Percutaneous microwave ablation for hepatic cavernous hemangiomas: a preliminary clinical result

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Summary. Purpose: To explore the clinical application value of microwave (MW) ablation treatment for hepatic cavernous hemangiomas (HCHs) under percutaneous ultrasound (US) guidance. Methods: From July 2006 to January 2011, 14 patients (9 female and 5 male) with 18 HCHs (mean maximum diameter, 36.6±26.1 mm) were treated by MW ablation under US-guidance percutaneously. The diagnoses of HCHs were proven pathologically in 78.6% (11/14) patients by US-guided core needle biopsy prior to ablation. The other 3 cases refused biopsy and had their diagnoses confirmed by typical presentations on contrast-enhanced imaging. Four inclusion criteria including symptoms related to HCH were recommended. The follow-up period was 22.7±16.0 months. *Results:* Average ablation MW energy and emission time were 55.2±53.3 kJ (range 13.5 to 207 kJ) and 1021.3±886.4 s (range 270 to 3450 seconds) for each lesion, respectively. Fifteen nodules (83.3%) were completely treated and no evidence of recurrence was found on contrast enhanced imaging during follow-up. The three large HCHs (16.7%) were partially ablated as being adjacent to the gastrointestinal tracts or an important hepatic hilum structure. After ablation, three patients' symptoms relating to HCHs were alleviated in differing degrees. No severe complications occurred in the peri-operation or follow-up periods. Minor complications mainly included fever, local pain and abnormal hepatic function. *Conclusion:* US-guided percutaneous MW ablation is a safe, feasible and effective treatment for selected patients with HCHs and can be considered as a minimally invasive alternative to surgical resection.

Key words: microwave ablation; hepatic cavernous hemangioma; ultrasound guidance

«Terapia ablativa percutanea con microonde per il trattamento degli emangiomi cavernosi epatici: risultati di uno studio clinico pilota»

Riassunto. *Obiettivo*: indagare l'efficacia della terapia ablativa con microonde (MW) mediante guida ecografica percutanea (US) come applicazione clinica per il trattamento degli emangiomi cavernosi epatici (HCHs). *Metodi*: quattordici pazienti (9 femmine e 5 maschi) portatori di 18 HCHs (media del massimo diametro, 36.6±26.1 mm) sono stati trattati con terapia ablativa con microonde mediante guida ecografica percutanea, nell'arco temporale compreso tra Luglio 2006 e Gennaio 2011. Le diagnosi di HCHs sono state patologicamente confermate pre-ablazione nel 78.6% (11/14) dei pazienti mediante prelievo bioptico ecoguidato. I rimanenti 3 casi hanno rifiutato di sottoporsi alla biopsia pertanto la loro diagnosi è stata effettuata mediante specifiche visualizzazioni rivelate dall'ecografia con metodo di contrasto. Sono raccomandati 4 criteri di inclusione, compresi i sintomi, correlati all'HCH. Il periodo di follow-up è stato 22.7±16.0 mesi. *Risultati*: per ciascuna lesione, la media dell'energia di ablazione con microonde ed il tempo di emissione sono stati rispettivamente 55.2±53.3 kJ (intervallo compreso tra 13.5 e 207 kJ) e 1021±886.4 s (intervallo compreso tra 270 e 3450 secondi). Quindici noduli (83.3%) sono stati completamente trattati e al follow-up, mediante ecografia con metodo di contrasto, non è stata rilevata alcuna recidiva. Tre HCHs di grandi dimensioni (16.7%) sono stati pazialmente ablati poiché situati in adiacenza ai tratti gastrointestinali o ad importanti strutture dell'ilo epatico. Dopo ablazione, i sintomi correlati ad HCHs dei corrispettivi pazienti sono stati alleviati

in diversa entità. Non si sono presentate complicazioni gravi nel periodo peri-operatorio o al follow-up. Le complicazioni di lieve entità che si sono presentate sono state principalmente febbre, dolore locale e funzione epatica anomala. *Conclusioni:* la terapia ablativa con microonde (MW) mediante guida ecografica percutanea (US) è una metodica sicura, fattibile e costituisce un trattamento effettivo per pazienti affetti da HCHs. Può pertanto essere considerata un'alternativa minimamente invasiva rispetto alla resezione chirurgica.

