Original article

Use of electrolysis as an adjunct to liver resection

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Background: Patients with hepatic metastases are potentially curable if all the diseased tissue can be resected. Unfortunately, only 10–20 per cent of patients are suitable for curative resection. Electrolysis is a novel non-thermal method of tissue ablation. When used in conjunction with surgery it may increase the number of resectable liver tumours with curative treatment.

Methods: All patients had been deemed inoperable using currently accepted criteria. Nine patients with hepatic deposits from colorectal carcinoma underwent combined surgical resection and electrolytic ablation of metastases.

Results: The treatment was associated with minimal morbidity. Within the electrolytically treated area seven patients had no radiological evidence of recurrence at a median follow-up of 9 (range 6–43) months; local recurrence was detected in two patients. Six of the nine patients had metastases elsewhere in the liver with four having extrahepatic metastases. Three patients remain tumour free. Three patients died. The median survival was 17 (range 9–24) months from the time of treatment.

Discussion: Electrolysis with resection may confer a disease-free and overall survival benefit. The small size of this initial study precludes statistical analysis, but preliminary results are encouraging.

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Introduction

Colorectal carcinoma is the third most common malignancy and the most common source of liver metastases, with the liver being the earliest and often the only site of metastatic disease[1]. These patients are potentially curable if all diseased tissue can be removed[2,3], but have a poor prognosis (measured in months) if this is not feasible[4]. The size, number or position of the metastatic lesions allows only 10–20 per cent of patients to be eligible for a formal resection[5].

Several ablative techniques have been investigated as alternatives to surgical resection for the treatment of colorectal metastases[4,6]. Electrolysis is a novel non-thermal method of tissue ablation[7]. A direct current is passed through a conductive medium between a pair of electrodes (cathode and anode). The electrolytic 'dose' is measured in coulombs (amperes × seconds). Tissue electrolysis produces sodium hydroxide and hydrogen at the cathode, and hydrochloric acid and chlorine gas at the anode[8,9]. The significant pH changes produced by electrolysis are cytotoxic and cause localized parenchymal necrosis with a negligible thermal effect[7–9].

Over the past few years electrolysis of liver tumours has been investigated extensively at this institution[7,10–13]. Not only has the process been shown to ablate liver tumours completely in experimental models[12,14], but it is also safe in terms of both its inherent tissue destruction and the inability to thrombose or damage large blood vessels in close proximity to the electrolytic lesion[13]. A pilot study was performed in five patients before tissue resection to determine whether this method could be used safely. No adverse effects resulted from the treatment (D. Berry, S. Wemyss-Holden, G. J. Madden, A. Dennison, unpublished results). Nine patients were then subjected to a formal liver resection, with electrolytic ablation of metastases that would have deemed the cancer irresectable using currently accepted criteria.

Patients and methods

The records of nine patients with a histologically confirmed diagnosis of secondary liver metastases from colorectal carcinoma between the dates of April 1997 to May 2000 were reviewed. The median age was 57 (range 44–66) years.

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Conventional surgical treatment was not possible because of the multiplicity of tumours, proximity to major vessels or distribution of metastases, or a combination of these factors. Patients were excluded from the study if they were ineligible for laparotomy, or had extrahepatic disease or multifocal liver metastases such that resection and ablation would compromise liver function. All patients included in the study had previously undergone resection of a primary colorectal tumour. Four patients had previously undergone hepatic resection and presented with irresectable hepatic recurrence over a period of 37 months (August 1997 to September 2000). One patient had undergone previous hepatic resection and was receiving electrolysis alone for a single irresectable metastatic deposit.

The patients underwent formal resection of hepatic metastases, followed by electrolytic ablation of metastases that could not be resected surgically. Ethics committee approval was obtained before any of the patients was treated. Before electrolysis, all patients were fully informed about the experimental nature of the study.

Two 6-Fr electrolysis catheters (Cordis Webster, Johnson and Johnson Medical, North Ryde, New South Wales, Australia) were inserted into the tumour, 9–24 mm apart, depending on the size of the tumour. Electrode positioning was confirmed ultrasonographically. The catheters were attached to a direct current generator (Medizintechnic, Soring, Quickborn, Germany), and a predetermined 'dose' was delivered at a constant current, calculated for the desired volume of necrosis. Tumour dimensions and position were determined using previous computed tomography (CT) scans and confirmed by intraoperative ultrasonography. The volume of each lesion was calculated using the formula $V = 4/3\pi(r_1 \times r_2 \times r_3)$. A 5-mm margin of normal parenchyma surrounding the tumour was also ablated. Previous experimental studies had shown a linear dose–response of 3·5 cm^3 per 100 coulombs (C)[10]. Tumour radius ranged from 5 to 30 mm. The 'dose' varied from 200 to 1000 C according to the calculated volume. The length of time taken for electrolysis ranged from 42 to 210 min. Platinum was chosen as the electrode material because of its inert nature, and theoretical antineoplastic properties[15].

