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In Vivo Single-Voxel Proton MR Spectroscopy in Intracranial Cystic Masses

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PURPOSE: **Our objective was to evaluate the proton MR spectroscopic pattern of the cystic contents of various intracranial masses and to report characteristic spectral patterns that may be helpful in the differential diagnosis of these lesions.**

METHODS: **We evaluated 40 proton MR spectra obtained from cystic contents of various intracranial cystic masses in 39 patients, including gliomas (n = 14), metastases (n = 3), abscesses (n = 8), cysticercosis (n = 4), epidermoids (n = 3), and others (n = 7). Proton MR spectroscopy was performed on a 1.5-T MR unit using a point-resolved spectroscopic sequence with a 2 × 2 × 2 cm^3 volume of interest. Assignment of the resonance peaks was based on previous studies.**

RESULTS: **Adequate proton MR spectroscopic data were obtained in 35 cases (88%). In most gliomas and metastases, only a lactate resonance was observed. There was a trend toward a higher lactate peak in high-grade gliomas. A few tumors, including malignant gliomas and metastases, showed lipid signal combined with lactate signal. In abscesses, there were various combinations of lactate, acetate, succinate, amino acids (including valine, alanine, and/or leucine), and/or unassigned resonances. In cysticercosis, resonances of lactate, succinate, alanine, acetate, and/or unassigned resonances were observed. Three epidermoid cysts showed only lactate signal. There were no identifiable resonances from the arachnoid and porencephalic cysts.**

CONCLUSION: **Only lactate is commonly observed in a variety of intracranial cystic masses, except for abscess and cysticercosis, in which resonances of acetate, succinate, amino acids, and/or unassigned metabolites can be seen in addition to a lactate peak.**

A variety of intracranial lesions, including gliomas, metastases, craniopharyngiomas, abscesses, parasitic disease (such as cysticercosis), epidermoids, and arachnoid cysts may appear as mainly cystic masses on magnetic resonance (MR) and computed tomography (CT) studies of the brain. The neuroimaging findings combined with clinical information usually enable a correct diagnosis, but they do not always characterize these lesions. For instances, it is sometimes impossible to differentiate cystic or necrotic tumor from abscess, low-grade glioma from high-grade glioma or metastasis, and epidermoid from arachnoid or other cyst.

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Proton MR spectroscopy has been used in the investigation of a variety of intracranial tumors (1–10). In most solid tumors, *N*-acetylaspartate (NAA) decreases and choline (Cho) compound and lactate are elevated. Although some previous studies have shown that low NAA/Cho ratios and high lactate signals tend to correlate with the malignancy of gliomas, the correlation between proton MR spectral data and histopathologic tumor grading is still a matter of controversy, and only a few reports on the proton MR spectroscopic patterns of nonneoplastic cysts have been documented (11–15).

The purpose of this study was to evaluate the proton MR spectroscopic pattern of the contents of various intracranial cystic masses and to determine whether there are any characteristic spectral patterns that may be helpful in the differential diagnosis of these lesions.

Methods

We evaluated 40 proton MR spectroscopic studies in 39 patients (21 men and 18 women; 26 to 60 years old, mean age, 43 years) with a variety of intracranial cystic masses. In one

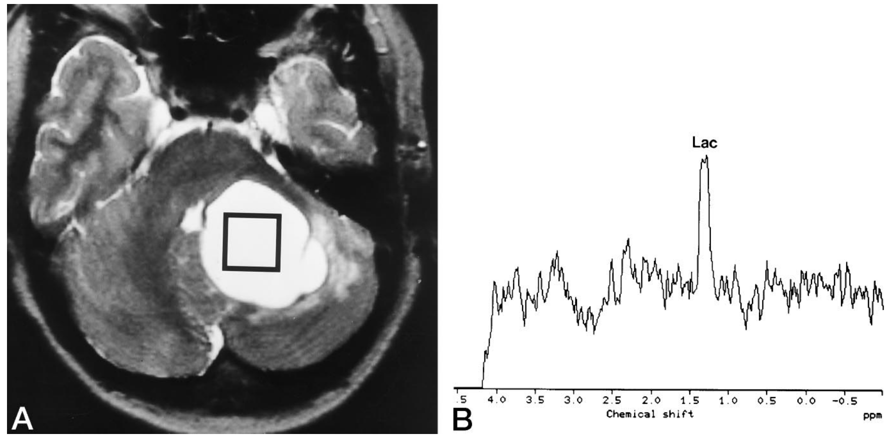

FIG 1. Pathologically proved pilocytic astrocytoma.