Parole chiave: terapia ablativa con microonde, emangioma cavernoso epatico, guida ecografica

Introduction

Hepatic cavernous hemangiomas (HCHs) are the most common benign neoplasms in the liver, with a prevalence in the general population as high as 20% according to autopsy studies (1). With widespread use of ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI), more than 90% of HCHs may fortunately be clearly differentiated from liver malignances. Currently, conservative management is recommended for HCHs (2), and treatment mainly focuses on the largest sized lesion or relieving the symptom related to the nodule. Resection is one of the common treatments for HCHs, but hepatectomy is a dangerous and complex procedure (3) and indications for surgery must be evaluated carefully (4). In recent years, one encouraging development is that a few imaging-guided therapies, such as transcatheter arterial embolization (TAE) (5) and radiofrequency (RF) ablation (6, 7), have become clinical alternatives to liver resection, proving safe, effective, and minimally invasive in selected patients with HCHs.

Imaging-guided thermal ablation using various energy sources, such as radiofrequency (RF) and microwave (MW), are increasingly attractive ways of treating malignant hepatic tumors (8). Compared with RF, the benefits of MW ablation are: less limitation by the heat sink effect and tissue charring and the ability to achieve a larger ablation volume in a shorter time (9), making MW ablation a better way of ablating hepatic nodules with rich blood flow. MW ablation techniques and equipment have undergone remarkable progress from non-cooled-shaft to cooled-shaft antenna, and the 2450MHz and 915MHz MW system with its cooled-shaft antenna is being successfully applied to clinical therapy for hepatocellular carcinoma (10). To our knowledge, there have still been no published documents about percutaneous MW ablation treatment for patients with HCHs under US-guidance using cooled-shaft antennae. The purpose of our retrospective study was thus to explore the clinical value of US-guided percutaneous MW ablation with cooledshaft antenna in the treatment of HCH.

Materials and methods

Patients

Between July 2006 and January 2011, fourteen consecutive patients with 18 HCHs underwent MW ablation therapy at our hospital. Ten patients had 1 nodule, 4 patients had 2 nodules (Table 1). The mean age of the patients (9 women and 5 men) was 41.9±7.4 years old (31-53 years). The diagnosis of HCH were proven pathologically in 78.6% (11/14) patients using US-guided core needle biopsy followed by ablation. The other 3 cases refused biopsy and the diagnosis had to be confirmed by typical presentation on contrast enhanced CT or MRI. The second hepatic nodule in a patient was determined as HCH because of having the same presentations on contrast-enhanced imaging as the first one in our study. The mean maximum diameter of the eighteen nodules was 36.6±26.1 mm (8-98 mm).

Four inclusion criteria used in present study were as follows. First, diagnoses of nodules before biopsy that were indeterminate by contrast-enhanced imaging, especially in patients with infection of hepatitis B or C virus, liver cirrhosis or a history of malignancy. Second, HCH was significantly enlarged with more than 1 cm increment of the maximum diameter in the follow-up period within one year. Third, the symptoms complained of by the patient, such as local pain or discomfort, were considered to relate to HCH. Fourth,

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Patients			HCH lesions		MW ablations				Histories
Number	Sex	Age	Segment	Maximum diameter (mm)	Sessions	Insertions	Time (s)	Energy (kJ)	
1	F	31	II VIII	10 21	1 1	1	300 360	15 18	Breast carcinoma
2	М	45	VI	12	1	1	420	21	Chronic hepatitis B
3	М	40	VI	38	1	2	360	18	Malignant insulinoma
4	F	45	V	10	1	1	600	30	Breast carcinoma
5	F	37	V	26	2	4	1560	78	Chronic hepatitis B
6	F	39	II VI	49 44	2 2	3 3	1140 930	57 46.5	None
7	М	42	III VI	38 45	1 1	2 2	850 1440	42.5 72	None
8	F	37	III	28	1	1	600	30	None
9	F	35	VII	50	2	3	1575	78.8	None
10	М	51	II	69*#	2	3	1260	75.6	None
11	F	52	V	98*#	2	5	2700	162	None
12	М	53	V	19	1	1	300	15	Renal clear cell carcinoma
13	F	31	II	82*#	2	4	3450	207	None
14	F	48	V VII	11 8	1 1	1 1	270 270	13.5 13.5	None

Table 1. Brief information on patients, HCH lesions, and MW ablation parameters in our study

Note: * Diagnosis was confirmed by typical presentations on contrast-enhanced imaging because biopsy was refused.

Partial ablation was adopted to treat the nodules.

