Tehran University of Medical Sciences Publication
http:// tums.ac.ir

Iran J Parasitol

Open access Journal at
http:// ijpa.tums.ac.ir

Iranian Society of Parasitology
http:// isp.tums.ac.ir

Short Communication

Role of Magnetic Resonance Spectroscopy and Susceptibility Weighted Imaging in Cerebral Alveolar Echinococcosis

***Guocai YANG, Qingxin ZHANG, Guibo TANG, Hui XU, Zhen YANG, Jianzhong GUO, Lin LIANG, Yonghong QI**

Dept. of Radiology (MRI), Qinghai Provincial People's Hospital, Xining, China

Received 15 Jun 2014
Accepted 16 Nov 2014

Keywords:
Cerebral alveolar echinococcosis, Magnetic resonance spectroscopy, Susceptibility weighted imaging

***Correspondence Email:**
Guocaiyangcn@163.com

Abstract

Background: To analyze the characteristic performance of magnetic resonance spectroscopy (MRS) and susceptibility weighted imaging (SWI) in cerebral alveolar echinococcosis (CAE).

Methods: We retrospectively analyzed 10 clinical-identified CAE cases MR performance, and summarized the MRS and SWI performance of CAE.

***Results*:** The 10 cases of CAE all had the history of primary HAE, among who 6 cases had single lesion (60%), while the rest 4 cases had multiple lesions (40%); and 4 cases were concomitant with lung metastases. MRI performance: T_2WI lesions were coal-like low-signal shadow, with multiple small vesicles inside the lesions; MRS performance: NAA, Cho and Cr significantly reduced, an abnormally high and steep crest was found at 1.4 ppm; the phase diagram and strength diagram of SWI showed isointensity.

***Conclusion*:** The MRS and SWI of CAE could provide important supplemental information for the diagnosis of CAE, especially the abnormally high and steep crest at 1.4 ppm provide the reliable image basis for the diagnosis and differential diagnosis of CAE.

Introduction

Cerebral alveolar echinococcosis (CAE) is a parasitic disease caused by the *in vivo* infection of *Echinococcus alveolaris* larva. CAE are almost 100% the results of hematogenous metastasis of hepatic alveolar echinococcosis (HAE) (1). When the oncosphere enters the liver, it would form numerous small vesicles, with 1-10 mm in diameter, and gather and form the irregular lumps. Meanwhile, it would continue the proliferative sprouting and infiltrate the whole liver, and in the late stage, it would usually invade vessels and transfer throughout the body. The easiest metastatic organ is the brain, followed by lung and other organs. The simultaneous metastasis of brain, lung and other or-

gans is also very common. Therefore, CAE mostly occurs during the HAE treatment or after the surgery (2).

Decided by the specific biological characteristics of HAE, the cerebral metastases would also form the multiple mixed masses, normally appearing multiple small vesicles and cross-sectional honeycomb-like changes. The single vesicle is rare, without the peplos and irregular shape, the edge would be ill defined, and the surrounding brain edema would be obvious. Lesions might distribute in any part of the brain, usually on the supratentorial part, while the simultaneous appearance in the supratentorial and infratentorial parts, even the involvement of brainstem and brain ventricle, could be observed sometimes.

Qinghai Province has a high incidence of CAE, therefore the definite diagnosis and early treatment would be of very important significance. In this article, 10 cases of CAE clinically identified in our hospital from Apr. 2009 to May 2013 were summarized. Combined the literatures, the characteristic performance and the corresponding pathological basis of MRS and SWI of CAE were discussed, aiming to provide a reliable image basis for the clinical diagnosis and differential diagnosis. Previously, because the clinical recognition of CAE was lack, as well as the imaging performance was complex, misdiagnosis and mistreatment would easily happen, especially towards the patients who complain mainly about the nervous system symptoms, this kind of patients would often be misdiagnosed as brain tumors and delayed the treatment. Great attention should be paid to the above kind of patients. In recent years, the study of the characteristic performance of MRS and SWI in CAE are carried out along with the application of high-field MRI, bringing a wide range of applications.

Case Presentation

Clinical data

The 10 cases were from the popular endemic area of echinococcosis, including 7 males and 3 females, aged form 39 to 53 years old, with the mean age as 45.5 years old. The first symptoms were headache, nausea, vomiting, blurred vision and epilepsy. Most patients had the symptoms of abdominal discomfort, jaundice and weight loss.

