Discrimination of Brain Abscess and Cystic Tumor by In Vivo Proton Magnetic Resonance Spectroscopy

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Abstract

Proton magnetic resonance (MR) spectroscopy was evaluated for the differentiation of brain abscesses and cystic brain tumors. Proton MR spectroscopy was performed in vivo in two patients with brain abscess and eight patients with various cystic brain tumors (anaplastic astrocytoma, glioblastoma, and metastatic brain tumor). MR imaging with contrast medium demonstrated ring-like enhanced mass lesions in all patients. The various resonance peaks in proton MR spectra were assigned to metabolites according to chemical shifts. Treatment of the cystic brain lesions was based on the information from proton MR spectroscopy. Aspirated pus from one patient with brain abscess was examined using ex vivo proton MR spectroscopy. The in vivo spectra of brain abscess contained resonance peaks attributed to acetate, lactate, alanine, amino acids, and lipids in both cases, and an additional peak of succinate in one case. In vivo spectra of the neoplasms contained resonance peaks corresponding to lactate, lipids, choline, creatine, and N-acetyl aspartate. Proton MR spectroscopy is useful for discriminating brain abscess from cystic tumors with similar neuroimaging appearance, which is very important for determining the treatment strategy.

Key words: brain abscess, brain neoplasm, cystic lesion, magnetic resonance spectroscopy

Introduction

Brain abscess is usually identified by neuroimaging, including computed tomography (CT) and magnetic resonance (MR) imaging, and the clinical manifestations. However, the neuroimaging appearance of some cystic brain tumors is similar findings to that of brain abscess. Brain abscess is especially difficult to identify in patients without clinical or laboratory evidence of infection.

The medical management strategies for brain abscess¹³⁾ and neoplasm definitely differ. The correct diagnosis must be obtained before the treatment of cystic brain lesion which involves surgical procedures.

In vivo proton MR spectroscopy permits non-invasive examination of the metabolic characteristics of the human brain in a clinical environment. MR spectroscopy can lead to a specific diagnosis when neuroimaging findings such as CT and MR imaging are not specific.^{2,11,21)} Proton MR spec-

troscopy has been performed in patients with brain abscess,^{3,5,6,8,10,12,14,17,19,20)} and some reports suggest that proton MR spectroscopy can distinguish brain abscess from brain tumors, such as malignant glioma or metastatic brain tumor.

This study evaluated proton MR spectroscopy for discriminating pyogenic brain abscess from cystic brain tumor with ring-like enhancement in patients by identifying lesion-specific spectroscopic patterns useful for differential diagnosis. Ex vivo proton MR spectroscopy of surgical aspirated pus was also performed to confirm the in vivo spectral assignments of brain abscess.

Materials and Methods

Ten patients, eight males and two females aged 12 to 73 years, with MR imaging evidence of ring-like enhanced lesions after administration of gadolinium-diethylenetriaminepenta-acetic acid were preoperatively evaluated with in vivo proton MR spectroscopy. The cystic lesions were located in the supratentorial region, except in one case. All cystic lesions were examined by evaluating the

pathology of operative specimens, except in one case. Informed consent was obtained from all patients or guardians.

MR imaging/spectroscopy was performed at 1.5 T using a clinical system (Gyrosan ASNT; Philips Medical Systems B.V., Best, the Netherlands) with a circularly polarized head coil. T_1 -weighted or T_2 -weighted MR images in three orthogonal planes were obtained to define the volume of interest (VOI) as a $2 \times 2 \times 2$ cm to $3 \times 3 \times 3$ cm region including the visual estimate of the cystic area. MR spectra of the VOI were acquired before administration of contrast materials for MR imaging. The spectra were obtained with an echo time (TE) of 136 msec and a repetition time (TR) of 2000 msec, and 128 or 256 signals were tested in all patients using a point-resolved spectroscopic (PRESS) sequence¹⁾ with water-suppression techniques from the VOI.

Field homogeneity was optimized for the selected VOI by measuring the proton MR signal of water in tissue before spectroscopic measurements. Typical full widths at half maximum of 4–8 Hz were achieved in all examinations. The water signal was suppressed by a frequency-selective saturation pulse at the water resonance. A sweep width of 1000 Hz was used with a data size of 512 points. Only the second half of the echo was acquired. After the zero filling of 1024 points for all free-induction-decay data, exponential line broadening and Gaussian multiplication were applied before Fourier transformation. Zero-order phase correction was applied to all spectra.

