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CASE REPORT

High-intensity focused ultrasound ablation: a non-surgical approach to treat advanced and complicated liver alveococcosis

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Abstract
Liver alveococcosis is a life-threatening parasitic disease with progressive growth and wide metastasis to neighboring tissues, lungs, and brain. The radical treatment option is surgery along with a few chemical therapies. However, the frequency of progression and recurrence, as well as postoperative complications and mortality, remains very high. The high-intensity focused ultrasound (HIFU) treatment system, a therapeutic application using ultrasound to deliver heat or agitation into the body, was initially designed to treat cancer. Advanced and complicated forms of liver alveococcosis usually require surgical treatment to provide partial ectomy of necrotized liver tissue along with alveococcal caverns and sanitation of the peritoneal cavity. In this article, we presented a case of successful HIFU ablation with transhepatic puncture and drainage in treatment of complicated and advanced liver alveococcosis to avoid wide surgical treatment.

Keywords High-intensity focused ultrasound (HIFU) · Liver alveococcosis · HIFU ablation

Introduction

Alveococcosis is a natural focus disease, the infectious agent of which is a helminth called *Echinococcus multilocularis* [1]. Unlike *Echinococcus monolocularis*, it is characterized by a more unfavorable course, poor prognosis, and high mortality rate [2, 3]. Liver alveococcosis is a life-threatening parasitic disease with progressive growth and wide metastasis to neighboring tissues, lungs, and brain [4–6]. It is often referred to as "parasitic liver cancer", because of infiltrating growth and the possibility of metastasis [7]. Along with a few chemical therapies, the radical treatment option is surgery of the affected area or liver transplantation [8–11]. Despite this, a 20-year survival rate can be achieved in less than 20% of infected patients [12, 13].

The high-intensity focused ultrasound (HIFU) treatment system, a therapeutic application using ultrasound to deliver heat or agitation into the body, is widely used to treat cancer [14]. As we previously reported, HIFU ablation has shown a high efficiency in non-complicated cases of liver alveococcosis [15, 16]. Morphological investigation of biopsy material after HIFU ablation has shown a destructive effect on protoscolexes, laminar, and cellular elements of the germinal layer of alveococcosis lavrocysts [15, 16]. The next stage after ablation of alveococcosis tumors was surgical removal of pathologically changed liver segments with alveococcal caverns, allowing us to achieve good clinical results. However, in advanced and complicated liver alveococcosis, wide surgical treatment such as semi-hepatectomy or liver transplantation is required to provide partial ectomy of necrotized liver tissue along with alveococcal caverns and sanitation of the peritoneal cavity. In this article, we presented a case of successful HIFU therapy in combination with transhepatic puncture and drainage in treatment of complicated and advanced liver alveococcosis to avoid wide surgical treatment.

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Case presentation

A 34-year-old male patient was admitted to our clinic with the complaints of epigastric pain, progressive faintness, absence of appetite, weakness, weight loss during the last 6 months, and typical symptoms of cholestasis (jaundice, dark urine, light-colored stools, and generalized itchiness). Baseline laboratory data (Table 1) confirmed the presence of cholestasis. The patient underwent contrast-enhanced abdominal computed tomography (CT) and ultrasound (US). Both liver CT and US investigations detected a mass with a liquid content in the right lobe of the liver (Figs. 1a, 2a) with an approximate length of 69 mm, height of 62 mm, width of 68 mm, and total volume of 153 ml. Approximately two-third of the right lobe of the liver tissue was affected by alveococcosis. A blood test for antibodies to alveococcosis was positive, confirming the diagnosis of liver alveococcosis.

Table 1 Baseline and control laboratory parameters

Laboratory parameters	Baseline data	After 7 months	Reference range
Bilirubin total, µmol/L	62.0	20.0	<22.2
Bilirubin direct, µmol/L	51.7	4.8	<5.1
ALT, µkat/L	1.60	0.64	<0.68
AST, µkat/L	0.80	0.58	<0.62
Serum protein total, g/L	69	74	66–87
Hemoglobin, g/L	125	140	130–160
WBC, $\times 10^9$/L	10.2	4.8	4.9–9.0
Eosinophils, %	10	3	0.5–5
ESR, mm/h	38	14	2–10

ALT alanine aminotransferase, *AST* asparagine aminotransferase, *WBC* white blood cells, *ESR* erythrocyte sedimentation rate

The patient consulted with surgeons, hepatologists, and other medical specialists to discuss different therapeutic approaches and possible complications, and it was ultimately decided to use multisession HIFU ablation to avoid large hepatobiliary surgery and risk of alveococcal seedings. After discussing the risk–benefits of HIFU therapy versus hepatobiliary surgery with the patient, we obtained signed informed consent from the patient and his relatives.