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Qinghai Provincial People's Hospital. Written informed consent was obtained from all participants.

ELISA

The serum enzyme linked immunosorbent assay test of echinococcosis in 8 cases was positive.

Results

General information

Ten patients all had the history of primary HAE, and 4 cases combined with pulmonary metastasis. Among the 10 cases of cerebral distribution, 6 cases had single lesion (60%), which all located in the cerebral hemispheres (4 cases in the right side, and 2 cases in the left side); 4 cases had multiple lesions (40%), 2 cases were in the supratentorial part, and 2 cases were both in supratentorial and infratentorial parts.

MR Performance

Eight cases appeared as slight T_1WI hypointensity, and 2 cases appeared as mixed signal; all the cases showed low T_2IW signal, with "coal-like" changes; the main T_2flair sequence all appeared as isointensity, mixed with stippled high signal shadow inside, the mass boundary was clear, surrounded by flaky edema, with significant position-occupation effect (Fig. 1 A ~ D). The multiple aggregated vesicles, with about 1 ~ 10 mm in diameter, could be seen in all cases. T_1WI was low intensity signal, T_2 IW was high intensity signal; DWI all appeared as slightly higher intensity signals with clear boundaries, ADC appeared as the

isointensity signal shadow, with stippled low signal shadow inside, while the peripheral edema appeared as the high signal shadow (Fig. 1E); SWI phase diagram and intensity diagram appeared as slabby isointensity (Fig. 1F ~ G), and the scope was slightly larger than T2WI, and the borders were more clearer, without significant vascular shadows peripherally. In the single voxel MRS, an abnormally high and steep peak approximately at 1.4 ppm could be seen, and NAA, CHO and Cr significantly reduced (Fig. 1 J-K); 10 cases all appeared the enhanced irregular ring-shaped enhancement, and the enhancement was obvious (Fig. 1 H-I).

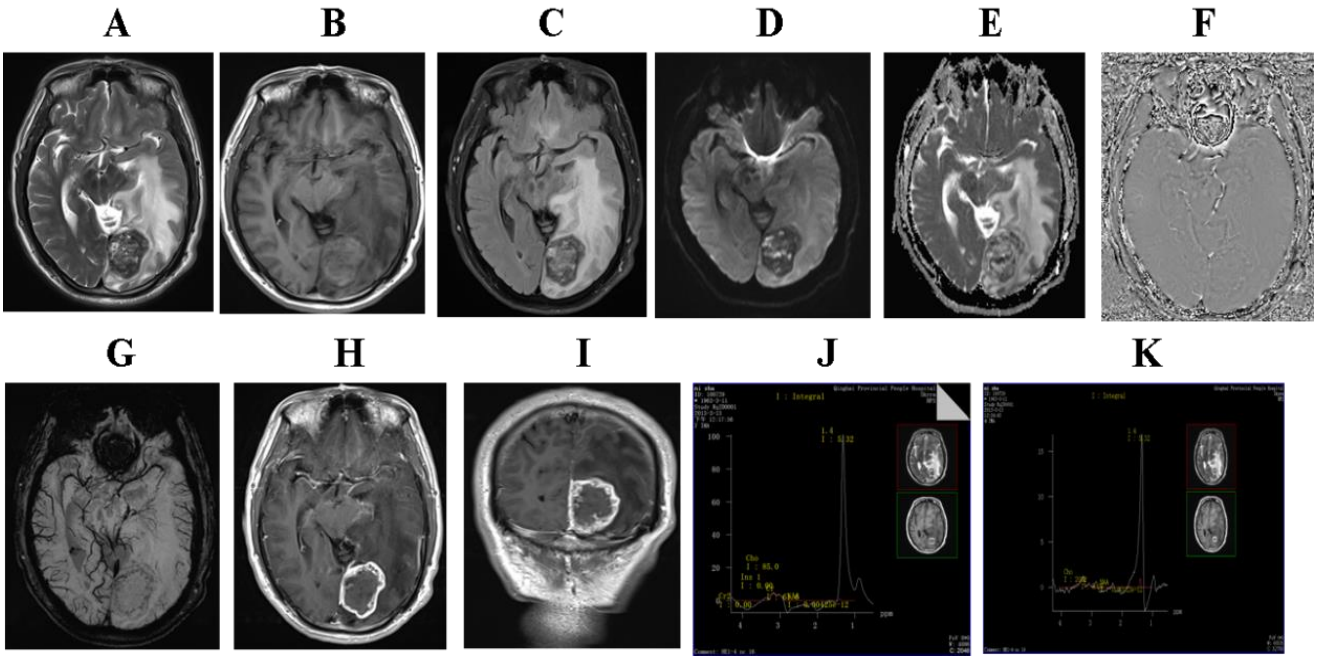

Fig. 1: Displayed the traditional, MRS and SWI imaging appearance of CAE on the left occipital lobe in 3.0T SkyraMRI