Resonance peaks were assigned based on previous MR spectroscopy examinations of brain abscess.^{3,5,6,8,10,12,14,17,19,20)} Resonance peaks were graded according to the ratio of the integral of the metabolite peak to the integral of the unsuppressed water peak. The ratios of all metabolite peaks

showed a wide range (2.8×10^{-5} to 1.0×10^{-3}). Peaks in the lower one-third of the range were assigned a grade of “small”; peaks in the middle one-third were graded as “moderate”; and peaks in the upper one-third were graded as “large.”

Patients with proton MR spectroscopy indications of brain abscess were treated by surgical aspiration. A specimen of the exudate of Case 1 was frozen in liquid nitrogen within 5 minutes of surgical aspiration. The frozen exudate was thawed and directly placed in a 5-mm nuclear MR tube. Ex vivo proton MR spectroscopy using the PRESS sequence with TR of 2000 msec and TE of 22, 136, and 272 msec was performed to confirm phase inversion of the peaks. With a TE of 136 msec, phase inversion occurs as a result of J-coupling in alanine, lactate, amino acids, but not in lipids,^{12,20)} which may be helpful to discriminate lactate or amino acid signals from lipid signals.

Results

Two patients had pyogenic brain abscesses, five had malignant astrocytomas (3 glioblastomas and 2 anaplastic astrocytomas), and three had metastatic brain tumors. Case 10 had a metastatic brain tumor identified by clinical findings. The MR spectra of all patients were of acceptable quality. The characteristics of patients and the in vivo proton MR spectroscopic findings are summarized in Table 1.

In vivo proton MR spectroscopy of brain abscess detected multiple resonance peaks. The main characteristic features in both cases were peaks tentatively assigned to acetate (1.92 ppm), alanine (1.5 ppm), lactate complex (1.37, 1.28 ppm), amino acids (0.8–1.1 ppm), and lipids (0.8–1.2 ppm) (Fig. 1A). The resonance peak of succinate (2.42 ppm) was also detected in Case 2. The N-acetyl aspartate

Table 1 Summary of magnetic resonance spectroscopic findings in 10 patients

Case No.	Age/Sex	Diagnosis	Ace	Succ	Ala	AA	Lip	Lac	NAA	Cho	Cr/PCr
1	72/M	brain abscess	‡	—	‡	+	+	‡	—	—	—
2	45/M	brain abscess	‡	+	‡	‡	+	‡	—	—	—
3	73/F	glioblastoma	—	—	—	—	—	‡	+	+	—
4	72/M	glioblastoma	—	—	—	—	—	+	+	‡	+
5	58/M	glioblastoma	—	—	—	—	+	—	‡	‡	‡
6	61/M	anaplastic astrocytoma	—	—	—	—	—	‡	+	‡	+
7	12/M	anaplastic astrocytoma	—	—	—	—	—	‡	‡	‡	+
8	68/F	metastatic brain tumor	—	—	—	—	‡	—	+	‡	+
9	68/M	metastatic brain tumor	—	—	—	—	—	‡	+	‡	+
10	69/M	metastatic brain tumor	—	—	—	—	—	‡	—	—	—

AA: amino acids, Ace: acetate, Ala: alanine, Cho: choline, Cr: creatine, Lac: lactate, Lip: lipids, NAA: N-acetyl aspartate, PCr: phosphocreatine, Succ: succinate. +: small peak, ‡: moderate peak, ‡: large peak.

Fig. 1 Case 1. **A:** Proton magnetic resonance (MR) spectra taken in vivo of the cystic lesion in the left frontal lobe. **B:** Proton MR spectra taken ex vivo of the exudate. Upper: echo time (TE) 22 msec, middle: TE 136 msec, lower: TE 272 msec, point-resolved spectroscopic sequence. AA: amino acids, Ace: acetate, Ala: alanine, Lac: lactate, Lip: lipids.

(NAA), choline, and creatine/phosphocreatine (Cr/PCr) peaks were absent in both cases, although seen in the parenchyma spectra of the normal brain.