The treatment protocol with HIFU ablation was comprised of three sessions with 3-month intervals. HIFU ablation was performed on the JC Focused Ultrasound Therapeutic System (Chongqing HIFU Technology Company, China) under general anesthesia. A therapeutic lens with a diameter of 15 cm and radiation frequency of 0.9 MHz was employed. The course of the focused ultrasound was in the vertical direction and 5-mm slices were used. The time-averaged radiation intensity power was 250–300 W (Fig. 3). After the first session of HIFU ablation, the patient was discharged for outpatient follow-up. The patient was admitted to the hospital after 3 months to receive the second course of treatment with HIFU ablation. Three days after the second HIFU ablation, the patient underwent percutaneous transhepatic drainage of the alveococcal cavity with insertion of a 12F dual lumen catheter by the Seldinger technique (same as the intravascular technique) under ultrasound guidance and local anesthesia. The aspirated liquid was sent to morphological electron microscopical study. The examination of the

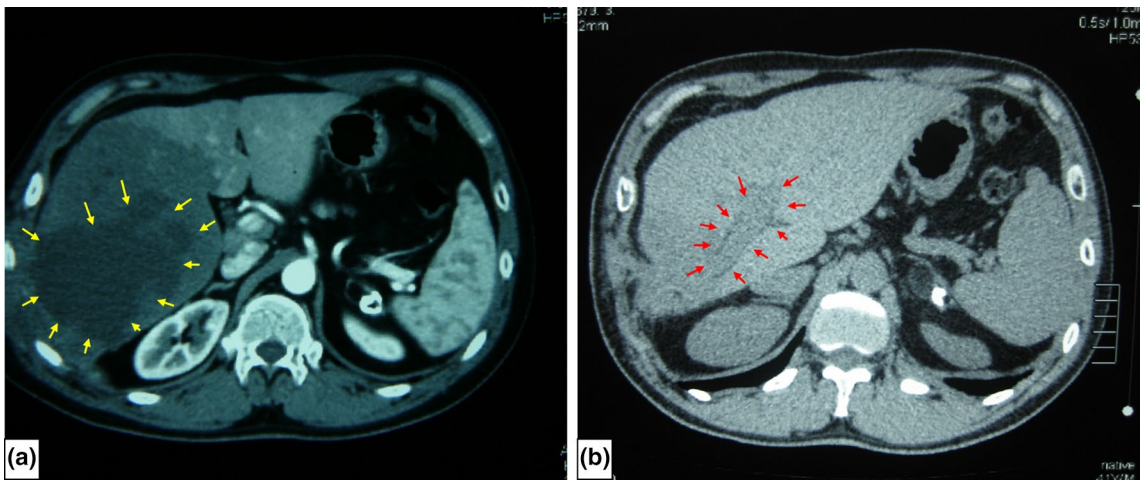

Fig. 1 Contrast-enhanced CT of alveococcosis mass in the left liver lobe before treatment (**a**) and CT after 9 months of treatment (**b**). On contrast-enhanced liver CT, the alveococcosis mass of the right lobe of the liver was seen as a solid hypodense and partially fluid formation of oval shape with relatively undefined and uneven contours (yellow arrow). After 9 months of treatment, in control CT, the alveococcosis mass had changed to fibrous tissue, and hypertrophy of the left lobe of the liver was also observed