Histories included infection of hepatitis B or C, liver cirrhosis and a history of malignancy.

the patient had evident psychological pressure due to the occurrence of the nodules, though the nodule was clearly diagnosed as benign on imaging. In our study, all cases fitted one or several of the above inclusion criteria. Exclusion criteria included severe blood coagulation dysfunction (prothrombin time >30 s, prothrombin activity <40%, and platelet count <30 × 10°/L cells); acute or active inflammatory and infectious lesions in any organ; and acute or severe renal failure, pulmonary insufficiency or heart dysfunction. This clinical application was approved by our institutional human research review committee. Written informed consent was obtained from all patients.

Preablation imaging work-up

Before MW ablation, all patients received US, contrast-enhanced US, and contrast-enhanced CT or gadolinium-enhanced MRI to delineate the target lesions. US and contrast-enhanced US were performed using the Sequoia 512 system (Acuson, Mountain View, California) with 3.5-5.0 MHz multifrequency transducers. The US contrast agent was Sonovue (Bracco, Milano, Italy). All CT studies were carried out with the same multi-detector row CT (Lightspeed 16; GE Medical Systems, Milwaukee, Wis) and contrast medium (iopromide, Ultravist 300; Schering, Berlin, Germany). All MRI studies were carried out with the same 1.5-T unit (Signa Echo-Speed, GE Medical Systems) and contrast medium (Magnevist, Schering; 0.1mmol per kilogram of body weight).

MW ablation device

The 2450MHz MW system (KY-2000, Kangyou Medical, China) consists of three independent MW generators, three flexible coaxial cables and three water-pumps, which can drive three 15-gauge cooledshaft antennae (1.1cm antenna tip) simultaneously. The 915MHz MW system (KY-2001, Kangyou Medical, China) consists of two independent MW generators, two flexible coaxial cables and two water-pumps, which can drive two 15-gauge cooled-shaft antennae (2.2cm antenna tip) simultaneously. The two MW system generators are capable of producing 1-100W of power output. The cooled-shaft antennae are surface coated with Teflon to avoid adhesion. Inside the antenna shaft there are dual channels through which distilled water is circulated by a peristaltic pump, continuously cooling the shaft to prevent overheating. A thermal monitoring system attached to the MW system could be used to monitor the real-time temperature during ablation.

MW ablation procedures

MW ablation lesions were confirmed according to the diagnoses of the nodules on contrast-enhanced imaging before therapy. For nodules of indeterminate diagnosis, the ablated lesion included the tumor and adjacent 5-10 mm normal liver tissue, especially for patients with infections such as hepatitis B or C virus, liver cirrhosis or a history of malignancy. For nodules determinately diagnosed as HCHs by imaging, the ablated lesion was commonly recommended to cover the entire nodule in order to decrease the damage to normal liver tissue. For nodules adjacent to important organs such as the gastrointestinal tract, main branches of the biliary tree, or the gallbladder, partial ablation of the nodular volume was adopted so as both to avoid injuring those important organs by overheating and to decrease the nodular volume.

Biopsy was routinely performed followed by ablation during the procedure to decrease the risk of bleeding and tumor seeding. MW ablation was monitored on US in real-time, the treatment session would stop if the hyperechoic zone induced by ablation covered the target region. When the antenna was withdrawn, the needle track was routinely cauterized to avoid bleeding and tumor seeding. If necessary, a compensatory treatment session was commonly performed within 3 to 7 days depending on the volume of residual tumor and the patient's recovery.

All treatments were performed at our institution and were carried out under US guidance with the patients under unconscious intravenous anesthesia (Propofol and Ketamine) in the operating room. All procedures were performed by two experienced doctors (LP, YXL); both had more than 10-years' experience in percutaneous MW ablation of liver tumors. A detailed ablation protocol including the number and placement of the antennae, power output setting, emission time and appropriate needle path worked out for each nodule on an individual basis before treatment. To decrease needle insertions, when the maximum nodule diameter was less than or equal to 5cm, 2450MHz MW ablation with a power output of 50 W was used, while 915MHz MW ablation with a power output of 60 W was selected for nodules with a maximum diameter of more than 5 cm. If the target nodule was adjacent to important organs such as main branches of bile ducts, the gallbladder, the stomach or the intestinal tract, one or two thermocouple needles connected to the MW system would be advanced into the tissue between the tumor and the important organ under US guidance and real-time temperature monitoring during ablation to avoid overheating.