A, Axial T2-weighted MR image (4000/100/1) shows a large cystic mass in the cerebellum. The VOI (*box*) of 2 × 2 × 2 cm^3 includes only the cystic fluid.

B, Proton MR spectrum (2000/270) from the cystic fluid shows only a lactate (*Lac*) peak. The lactate peak was inverted with an echo time of 135 (not shown).

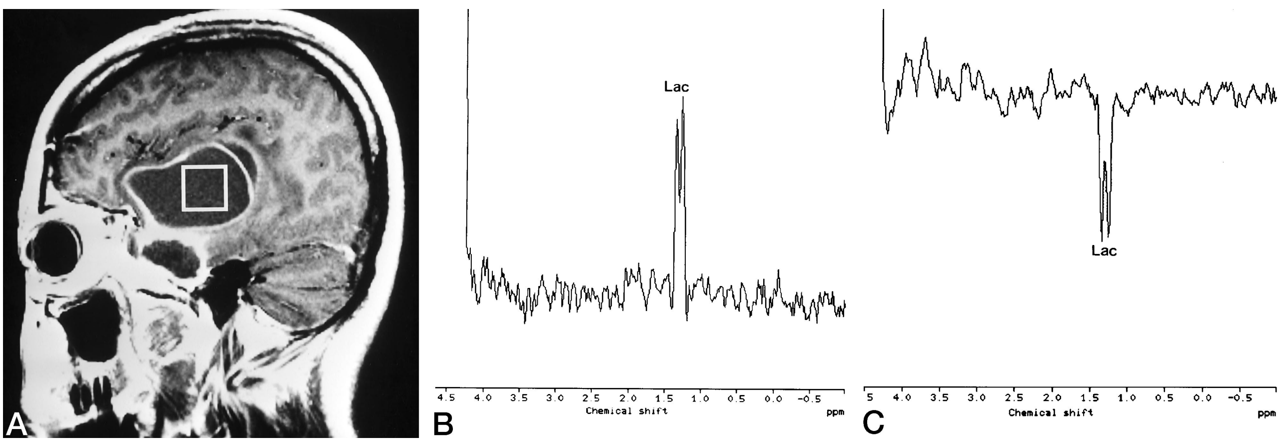

FIG 2. Pathologically proved glioblastoma multiforme.

A, Sagittal contrast-enhanced T1-weighted MR image (500/16) shows a large ring-enhancing cystic mass in the left temporal lobe. The VOI (*box*) of 2 × 2 × 2 cm^3 is entirely within the cystic fluid.

Proton MR spectra at 2000/270 (*B*) and 2000/135 (*C*) from the cystic fluid show only a lactate (*Lac*) peak. Note inversion of the lactate peak in *C* due to J-coupling.

patient with multiple brain abscesses, proton MR spectroscopy was performed for two abscesses. The cystic masses included low-grade gliomas (grades I and II) (n = 3), high-grade gliomas (grades III and IV) (n = 10), ganglioglioma (n = 1), metastases (n = 3), trigeminal neurinoma (n = 1), craniopharyngioma (n = 1), abscesses (n = 8), cysticercosis (n = 4), epidermoids (n = 3), arachnoid cysts (n = 2), peritumoral meningioma cysts (n = 2), and porencephalic cyst (n = 1). All neoplasms, epidermoids, and abscesses were confirmed pathologically. For the abscesses, the etiologic agents were confirmed microbiologically in six patients: *Streptococcus intermedius* in three, *Eubacterium lentum* in two, and *Staphylococcus epidermidis* in one. In patients with cysticercosis, the diagnosis was based on both the CSF enzyme-linked immunosorbent assay (ELISA) test for cysticercus-specific antibody and the MR imaging findings, and was verified at surgery in two patients. In patients with non-neoplastic cysts, such as arachnoid cyst or porencephalic cyst, diagnosis was based solely on the MR findings.