A.T2WI mass mainly appeared as low signal, within spotted high signal inside, and the lesion edge could see high signal vesicles shadow, with obvious position-occupation effect and the perifocal edema; B. T1WI mass showed a slightly higher signal, the boundary was less clear, and the small vesicles was unclear; C. Blackwater sequence showed that lesions had a clear boundary, mixed with signal shadow, while the peripheral edema was obvious; D. DWI showed that the lesions appeared as mixed but slightly high signal, within which the spotted high signal could be seen; E. ADC image was ill-defined isointensity, within which spotted lower signal could be seen; F and G were the SWI phase diagram and intensity diagram, respectively, the lesions appeared as slabby isointensity shadow, the intensity graph showed multiple small blood vessels shadows around; H and I contrast-enhanced T1WI showed that apparent, irregular ring enhancement appeared around the lesions; J. in PRESS sequence with 135ms echo time of ^{1}HMR spectroscopy, the low signal center of the lesion was focused on the 1cm^{3} interest region, which exhibited the abnormal steep peak at 1.4ppm, while NAA, Cho and Cr significantly reduced; K. in PRESS sequence with 30ms echo time, the interest region of the lesion exhibited abnormal steep peak at 1.4 ppm, while NAA, Cho and Cr all significantly reduced.

Discussion

Two common types of echinococcosis are echinococcosis granulosa and alveolar echinococcosis, the disease sites are much more common in liver, followed by lung. CAE is rare, with the incidence rate as only 1% -2% of all echinococcosis (3, 4). The patients would be infected because of swallowing the foods, which contain the tapeworm eggs. After entering the stomach, the shell of the tapeworm eggs would be dissolved by the stomach acid hatch, and then the eggs would hatch into larvae, most insect larvae would pass through the intestinal wall and enter the liver via the portal vein, a small number of insect larvae would enter the inferior vena cava through the hepatic vein and then form CAE, so, most CAE come from HAE. Alveolar echinococcosis would form local mass in the brain, which is exactly like malignant tumor, and the multiple lesions would appear as the metastasis tumor of brain. The clinical symptoms of CAE are mainly intracranial hypertension, usually appearing as headache, vomiting, paralysis, visual disturbances (papilledema) and dizziness, epilepsy, etc. Most patients would be concomitant with HAE, suffering from upper abdominal discomfort, jaundice and weight loss, etc.

The growth pattern of alveolar echinococcosis in the cerebral parenchyma mainly appears as the unlimited outward sprouting propagation, forming numerous honeycomb-like asci; the vesicles would contain gel-like substances, stimulating the surrounding tissues to form the inflammatory granuloma, while without the formation of fibrous capsule. Inside the old lesions, there normally exists necrosis, calcareous infarct, and small asci. The asci would have a thin outer membrane and scolex; therefore, it has the capabilities of growth and development. Under the electron microscope, a homogeneous cuticle could be seen inside the intracapsul, while the surrounding granuloma changed to epithelioid tissue cells, arranged in palisade, with multinucleated giant cells scattered inside and surrounded by the fibrous tissues. Eosinophils, lymphocytes, and plasma cells were entrapped inside. Some scholars have studied the reactions inside granuloma of alveolar echinococcosis patients, and found that the CD^{8+} T cells were predominant in the surrounding of active granulomas, while CD^{4+} T cells were more common in the surrounding of "dysplastic" or "dead" granulomas. Since 2000, the diagnosis has relied on the 3 low molecular weight antigens (26-28, 8 and 7-8KDa) in Hokkaido region (Japan), because they had a higher sensitivity (5-7).