White cell count and liver function tests were carried out before and after treatment. Carcinoembryonic antigen (CEA) levels were monitored after operation to assist in determining any tumour recurrence.

CT scans were reviewed retrospectively by a radiologist, who was blinded to treatment details for each patient. The radiologist interpreted and compared CT findings before electrolysis with those obtained at 1 week, 3, 6 and 9 months, and annually after electrolysis to determine the effectiveness of treatment. The electrolytic lesion was evaluated for size, shape and location following electrolysis as well as for evidence of recurrence. Successful treatment was associated with no tumour recurrence within the electrolytically treated lesion, while failure of electrolytic treatment was associated with recurrence within the treated area. Recurrence elsewhere was considered to be due to the natural course of the metastatic disease and not a failure of treatment.

Results

Of the nine patients treated, six are still alive. The procedures were performed with a median hospital stay of 9 days. Median follow-up was 9 (range 6–43) months. In two patients who had electrolysis of lesions lying adjacent to the inferior vena cava, there was no damage to the vascular structure.

Seven of the nine patients with hepatic metastases from colorectal carcinoma showed no evidence of radiological recurrence within the electrolytically treated lesion in the follow-up period. In each of these patients, electrolytic treatment was deemed successful. Recurrence within the electrolytically treated area occurred in two patients.

Six of the nine patients experienced hepatic recurrence of tumour outside the electrolytically treated area, which was not related to the previously treated area. There was no evidence of recurrence around the position of the electrodes due to seeding in any patient. Four patients had extrahepatic disease that was histologically confirmed to resemble adenocarcinoma, consistent with metastasis from the primary colorectal carcinoma.

CEA levels were increased after operation in four of the seven patients who had tumour recurrence. One patient, who experienced shrinkage of the treated tumour and no recurrence, had reduced CEA levels after operation. Liver enzyme levels and white cell counts were raised in the early postoperative period, but returned to normal within 3 months of treatment. No major complications occurred either during or after treatment.

All patients received chemotherapy before or after treatment.

Discussion

In recent years there has been an increasing interest in the use of ablative techniques for treating previously irresectable disease[4,16–19]. These techniques have the advantage of preserving more liver parenchyma, and are associated with fewer complications than resection[4]. The use of ablation as an adjunct to surgical resection is not yet established.

Electrolytic ablation of liver tumours has previously been described in China[20,21], with promising results. It is a non-

thermal technique, and therefore not limited by the 'heat sink' effect of nearby vessels[7]. It is also safe in terms of its inherent tissue destruction and inability to thrombose or breach large blood vessels in close proximity to the site of electrolysis[13]. Electrolysis is also predictable, with the volume of the lesion created being proportional to the electrolytic 'dose' (in coulombs) administered[10]. Currently, a limitation of the technique is that it is time consuming, with an increase in tumour size necessitating an exponential increase in treatment time. At present it is limited to lesions of less than 5 cm in diameter and requires a laparotomy. However, further development of appropriate electrode delivery systems may result in the treatment being administered percutaneously.

CT has been used in this study for follow-up evaluation as it has been proven to be sensitive in characterizing hepatic lesions[22]. A small margin of normal tissue at the periphery of the tumour is ablated to prevent residual viable tumour cells persisting at the margin and leading to recurrence. An initial increase in size of created lesions in the first week after operation is expected on the CT scan as this represents ablation of a margin of normal tissue (*Figs 1* and *2*). A decline in lesion size after the first week reflects successful treatment, while an increase in size suggests failure[23]. Conservative electrolytic treatment in the early stages of the trial may have resulted in undertreatment of tumours, allowing residual viable tumour cells to persist within the lesions, causing recurrence. With greater experience more accurate 'doses' of current were delivered, based on tumour geometry.

Necrosis in the electrolytically treated area appears hypodense on CT. Fibrosis within the treated area of some patients is evidence of shrinkage of the electrolytically treated area from a fluid-filled necrotic zone to a smaller fibrosed area (*Fig. 3*). Areas of fibrosis appear enhanced on contrast CT. Magnetic resonance imaging may be useful in evaluating these patients and a study to investigate this has been initiated.