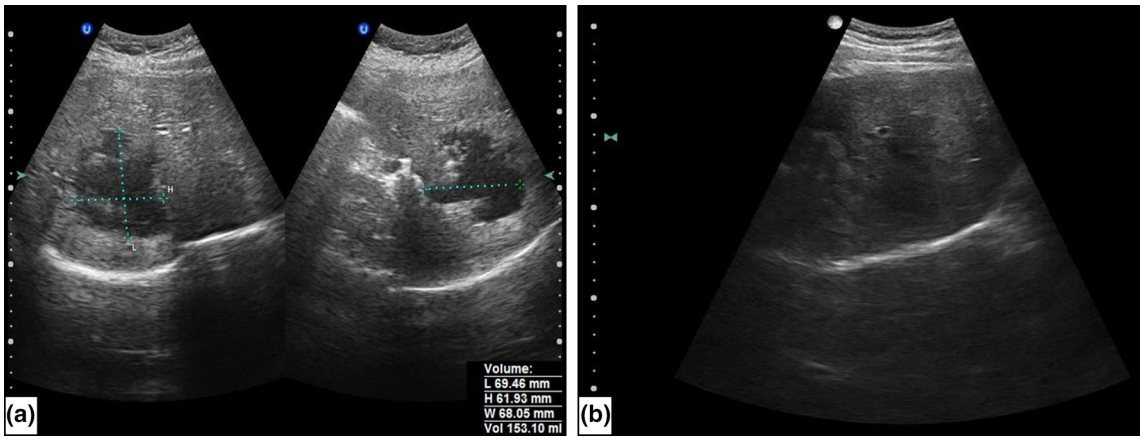

Fig. 2 US of alveococcosis mass in the left liver lobe before treatment (**a**) and after 9 months of treatment (**b**). On B-mode ultrasound, the alveococcosis mass was imaged as liquid content with an approximate length of 69 mm, height of 62 mm, and width of 68 mm in the right lobe of the liver (**a**). This alveococcosis mass disappeared after treatment on control B-mode ultrasound (**b**)

