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Risk factors of haemoglobinuria after microwave ablation of liver tumours

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AIM: To explore the risk factors predicting haemoglobinuria after ultrasound-guided percutaneous microwave ablation (MWA) of liver tumours and discuss the treatments and outcomes.

MATERIALS AND METHODS: The present study comprised 2,829 patients admitted for liver tumours treated with MWA from Jan 2011 to April 2017. Ethics committee approval was waived and informed consent for treatment procedures were obtained from the patients. Haemoglobinuria after MWA was found in 149 patients. The influence of 19 risk factors was assessed. Binary logistic regression and receiver operating characteristic (ROC) curve analysis were used for statistical analysis. The treatments and outcomes of patients with haemoglobinuria were summarised.

RESULTS: By univariate analysis, histopathology, liver cirrhosis, MWA volume, MWA energy, and MWA duration were significant risk factors. By multivariate analysis and ROC curve, MWA energy, duration, and volume were identified as predictors of haemoglobinuria after MWA. Drug treatments including kidney protection, adequate hydration, alkalisation of urine, and diuresis were administrated to the patients with haemoglobinuria. One patient progressed to acute kidney injury (AKI) while others had good clinical outcomes.

CONCLUSION: Haemoglobinuria is a controllable side effect after MWA of liver tumours, which is related to high MWA energy, long MWA duration, and great MWA volume. It usually caused few side effects on renal function with correct treatment.

Introduction

Microwave ablation (MWA) is a favourable therapy for solid tumours in multiple organs.[1–4] It is recommended in treating single hepatocellular carcinoma <3 cm by the Barcelona Clinic Liver Cancer (BCLC) system.[5] It is also an effective therapy in treating medium (diameter of 3–5 cm) and large (diameter >5 cm) liver malignancies, and even benign liver lesions.[3,6,7] As a minimally invasive therapy, MWA is safe with a low incidence of major complications, including 0.1–0.4% intraperitoneal haemorrhage, 0.1–0.4% hepatic abscess, 0.1–0.7% bile duct injury, and 0.1–0.2% gastrointestinal tract perforation. The mortality and morbidity rates of MWA were 0–1.9% and 1.9–7.9% based on the large series studies, respectively.

Haemoglobinuria after MWA of liver tumours has become a recently discovered side effect. Haemoglobinuria

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is a type of abnormal urine (black-tea-coloured) with haemoglobin (Hb), which is often found in intravascular haemolysis leading to cell-free Hb released into the circulatory system.[8] Cell-free Hb is toxic as a result of triggering oxidative tissue damage.[9,10] Under physiological conditions, cell-free Hb is believed to be ultimately cleared by liver macrophages and its toxicity remains controlled.[9] When this protective system is saturated, the extra cell-free Hb is removed from the kidney through glomerular filtration. The kidney has less capacity for anti-oxidation than blood[11] and when it is exposed to large quantities of Hb, acute kidney injury (AKI) may occur as a severe complication because of tubular dysfunction and damage caused by intrarenal oxidative reactions and free-haem triggered toxicity.[9,12–16] There are only a few case reports of haemoglobinuria, which was observed after radiofrequency ablation of hepatocellular carcinoma[17,18] or MWA-assisted liver resection[19] with the possible risk factor of great ablation volume; however, no reports have included analysis of a large patient sample. To the authors' knowledge, no severe complications associated with haemoglobinuria after ablation, such as AKI, have been reported. In the present study, the clinical data of 2,829 patients with liver tumours treated by MWA were analysed retrospectively to explore the risk factors of haemoglobinuria. The treatments and outcomes of 149 patients with haemoglobinuria were analysed and summarised. One of the patients with haemoglobinuria underwent AKI after MWA of a hepatic haemangioma, a brief case report of which is provided in this article. The prevention and prognosis of haemoglobinuria after MWA are also discussed.

Materials and methods

Patients

The clinical data of 2,829 adult patients admitted for liver tumours with histopathological diagnosis and treated with ultrasound-guided percutaneous MWA from Jan 2010 to April 2017 were reviewed in this study. Ethics committee approval was waived and informed consent for treatment procedures was obtained from all patients. The histopathological types of liver tumours included primary liver cancer, metastatic liver cancer, and benign focal liver lesions (focal nodular hyperplasia, hepatic adenoma, and hepatic haemangioma). As for benign focal liver lesions, the final diagnoses were all proved by histopathological ultrasound-guided core needle biopsy performed before the MWA. Focal nodular hyperplasia and hepatic adenoma were treated by the MWA for highly doubtful malignancy. The hepatic haemangiomas were initially diagnosed at contrast-enhanced computed tomography (CT) or contrast-enhanced magnetic resonance imaging (MRI). The indications of MWA for hepatic haemangioma included (1) clinical symptoms were caused typically by the hepatic haemangioma and (2) patient refusal of surgical resection. All 2,829 patients showed normal renal function and urine before the procedure as confirmed by laboratory tests. Among them, 149 patients (including 119 men and 30 women; mean age of 57.8±11.4 years range, 30–85 years) had haemoglobinuria (black-tea-coloured) confirmed by urine routine after MWA. One patient had the severe complication of AKI after the procedure. Among the 149 patients with haemoglobinuria, 109, 23, and 17 patients were diagnosed as having primary liver cancer, metastatic liver cancer, and benign focal liver lesions (hepatic haemangioma), respectively. The concomitant conditions included high blood pressure (five patients), diabetes mellitus (29 patients), liver cirrhosis (63 patients), and hepatectomy (12 patients). Baseline characteristics of the 2,829 patients are described in Table 1.

MWA equipment and technology

The MWA unit used was a 100 W two-cooled-shaft system (KY-2000, Kangyou Medical, Nanjing, China) with frequencies of 2,450 MHz and 915 MHz. The antennae were percutaneously inserted into the tumour and placed at a designated location under ultrasound guidance. A thermal monitoring needle was inserted into the tumour margin for real-time temperature monitoring during ablation under ultrasound guidance to ensure that the heat-generated hyperechoic water vapour completely encompassed the entire tumour. The detailed procedures of ultrasound-guided MWA in patients with liver tumours were described in previous publications. The example images of ultrasound-guided MWA of hepatic haemangioma and primary liver cancer were showed in Fig 1.

Evaluation methods

The patients' blood tests (hepatic and renal function) and urine routine were taken before and after MWA. In the urine routine, urine dipstick tests were used to detect haemoglobinuria.[14] In the urine analysis, the minimal detecting sensitivity of haemoglobin was 0.03 mg/dl with the range of 0.03–1 mg/dl. Haemoglobinuria was determined with the results of Hb positive and red blood cell (RBC) negative.[8,14] After MWA in the 2,829 patients, hepatic and renal functions were tested every other day, and urine would be tested every time the patient urinated until the results were normal. The data of MWA volume (V), energy (E), duration (T) and power (P) in this study were all from a one-session procedure. The MWA zone was a spherical shape. The MWA volume (V) was calculated by the volume equation for a spherical shape as

$$V = \pi \times a \times b \times c \div 6,$$

where a, b and c were the maximum diameter in the three dimensions (vertical, sagittal, and coronal planes of the MWA zone when the patients were in supine position) of the tumour measured at contrast-enhanced CT or MRI. The ablation energy was calculated using

$$E = \sum_{i} PiTi$$

(E represented for the summation energy of each MWA session).

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