Follow-up

The follow-up period was calculated starting from the beginning of MW ablation procedure in all patients. Contrast-enhanced US or CT or MRI were repeated at 1, 3, 6, 9, 12 months in the first year and then at 6-month or 12-month intervals after year 1. The mean follow-up period was 22.7±16.0 months (2 to 55 months) in the present study.

Statistical analysis

Data analyses were performed using SPSS 11.0 for windows (SPSS Inc, Chicago, IL, USA) and continuous data were expressed as means ± standard deviations (SD).

Results

MW ablation

Eighteen nodules were successfully treated. Average ablation sessions and needle insertions were 1.4 ± 0.5 (one to two sessions) and 2.2 ± 1.3 (1 to 5 in-

sertions) for each nodule, respectively. Average MW energy and emission time were 55.2±53.3 kJ (range 13.5 to 207 kJ) and 1021.4±886.4 s (range 270 to 3450 seconds) for each nodule, respectively.

The three large HCHs (16.7%) shown in table 1 were partially treated as being adjacent to the gastrointestinal tract or an important structure of the hepatic hilum. Partial ablations were performed and the ablated volumes were 85%, 81% and 86%, respectively in 1-month follow-up. The residual tumors did not progress or grew very slowly over the 1 year follow-up period. The other fifteen nodules (83.3%) were completely ablated and no evidence of recurrence was found around ablated lesions on contrast-enhanced imaging during the follow up. Imaging data of two patients before and after treatment are shown in figures 1 and 2, respectively.



Figure 1. An HCH presentation in hepatic segment V of a 53 year-old male patient on US and MRI before and after MW ablation. (a) Grey-scale US shows a 19 mm HCH in its maximum diameter, slightly hyperechoic (white solid arrow) before treatment. (b) Contrast-enhanced US shows the HCH peripheral hyper-enhancement (white solid arrow) in the arterial phase before treatment. (c) Contrast-enhanced US shows ablated lesion non-enhancement (white solid arrow) in the portal phase 1 month after treatment. (d) Contrast-enhanced MRI shows ablated lesion non-enhancement (white solid arrow) in the portal phase 1 month after treatment.



Figure 2. Two HCH presentations in hepatic segments III and VI of a 42 year-old male patient on contrast-enhanced US and MRI before and after MW ablation. (a) Contrast-enhanced MRI shows two HCHs' peripheral hyper-enhancement (white solid arrow) in the arterial phase before treatment, one with a maximum diameter of 38 mm and the other with a maximum diameter of 45 mm in hepatic segments III and VI, respectively. (b) Contrast-enhanced MRI shows two HCHs' hyper-enhancement (white solid arrow) in the delay phase before treatment. (c) Contrast-enhanced US shows a shrunk ablated lesion in segment VI (white solid arrow), and no recurrence around the lesion in the delay phase, 1 year after treatment. (d) Contrast-enhanced US shows a shrunk ablated lesion in segment III (white solid arrow), and no recurrence around the lesion in the delay phase, 1 year after treatment. I year after treatment.

After ablation, the symptoms relating to HCHs in three patients were alleviated to a different extent and the psychological pressure in 5 cases due to the finding of a hepatic tumor pre-operation were relieved.

Complications

Severe complications such as abscess, bile duct injury, perforation of gastrointestinal tracts and hemorrhage requiring embolization did not occur in peri-operation and follow-up periods. Minor complications in the present study were mostly similar to presentations after MW ablation of hepatic malignancies. The highest body temperatures in 9 cases (64.3%) lay between 37.2 and 38.5 Celsius degrees lasting 1 to 2 days. There was no need to manage this in most patients, though medicine to lower the temperature was adopted in two cases. According to the common toxicity criteria for reporting pain at the National Cancer Institute (11), grade 1 local pain was complained of in 57.1% (8/14) of all cases, lasting 1 to 3 days without using any drug. No patients complained of grade 2 or more local pain after ablation. The liver function study showed that serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were increased in 85.7% (12/14) of all cases. The incremental levels varied, but the highest one was less than three times higher than baseline values. Both of these two enzymes normalized in one month after ablation. No obvious changes were observed in other serum elements relating to liver and renal function, such as total bilirubin (TB) and direct bilirubin (DB). Hemoglobinuria was found at the first urination after ablation in two cases of large HCHs. Subsequently, the urine color gradually returned to normal without any remedy. The hospitalization time was 3.4±1.7 days (2 to 7 days) according to patient recoveryand no changes occurred because of complications.