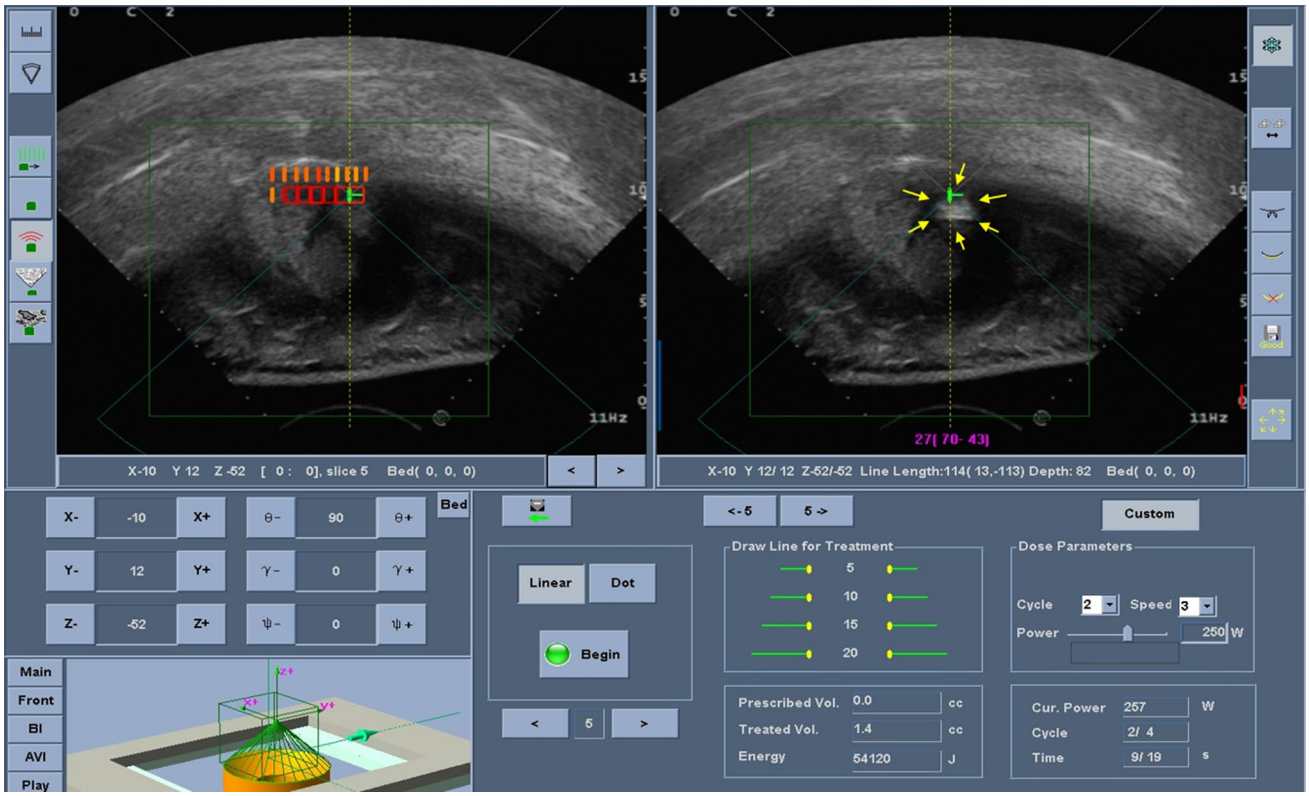

Fig. 3 Illustrative screenshot from HIFU ablation during the procedure. This is a real-time working moment of HIFU ablation of liver alveococcosis. In the left panel of the figure, the point strike (upper group of perpendicular lines) and the linear strike (lower group of square pictograms) of the focused high-intensity ultrasonic beams were directed for ablation of the alveococcosis mass. At the same time, in the right panel of the figure, the "cloud" effect of HIFU is seen (yellow arrow). This is a hyperechoic region of the boiled alveococcosis caverns in response to ablation. The technical and therapeutic characteristics of HIFU ablation at the time of treatment are presented in the bottom part of the figure

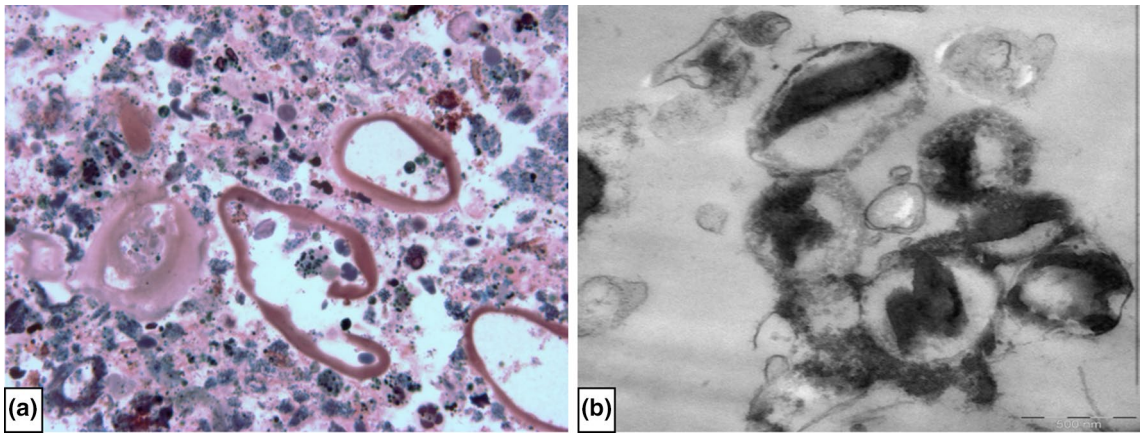

Fig. 4 **a** Destruction of membranes and cell elements of an alveococcosis larvocyst (semi-thin section stained with methylene blue, azure-2, and basic fuchsin. Magnification: 1×1000); **b** Destruction of calcium-containing cell of the germinal layer (electron diffraction photograph. Magnification: 1×7500)

puncture biopsy content showed the destruction of laminar and cellular elements of the germinal layer of alveococcosis larvocysts due to the cavitating and necrotizing effects of HIFU therapy (Fig. 4). In the outpatient clinic, the cavernous cavity was irrigated with an aseptic solution (dioxidine solution 1%) daily for 2 weeks, then alternate days during the next 9 weeks, and then twice a week with subsequent removal of the drainage. The last HIFU ablation was conducted 3 months after the second ablation. The patient's clinical condition significantly improved, and cholestatic symptoms disappeared during the overall 6 months (Table 1). On control liver CT and US, the area of the cavernous cavity changed to fibrous and calcifications without any liquid content. Compensatory hypertrophy of the liver left lobe was observed (Figs. 1a, 2b). The patient was followed up over the next 5 years with control liver CT and US. During the follow-up period, there were no signs of recurrence.