The conventional MRI of CAE would appear as: irregular masslike lesions inside cerebral parenchyma, perifocal edema is obvious, with significant position-occupation effect, T1WI mostly manifests as the slight hypointensity, few of which would appear as the mixed signal; T2WI appears as low signal, with "coal-like" changes (5); the main body of T2flair sequence appears as the isointensity, mixed with spotted high signal shadow inside and clear mass boundary; DWI appears as a slightly higher signal with clear boundary, with spotted high signal shadow inside, while the signal shadow of the peripheral edema is unclear; ADC is signal shadow with unclear boundary, with spotted low signal shadow inside, and the peripheral edema shows a high signal shadow. T1WI and T2WI could appear vesicles of different signals and honeycomb-like changes, and the enhanced images would appear that the lesions exhibit irregular chaplet-like enhancement, among which the coal-like changes and multiple small within the lesions in T2WI images are the conventional MRI performance of CAE.

Image features and pathological comparison analysis: 1. T2WI exhibited low signals, with the sameness as the "coal-like" changes. In recent years, 1.5T and 3.0T MR SWI have been widely used, the SWI diagram and SWI images of CAE showed no significant changes of the high and low signals, instead, they showed changes of isointensity, (Fig. 1F ~ G)

SWI image did not support the theoretic deductions that the jelly-like substance was paramagnetic, as well as the secondary calcium deposition in lesions. 2. In DWI, CAE would exhibit slightly higher signals with clear boundary, while the boundary of the signal shadow was unclear in AD, suggesting that diffusion of CAE was not limited, because ADC could better reflect the degree of tissue diffusion. In DWI, CAE appeared as slightly higher signals. Because there were a number of small vesicles, and the cyst fluid inside the small vesicles appeared as long T1 and long T2 signal in MRI, showing permeation effect in DWI images, so slightly higher signal would appear in DWI images. 3. The enhanced lesions exhibited the irregular chaplet-like performance, according to the literature, the invasion of CAE into the brain tissue might generate reactions in the surrounding tissues, the capillary would proliferate and the blood-brain barrier would be destroyed, thus the enhanced scanning could exhibit significant irregular chaplet-like enhancement in lesions (8).

In the MRS study of 10 CAE cases, it was surprising to find that the characteristic spectral lines appeared in the central region of lesion in every CAE case, no matter in the long and short TE in 1.5T or 3.0T, MRS, there appeared an abnormal high and steep peak at approximately 1.4 ppm (Fig. 1J ~ K). The analysis revealed that the common three metabolites at this position were different. Lactate (Lac) was the most common, which often appeared the relative peak at 1.33ppm. Many states would cause the increase of lactic acid, such as the decrease of oxygen supply, acceleration of glycolysis, mitochondrial dysfunction, inflammation and fermentation, *etc*, among which the glycolysis is the main pathway to produce lactic acid (9). There is steep lactic acid peak in tumor tissue necrosis or cystic degeneration. After the surgery of CAE, it was pathologically confirmed that jelly-like substances and a small amount of fiber-like clast were inside the lesions, and the lactate acid peak appeared as the erected bimodal in short TE, while as the inverted bimodal in long TE. In this study, the MRS in long and short TE of 1.5T and 3.0T MR both showed erected bimodal, therefore we could eliminate the possibility of the abnormal peak as the lactic acid. Secondly, the lipid peak (Lip) appeared at 1.3ppm and 0.9ppm, which was the characteristic in short TE of high-grade tumors, but only 41% high-grade tumors would be able to be observed Lip in long TE (9-12). According to the author's observation, Lip peak, which was rare in tumor MRS, had never appeared as such a steep peak, and the Lip peaks resonanced in MRS came from the free lipid inside vesicle cells or extracellular free fat particles, while the free Lip was caused by the damaged cell membrane structures and membrane disintegration with various reasons causes, such as hypoxia, necrosis, apoptosis and inflammation (13). In lymphoma (NHL), Lip would appear as the obvious steep peak, which might be related with the phagocytosis of free fatty acid (FFA) into the tumors by the large number of phagocytes inside (14). No large number of lipid substances was found in the pathological section of CAE, therefore we found it difficult to identify the abnormal steep peak as the lipid peak. Third, alanine (Ala) would be at 1.47 ppm, while Ala was generally undetectable in normal human brain. In most *in vivo* systems, the synthesis of Ala is mainly from pyruvate, according to the literature, it is now generally believed that Ala peak would mainly appear in meningiomas and brain abscess (15). From the peak position in the abscissa and the substances contained inside, we could hardly connect it with the Ala peak. Therefore, the low and flat NAA, Cr and CHO peaks could more support the imaging diagnosis of non-tumorous lesions outside the brain.