Discussion

For most patients with HCH, surgical resection tends to be considered the preferred choice of treatment (12). However, some patients are nonsurgical candidates or reject an opening operation for various reasons such as multiple comorbidities and cosmetic requirement. As minimally invasive treatments for HCHs, TAE (5, 13) and RF ablation (6, 7) have been suggested as alternatives to surgery. It is generally acknowledged that MW ablation has similarities RF ablation in terms of complete ablation rates, local tumor control, complications related to treatment and longterm survival rates (14-16). Thus, US-guided percutaneous MW ablation might stand as a new alternative way to treat HCHs in nonsurgical candidates. One of the essential considerations in treating HCHs is to decrease the risk of rupture. As the size of HCH increases, so does the chance of rupture (17, 18), especially when the tumor is located on the surface of the liver or shows extrahepatic growth. Additionally, large tumors might be adjacent to important organs including the gastrointestinal tract, main branches of the biliary tree and gallbladder. In the present study, besides thermocouple needles monitoring temperature in real-time during therapy, partial ablation was adopted to minimize the tumor size and avoid major complications. With the 3 large HCHs more than 80% of the nodular volumes were successfully ablated in the 1-month follow-up, and the residual tumors did not progress or only grew very slowly during follow-up.

Keeping definitions of complications and side effects consistent with the standardization of terminology and reporting criteria for image-guided tumor ablation (19), a major complication was defined as an event that led to substantial morbidity and disability, increasing the level of care, or that resulted in hospital admission or a substantially lengthened hospital stay. All other complications were considered minor. In our study the complications of all patients were minor ones such as fever, grade 1 local pain and increment of liver enzymes. The incidence rates were similar to those after MW ablation of liver malignancies (20). Hemoglobinuria was found after therapy in two cases and then tended to improve without additional remedy or management. The reason for hemoglobinuria occurring was presumably a mass of blood cells that were ruined in an HCH ablation procedure.

For the treatment of HCHs, conservative management such as regular observation is commonly recommended (21), and surgical removal is a cautious advice. Though MW ablation is a minimally invasive therapy compared to open hepatectomy, the same serious attitude should still be advocated and the above inclusion criteria should be strictly abided by in clinical MW ablation when treating HCHs. All cases in our study matched at least one of the four inclusion criteria. The nodules of four patients who had a history of hepatitis B or malignancies were indeterminately diagnosed on imaging before being proven pathologically. The possible reasons why it was difficult to draw a definite diagnosis before biopsy were atypical presentation on imaging and a small hepatic neoplasm detected in the follow-up period of patients with a malignant tumor history.

In the treatment of large liver cancers application of 915MHz MW can significantly reduce the insertion numbers as compared to 2450MHz MW (10), and fewer insertions tend to increase the safety of therapy and decrease the risk of complications such as bleeding. In our study, for the HCHs with maximum diameters over 5 cm, ablation system 915MHz MW was applied to decrease the number of insertions, so the average needle insertions were 2.2±1.3 (1 to 5 insertions) for each nodule. Massive hemorrhage requiring embolization did not occur in the peri-operative phase and blood transfusion was not necessary after ablation. One important point was that the needle tracks were routinely cauterized when the antennae were withdrawn. Average MW energy and emission time were 56.1±53.9 kJ (range 13.5 to 207 kJ) and 1021.4±886.4 s (range 270 to 3450 seconds) for each nodule. In our experience, a longer time and higher energy were needed in treating HCHs, especially large ones. One possible reason is that the HCH vessels are not easily destroyed by thermal ablation because they have a normal vascular wall structure with good properties of heat dissipation. A meta-analysis study (22) indicated that the combination of transcatheter arterial chemoembolization (TACE) with local ablation was superior to monotherapy in treatment of patients with HCC, so it might be a promising method to treat large HCHs with combined TAE and ablation after further clinical exploration.

This study had some limitations. First, because of the strict inclusion criteria, only 14 patients were included in our study and the follow-up period was not long. Further study on a large series of cases with longterm follow-up is clearly necessary. Second, this was only a single center and a retrospective study: a multicenter prospective study would be more convincing.

Conclusion

In conclusion, US-guided percutaneous MW ablation is a safe, feasible and effective treatment for selected patients with HCHs and can be considered as

a minimally invasive alternative to surgical resection. Clinically, it should be applied seriously and the inclusion criteria mentioned in our study are recommended.

Acknowledgement

This study was financially supported by grants from the National Scientific Foundation Committee of China (No. 30825010 and No. 81071210).

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Received: 6.8.2014

Accepted: 24.9.2014

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