Discussion

To the best of our knowledge, this is the first case in the literature demonstrating successful implementation of HIFU ablation followed with transhepatic drainage in the treatment of advanced and complicated liver alveococcosis, which helped us avoid wide hepatobiliary surgery.

Liver alveococcosis is a surgically dependent disease. The primary goal in the treatment of liver alveococcosis is radical removal of a parasitic lump [8, 13, 17]. Unfortunately, alveococcosis is characterized by a long-term asymptomatic course and is frequently diagnosed at a late stage; therefore, in 60–70% of cases it is impossible to perform radical surgery [18, 19]. Applied methods of local destruction, such as radiofrequency ablation, cryodestruction, plasma coagulation, and laser irradiation, are minimally invasive methods [20], but the efficacy of these palliative approaches is disputable in advanced and complicated cases of liver alveococcosis. The efficiency of single antiparasitic therapy for alveococcosis without radical surgery is low. Despite adjuvant antiparasitic therapy in combination with palliative surgery (partial hepatectomy by 90% resection of the alveolar lump), recurrence or progression occurred in 12.5% during 15 years of follow-up [13].

The morphological study confirmed the existing opinion that the noninvasive remote effect of HIFU ablation causes destructive changes in protoscolexes, laminar, and cell elements of the cuticular and germinal membrane of the alveococcosis larvocyst [15, 21, 22]. In our earliest study, we demonstrated the efficacy of HIFU ablation in non-complicated cases as a pre-surgical preparation of patients [15]. The noninvasive nature and possibility of multiple application of HIFU ablation allow us to methodically separate the sites damaged by alveococcosis liver parenchyma from the healthy ones. This makes it easy to remove almost "dead" or "inactivated" alveococcosis via a surgical approach.

In our current case, radical resection of a parasitic lump was impossible due to its large size, localization, and patient's clinical condition. The only available surgical option was to perform either hemi-hepatectomy, which also could not prevent possible recurrence, or liver transplantation, which was not possible by this point. After the second HIFU therapy, it was decided to limit abdominal drainage with further conservative antiparasitic and symptomatic treatment. The third HIFU session finally destroyed all parasitic regions and subsequently led to right lobe fibrosis and left lobe compensatory hypertrophy of the liver.

The main benefits of HIFU ablation for liver alveococcosis are as follows. First, the hospital stay will be reduced from approximately 14 days (with traditional surgery) to 5 days (HIFU therapy with minimally invasive drainage),

and the cost of the hospital stay will also be reduced. According to our experience, the estimated cost for HIFU ablation is half the cost of hepatobiliary surgery, and approximately $800 was spent in our current case. Second, quality of life is significantly higher after HIFU therapy compared to traditional hepatobiliary surgery. Third, the intercostal approach of HIFU ablation makes it easy to reach the lesions located in the liver right lobe (behind the ribs) during the inspiration/expiration phases of the breath supported by general endotracheal anesthesia.

The main indication for HIFU therapy is the presence of an alveococcal mass in any part of the liver confirmed by CT and laboratory tests. Percutaneous transhepatic drainage should be performed if the cavernous cavity diameter is more than 3 cm. The optimal timing of percutaneous drainage depends on the amount of liquid produced from alveococcal caverns, but no longer than 6 months.

Using HIFU therapy combined with percutaneous transhepatic drainage of the cavernous cavity can be considered in cases of complicated extended liver alveococcosis. The clinical example given by us demonstrates that using a two-stage treatment approach combining HIFU therapy and minimally invasive drainage allows us to achieve positive results. Further investigations are needed to assess patient quality of life and long-term outcomes.

Conclusion

HIFU ablation in combination with minimally invasive percutaneous liver drainage was effective in the treatment of advanced and complicated liver alveococcosis with no recurrence or progression during the subsequent 5 years. This treatment approach might be preferred as an alternate therapy in individual cases with liver alveococcosis.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

Ethical statements The Institutional Ethics Committee approved application of HIFU ablation in treatment of liver alveococcosis. Additional informed consent was obtained from the patient for which identifying information is included in this article.

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