Ex vivo proton MR spectroscopy of the exudate specimen from Case 1 confirmed the tentative as-

signment of peaks in vivo (Fig. 1B). The upper, middle, and lower spectra were obtained with TEs of 22, 136, and 272 msec, respectively, and show essentially the same resonance seen in vivo. The inversion of the 0.95, 1.05, and 1.09 ppm triplet in the ex vivo spectrum at TE of 136 msec tends to confirm the initial assignment of these peaks to amino acids. The lipid peak does not invert at this TE value,¹²⁾ so that the peaks of 1.2 and 0.89 ppm arose from lipids.

In vivo proton MR spectroscopy of malignant astrocytoma found large peaks of choline in four cases and an elevated peak of choline relative to that of NAA in another case, and elevated peaks of lactate complex in four cases and lipids in one case. Proton MR spectroscopy of metastatic brain tumor had a strong resemblance to that of malignant glioma, and the tumors could not be distinguished. Proton MR spectroscopy revealed only peaks of lactate complex in one case. Proton MR spectroscopy of both malignant glioma and metastatic brain tumor showed no peaks of either acetate or succinate, nor detectable peaks of amino acids.

Representative Cases

Case 1: A 72-year-old male complained of headache and presented with right hemiparesis. He had no fever or inflammatory signs. CT and MR imaging showed a ring-enhanced mass lesion in the left frontal lobe (Fig. 2). Proton MR spectroscopy suggested a brain abscess (Fig. 1A), and puncture of the lesion yielded 8 ml of yellowish, cloudy pus. Standard microbiological studies of the purulent material isolated microaerophilic streptococcus. Drainage of the abscess and treatment with antibiotics led to a favorable neurological and radiological outcome.

Case 3: A 73-year-old female presented with left hemiparesis. CT and MR imaging showed a round mass with ring-shaped enhancement in the right parietal lobe (Fig. 3). Angiography revealed no tumor stain. Proton MR spectroscopy suggested malignant neoplasm (Fig. 4), so the tumor was completely removed by craniotomy. Histological study demonstrated glioblastoma multiforme. The patient had left mild hemiparesis when discharged.

Discussion

Proton MR spectra of brain abscess are available for 61 cases of brain abscess.^{3,5,6,8,10,12,14,17,19,20)} We selected 42 cases with MR spectra appropriate for analysis. Some authors have erroneously interpreted acetate resonance as NAA.^{10,17)} Lactate resonance was found in all cases, acetate in 37 cases, amino acids in 34, alanine in 31, succinate in 14, and lipids

Fig. 2 Case 1. Axial T_1 -weighted magnetic resonance image with contrast medium before surgery demonstrating a cystic mass with a ring-shaped enhanced area in the left frontal lobe and perifocal edema around the mass.

Fig. 3 Case 3. Axial T_1 -weighted magnetic resonance image with contrast medium before surgery demonstrating a cystic mass in the right parietal lobe with massive edema mimicking a brain abscess, but found to be glioblastoma multiforme.

Fig. 4 Case 3. Proton magnetic resonance spectra of the cystic lesion. Cho: choline, Lac: lactate, NAA: N-acetyl aspartate.

in 16 cases.

Our results generally agreed well with previous reports. The present study supports the idea that acetate and succinate may be key markers for brain abscess.^{3,5,6,8,9,12,14,19,20} Proton MR spectroscopy has never detected acetate and succinate in brain neoplasm. Acetate and succinate are end-products of protein and carbohydrate metabolism in various bacterial strains that cause abscess.⁵ Gas-liquid chromatography demonstrates that these end-products are detectable in the various bacteria strains present in abscess.^{4,7,18} In addition, acetate and succinate peaks are easy to identify because of the single appearance and no overlap with other peaks, unlike undefined peaks for amino acids and lipids. However, the peaks of acetate and succinate were also observed in cysticercosis.³ Strictly, the presence of the peaks of acetate and succinate indicate exclusion of brain neoplasm and suggest infection.

Acetate and lactate are produced by most bacteria strains, but succinate is also produced by some strains, so that absence of succinate in the proton MR spectra from patients may reflect a low concentration in the pus.²⁰ Succinate may be a marker of anaerobic infection.⁷ However, the findings of a culture study of aspirated pus, gas chromatography of pus, and proton MR spectroscopy taken of abscess did not always agree. Proton MR spectroscopy is a relatively less sensitive analytic method compared with gas chromatography,^{2,7} and the environmental conditions associated with bacterial growth have different factors such as oxygen pressure, carbon di-

oxide pressure, glucose concentration, and presence of different bacteria species.