All proton MR spectroscopic studies were performed on a clinical 1.5-T MR system with a circularly polarized head coil before any treatment was initiated. MR imaging, with either T1- or T2-weighted sequences in three orthogonal planes, preceded proton MR spectroscopy in order to define the volume of interest (VOI) of 2 × 2 × 2 cm^3. The VOI was confined to the central cystic contents in all but five lesions (one glioma, one metastasis, two abscesses, and one cysticercosis), in which approximately 10% to 20% of the VOI contained solid components. The spectra were obtained using a point-resolved spectroscopic (PRESS) sequence with parameters of 2000/270/128 (repetition time/echo time/excitations) in all patients. In two thirds of the patients, MR spectra were additionally obtained with an echo time of 135 to confirm the phase reversal shown by J-coupled metabolites (ie, lactate and amino acids). Before spectroscopic measurements were obtained, the field homogeneity was optimized over the selected VOI by observing the proton MR signal of tissue water with the spatially selective PRESS sequence. Typical full widths at half maximum of 4 to 8 Hz were achieved in most 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 1024 points. Only the second half of the echo was acquired. Following the zero-filling of 4096 points in all free-induction-decay data, an exponential line broadening (center, 0 milliseconds; half time, 150 milliseconds) was done before Fourier transformation. A zero-order phase correction was applied to all spectra.

Assignment of resonance peaks for the metabolites, including acetate, succinate, and amino acids, was based on previously documented studies of brain abscess (11–14, 16). The resonance peak of lactate was arbitrarily assigned to one of three grades, low (+), medium (++), or high (+++), relative to the peak height of water. The proton MR spectroscopic patterns of some abscesses and cystic or necrotic tumors in this study and the method by which arbitrary lactate peak grades were assigned have been described in detail elsewhere (16).

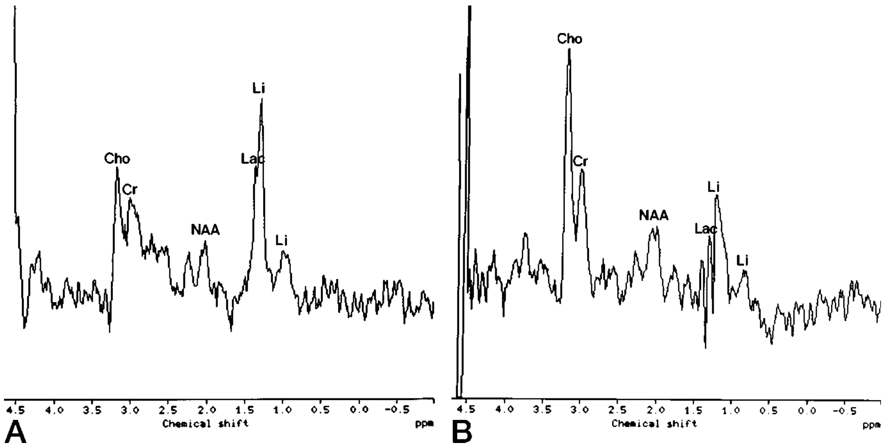

FIG 3. Pathologically proved metastasis from lung cancer.

Proton MR spectra at 2000/270 (*A*) and 2000/135 (*B*) from the central cystic fluid of a metastatic tumor in the right cerebellum show elevated lactate (*Lac*) and lipid (*Li*) peaks. Cho, Cr, and NAA peaks are also seen, probably resulting from inclusion of the solid portion of the tumor. At MR imaging, the VOI of 2 × 2 × 2 cm^3 mostly included the cystic portion, but small parts of the solid wall were also included (not shown).