Conclusion

The coal-like changes and multiple small vesicles within the lesions in the conventional T2WI, as well as SWI signals and the high and

steep peak at about 1.4 ppm in MRS, could provide a typical imaging of CAE, and could be identified with any short-T2 lesions (8, 16-18).

Acknowledgements

The authors declare that there is no conflict of interests.

References

1. Torgerson PR. The emergence of echinococcosis in central Asia. Parasitology. 2013; 10: 1-7.
2. Matsuhisa T. The mechanism of distantm etastases of alveolar hydatid diaease Hokkaid lgaku Zasshi. 1996; 71: 369-376.
3. Ernest E, Nonga HE, Kynsieri N, Cleaveland S. A retrospective survey of human hydatidosis based on hospital records during the period 1990-2003 in Ngorongoro, Tanzania. Zoonoses Public Health. 2010; 57: 124-129.
4. Demir K, Karsli AF, Kaya T, Devrimci E,Alkan K. Cerebral hydatid cysts: CT finding. Neuroradiology. 1991; 33: 22-24.
5. Algros MP, Majo F, Bresson-Hadni S,Koch S, Godard J, Cattin F, Delbosc B, Kantelip B. Intracerebral alveolar echinococcosis. Infection. 2003; 31: 63-65.
6. Senturk S, Oguz KK, Soylemezoglu F,Inci S. Cerebral Alveolar Echinoccosis Mimicking Primary Brain Tumor. Am J Neuroradiol. 2006; 27: 420-422.
7. Kodama Y, Fujita N, Shimizu T, Endo H,Nambu T,Sato N,Todo S, Miyasaka K. Alveolar Echinococcosis: MR Findings in the Liver. Radiology. 2003; 228: 172-177.
8. Reittner P, Szolar DH, Schmid M. Case report. Systemic manifestation of *Echinococcus alveolaris* infection. J Comput Assist Tomogr. 1996; 20: 1030-1032.
9. Imamura K. Proton MR: spectroscopy of the brain with a focus on chemical issues. Magn Reson Med Sci. 2003; 2: 117-132.
10. Opstad KS, Provencher SW, Bell BA, Griffiths JR, Howe FA. Detect ion of elevated glutathione in meningiomas by quantitative in vivo 1 H MRS. Magn Reson Med. 2003; 49: 632-637.
11. Magalhaes A, Godfrey W, Shen Y, Hu J, Smith W. Proton magnetic resonance spectroscopy of brain tumors correlated with pathology. Acad Radiol. 2005; 12: 51-57.
12. Tate AR, Majos C, Moreno A, Howe FA, Griffiths JR, Arús C. Automated classification of short echo time in vivo 1 H brain tumor spectra: a multicenter study. Magn Reson Med. 2003; 49: 29-36.
13. Gujar SK, Maheshwari S, Björkman-Burtscher I, Sundgren PC. Magnetic resonance spectroscopy. Neuro Ophthalmol. 2005; 25: 217-226.
14. Brennan L, Hewage C, Malthouse JP, McBean GJ. NMR study of alterations in (1-13C) glucose metabolism in C6 glioma cells by gliotoxic amino acids. Neurochem Int. 2003; 42: 441-448.
15. Kantarci M, Bayraktutan U, Karabulut N, Aydinli B, Ogul H, Yuce I, Calik M, Eren S, Atamanalp SS, Oto A. Alveolar echinococcosis: spectrum of findings at cross-sectional imaging. Radiographics. 2012; 32: 2053-2070.
16. Atanasov G, Benckert C, Thelen A, Tappe D, Frosch M, Teichmann D, Barth TF, Wittekind C,Schubert S, Jonas S. Alveolar echinococcosis-spreading disease challenging clinicians: A case report and literature review. World J Gastroenterol. 2013; 19: 4257-4261.
17. Koroglu M, Akhan O, Gelen MT, Koroglu BK, Yildiz H, Kerman G, Oyar O. Long-term follow up of patients with alveolar echinococcosis. Cardiovasc Intervent Radiol. 2006; 29: 473-478.
18. Marti B, Menor S. Complication of hepatic hydatid cysts: ultrasound, computed tomography, and magnetic resonance diagnosis. Gastrointest Radiol. 1990; 15: 119-125.