Two cases of brain abscess contained neither acetate nor succinate signals.¹²⁾ However, amino acids, such as valine and leucine, that are end-products of proteolysis caused by enzymes released from neutrophils,¹⁵⁾ were detected in these cases. Certain amino acids, such as valine and leucine, may be markers for abscess. The 0.9 ppm peaks from amino acids ($-\text{CH}_3$ moieties from valine, leucine, and isoleucine) are also useful for the differentiation of brain abscess and tumor at in vivo proton MR spectroscopy.⁹⁾ In our study as well as in this previous study, amino acid peaks were observed in patients with brain abscess but not in patients with tumor necrosis.

Proton MR spectroscopy detected hardly any resonances indicating NAA, choline, or Cr/PCr complex in brain abscesses. NAA and Cr/PCr complex were detected in only one case,¹²⁾ and choline in one case.¹⁰⁾ These peaks were very small and may reflect contamination of the VOI by a portion of normal brain parenchyma. Smaller VOIs will provide more specific spectra of the lesion. Proton MR spectroscopy took us about 20 minutes to obtain the spectrum of one VOI within the cystic lesion, to minimize the time required for the examination.

The proton MR spectrum of brain abscess is affected by conditions such as location, size, and time of infection. Some patients may have non-specific MR spectra, so other information is needed, such as neuroimaging findings and clinical manifestations. A recent study reported that diffusion-weighted echo-planar MR imaging can also be used for distinguishing between brain abscess and tumors.¹⁶⁾ The combination of proton MR spectroscopy and other methods including diffusion-weighted echo-planar MR imaging has great potential for establishing the differential diagnosis between pyogenic brain abscess and other cystic tumors with similar neuroimaging appearance.

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Commentary

This is a very interesting contribution, in which Kadota et al. evaluated the possibility to differentiate brain abscess from malignant brain tumors, using PMRS. Although their imaging has demonstrated the typical ring-like enhanced mass lesions in all patients, PMRS allowed the distinction between abscesses from other malignant brain tumors, such as GBMs or metastatic neoplasms. Their study supports the finding that the presence of acetate and succinate peaks in the PMRS may be the important key markers for brain abscess, since this examination has never detected this spectra in brain tumors. It is also suggested that acetate and succinate are end-products of protein and carbohydrate metabolism from several bacteria strains, present in these lesions. It was interesting to note that this finding may also be present in cysticercosis, which is an endemic plaque in many tropical countries, and also a granulomatous lesion that may produce any kind of neurosurgical complications, including meningitis, hydrocephalus, expanding lesions or even abscesses. Other Japanese studies like the one reported by Noguchi et al. (see ref. 16) have also demonstrated that diffusion weighted echo-planar MR imaging may be complementary to the distinction between brain abscess and tumors.

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Kadota et al. studied proton MR spectroscopy in two cases of brain abscess and found the resonance peaks corresponding to acetate, lactate, alanine, amino acids, and lipids in both cases and an additional peak corresponding to succinate in one case. These findings were specific to brain abscess as compared to the spectra of cystic lesions associated with brain tumors they studied. Usually it is not difficult to make a diagnosis of brain abscess, however, from time to time we encounter cystic lesions that are difficult to differentiate by conventional examinations including MRI. This careful study has supported the idea that proton MR spectroscopy is useful for establishing the differential diagnosis between brain abscess and other cystic lesions in the brain.

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The possibility to differentiate between brain abscess and malignant tumor is highly appreciated in two situations: Patients in whom an operation is not possible due to a general bad condition or bad parameters of coagulation; patients with one or multiple lesions in deep or highly sensible regions of the brain. In these cases it is desirable to have a reliable diagnosis without operation or biopsy. In order to treat such cases according to the results of in vivo magnetic resonance spectroscopy, the empirical experience should be grounded on a higher number of cases to achieve statistical evidence. Especially coefficients of sensitivity and specificity should be estimated. Further, the volume of interest which should allow a clear diagnosis sometimes requires smaller volumes than $2 \times 2 \times 2$ cm in order to avoid partial volume effects. In the case of very small lesions the use of segmentation techniques might be helpful. Following these guidelines the study using in vivo magnetic resonance spectroscopy as a promising tool for these purposes should be continued.

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