμ/L) were normal. The mass had not changed significantly over a 3 month period and a laparoscopy with ultrasound was performed to further assess the pathology. Biopsies taken at laparoscopy confirmed the presence of a HCC without extrahepatic disease. The extent of cirrhosis and the tumour size precluded resection or ethanol injection. The patient declined systemic chemotherapy but requested some form of treatment. Electrolytic ablation was offered as a possible option for managing the tumour.

The tumour was approached via a bilateral subcostal incision. It measured 4.2 cm × 4.2 cm × 2.6 cm on intraoperative ultrasound. Two 2 mm-diameter electrolysis catheters (supplied by Cordis Webster, Johnson and Johnson Medical, North Ryde, NSW, Australia), each housing a 4 mm platinum anode and cathode with 2 mm separation, were inserted into the tumour 8.2 mm apart. The positions were confirmed on ultrasound. The catheters were attached to a direct current generator (Soring, Medizintechnic, Quickborn, Germany) that delivered a predetermined ‘dose’ of Coulombs at a constant voltage for the desired volume of necrosis. The rate of current delivery is dependent on tissue resistance. Previous experiments have established that the volume of necrosis is directly proportional to the amount of Coulombs delivered,[7] with a mean rate of 3.5 cm^3 per 100 C. Tumour volume was 54.3 cm^3, corresponding to an electrolytic dose of 1500 C. Electrolysis took 288 min. There was no haemorrhage or bile leakage but the patient developed pulmonary atelectasis with a small pleural effusion. The white cell count remained normal. Liver enzymes rose by <3 times the upper limit of normal in the first week, but returned to normal by 6 weeks. The patient was discharged 7 days after the procedure.

Follow-up CT scans at 1 week and 3 months were compared with the preoperative images (Fig. 1; Table 1). At 1 week after the procedure there was no evidence of viable tumour (Fig. 1b) and a central area of necrosis with gas was noted. An irregular hypodense area leading to the lesion superiorly most likely represented the catheter tract. At 3 months the electrolytic lesion was cystic and smaller, but showed an area of peripheral enhancement. The enhancement could represent postoperative granulation tissue or fibroblastic activity from the electrolytic treatment, or may indicate tumour recurrence. The patient continues to be followed up.

DISCUSSION

Hepatocellular carcinoma is the most common solid cancer worldwide, with a median survival of 4–6 months if untreated.[10] Surgical resection offers the best chance for a cure but it is appropriate for only up to 20% of patients with HCC.[3] Ablative techniques remain attractive methods of treating unresectable disease.[3] These techniques preserve more normal parenchyma

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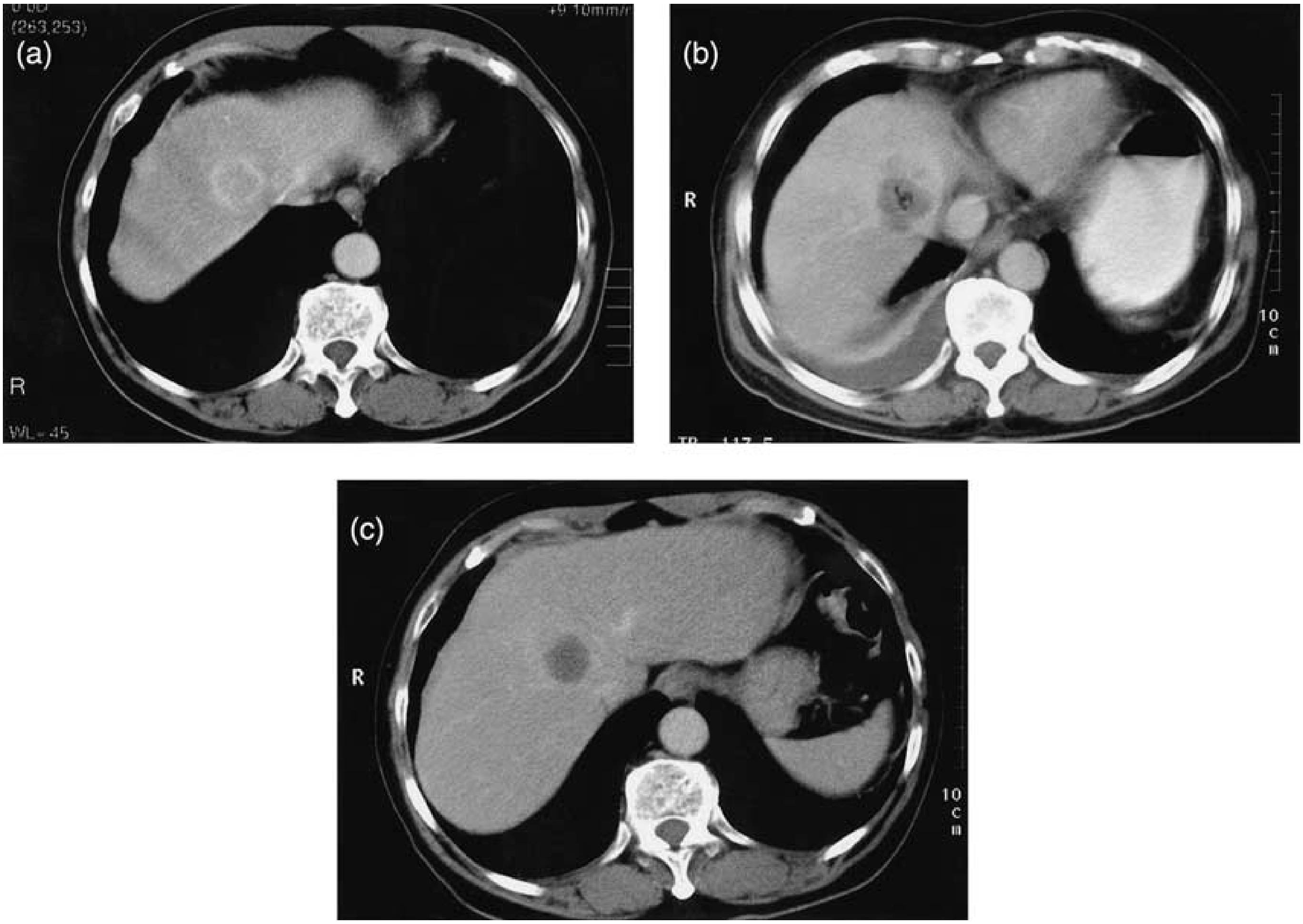