The increase in liver enzyme levels after electrolysis was transient and short-lived. In most patients enzyme levels had returned to normal within 3 months of treatment.

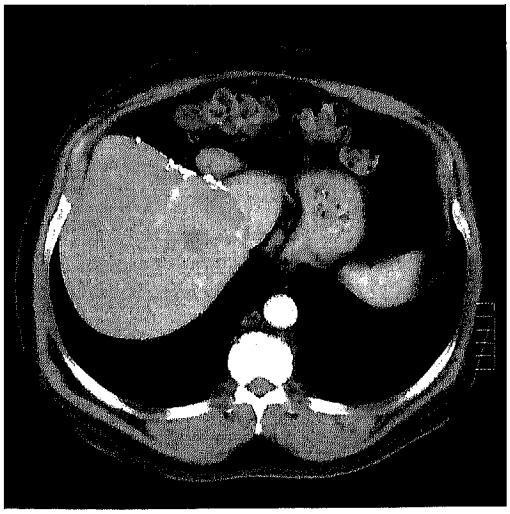

Fig. 1 Computed tomogram of a lesion before treatment

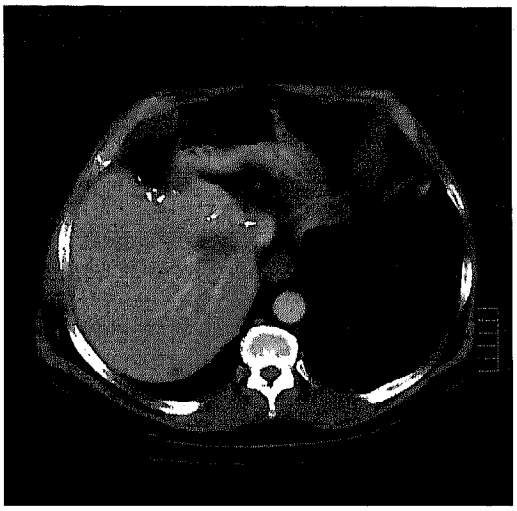

Fig. 2 Computed tomogram of the electrolytically treated lesion in the same patient 1 week after operation, showing ablation of a margin of surrounding normal tissue

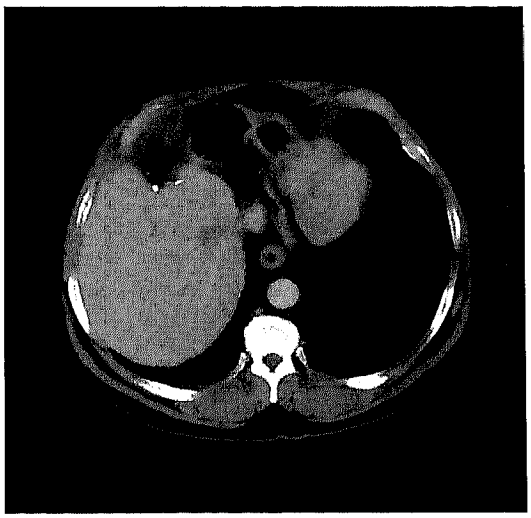

Fig. 3 Computed tomogram of the electrolytically treated lesion in the same patient 3 months after electrolysis, showing fibrosis and shrinkage of the treated area

In patients with colorectal hepatic metastases CEA is a serum tumour marker that can be useful in detecting tumour recurrence. CEA is not associated specifically with colorectal carcinoma but may be raised in up to 70 per cent of patients affected[22]. Four patients had a significantly increased CEA level after electrolysis, consistent with the tumour recurrence noted. One patient in whom treatment was effective had a reduced CEA level following electrolysis.

There was no detectable additional morbidity associated with the electrolytic treatment when used as an adjunct to surgical resection. The lack of major complications associated with electrolysis suggests that it is safe as a method of local ablation.

The median survival from the time of the procedure was 17 (range 9–24) months. This result should be interpreted in the context of the natural history of untreated colorectal liver metastases, for which untreated median survival is of the order of 3–6 months[6,24,25]. The increased survival time in this group of patients receiving electrolysis with resection may have an overall survival benefit. The small size of this initial study precludes statistical analysis of the results. The use of electrolysis in the ablation of liver tumours requires further long-term studies and evaluation; however, preliminary results are encouraging.

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