Fig. 1. (a) Computed tomography (CT) scan 3 months preoperatively showing the hepatocellular carcinoma (HCC) in segment IV; (b) CT scan 1 week after electrolytic treatment showing a necrotic lesion containing gas; (c) CT scan 3 months postoperatively, showing a reduction in size of the lesion.

Table 1. Pre- and post-electrolysis CT changes

Lesion	3 months before operation	1 week after operation	3 months after operation
Size	3.3 × 3.4 cm	3.1 × 3.4 cm	2.5 × 2.8 cm
Shape	Spherical	Spherical	Spherical
CT features	Solid, enhanced	Necrotic with gas	Cystic and rim of enhancement

CT, computed tomography.

and are considered less morbid compared to that of surgical resection.[11] Ablative techniques involve either the injection of a cytotoxic agent (e.g. alcohol, acetic acid), or the delivery of a thermal insult (heating or freezing). An inherent limitation of these ablative techniques is the inability to reliably destroy tumours more than 4–5 cm in diameter.[12] All thermal techniques may be influenced by the 'heat sink' phenomenon. There is equilibration of thermal energy by convection to nearby vascular structures, where the effect of heating or cooling is minimized and reduces the reliability of ablation.[13] Cryotherapy may also be complicated by 'cryoshock', which is mediated by the release of inflammatory cytokines.[14]

Electrolysis has been shown to completely ablate liver tumours in animal models and in humans.[12,15] As a non-thermal technique, it is not susceptible to the heat sink effect.[5] When adjacent to vascular structures electrolysis does not ablate or thrombose larger vessels, although it destroys the immediately adjacent parenchyma.[16] This is most likely due to the increased resistivity of larger vessel walls. The limitations to this method are that it is time-consuming, although steps to improve this are being investigated. Also the technique is available only at laparotomy at present.

The use of electrolysis for the ablation of primary HCC has previously been described in China, although the article is lacking in statistical interpretation.[8,9] Patients with surgically unresectable cases of HCC experienced tumour shrinkage and prolonged survival following electrolysis, and when given to patients with very large tumours and severe cirrhosis, electrolysis did not cause further impairment of liver function.[8] A study by Lao *et al.* showed an 88% 6 month survival rate and a 69% 1 year survival rate for patients following electrolytic treatment for primary liver cancer.[8] The main side-effect noted following treatment was short-term fever, which returned to normal within 3 days and had minimal interference with general physiology of the patient.[8]

Computed tomography has been used for follow-up evaluation after radiofrequency ablation. An initial increase in size of radiofrequency-created lesions at 1 week represents ablation of a margin of normal tissue, and a subsequent progressive decline in lesion size reflects successful treatment. An increase in size after the initial week suggests local failure of treatment.[17] Following a single treatment with electrolysis, the size of the HCC lesion in the present patient has reduced significantly, from 3.1 cm × 3.4 cm at 1 week after procedure to 2.5 cm × 2.8 cm 3 months after procedure. However, there was no increase in the size of the lesion when comparing pre- and post-procedure scans. This may indicate that the lesion may not have been adequately treated with a suitable margin, although measurements are approximate. Because there was only one patient in the present case study we cannot be certain whether the enhancement in the periphery of the lesion is a normal preoperative and postoperative finding. Other features of the CT scan included necrosis, which appears hypodense, and gas in the lesion at 1 week after procedure. Possible reasons for the presence of gas within the lesion include production by reactions at the electrode site, production by bacteria within the necrotizing tissue, or introduction of air via the insertion path of the electrode. There was no gas evident in the 3 month post-procedure CT scan. A limitation with interpretation of CT scans was the inability to accurately determine superior–posterior tumour dimension, and its resultant omission from results. The patient also had a preoperative scan performed at a different hospital on a different CT scanner.

As far as we know this is the only case to be treated with electrolysis in the Western world. In the present patient, electrolysis has significantly reduced the size of the HCC lesion and the reduction in size is a promising sign, which may encourage further investigations of the use of this technique in patients with this disease.

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