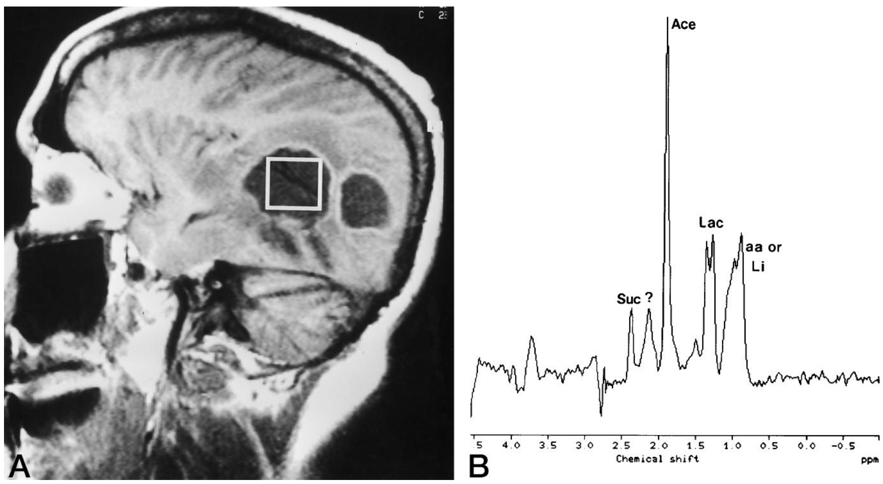

FIG 4. Pathologically proved abscess.

A, Sagittal contrast-enhanced T1-weighted MR image (500/16) shows two ring-enhancing masses with surrounding edema in the left posterior temporal lobe. The VOI (*box*) of 2 × 2 × 2 cm^3 is confined to an abscess cavity.

B, Proton MR spectrum (2000/270) shows tall acetate (*Ace*, 1.9 ppm) peak and succinate (*Suc*, 2.4 ppm), lactate (*Lac*, 1.3 ppm), amino acids or lipids (aa or Li, 0.9 ppm), and unassigned (*?*, 2.2 ppm) peaks. The phase reversal of the lactate (1.3 ppm) and the amino acid (valine or leucine, 0.9 ppm) was well documented on an MR spectrum at 2000/135 (not shown).

Results

The MR spectra were of analyzable quality in all but five patients in whom the spectra were unacceptable because of either poor shimming conditions (one each with high-grade glioma, craniopharyngioma, or peritumoral meningioma cyst) or contamination from neighboring fat (one each with arachnoid cyst or cysticercosis in the superficial brain surface close to the calvaria).

In all three cases of low-grade glioma (Fig 1) and in eight of nine cases of high-grade glioma (Fig 2), only a lactate resonance (1.3 ppm) was observed. In the remaining cases of high-grade glioma, a lactate resonance plus a lipid signal were found. The peak height of the lactate signal was low (+) in all low-grade gliomas and in three high-grade gliomas. Of the remaining six high-grade gliomas, five showed a medium lactate peak (++) and one showed a high lactate peak (+++). One cystic ganglioglioma in the cerebellum also showed only a lactate resonance, which was of medium peak (++). Among the three metastases, two showed only a lactate resonance of medium peak (++); the remaining metastasis, from lung cancer, showed multiple peaks: lactate, at 1.3 ppm; broad signal (presumably from lipid), at 0.8 to 1.2 ppm; Cho, at 3.2 ppm; creatine (Cr), at 3.0 ppm; and NAA, at 2.1 ppm (Fig 3). The resonance peaks representing NAA, Cho, and Cr were also identified in the other patients in whom the VOIs contained some adjacent solid tissues. One trigeminal neurinoma revealed a lactate resonance of medium peak (++) and two unassigned resonances at 3.4 and 3.6 ppm.

In seven of the eight patients with abscesses (Fig 4), there were various combinations of resonances from lactate; acetate (1.9 ppm); succinate (2.4 ppm); amino acids, including valine, alanine, and leucine (0.9, 1.5, 3.6 ppm, respectively); lipid; and unassigned metabolites (one each at 2.2, 2.9, 3.2, 3.4, 3.8 ppm). The resonance of lactate had a high peak (+++) in three patients and a medium peak (++) in five. Resonance peaks from acetate and succinate were observed in five and four patients, respectively. Resonances from alanine (1.5 ppm) and leucine (3.6 ppm) were found in four and two patients, respectively. A peak at 0.9 ppm on MR studies obtained with an echo time of 270, which had a phase inversion at an echo time of 135, was seen in four abscesses, highly suggestive of amino acid (valine or leucine), but not lipid. In the other patients who were not studied with an echo time of 135, the peak at 0.9 ppm remained undifferentiated between lipid and amino acid. There were five unassigned peaks at 2.2, 2.9, 3.2, 3.4, and 3.8 ppm, respectively, in three patients with brain abscess. In

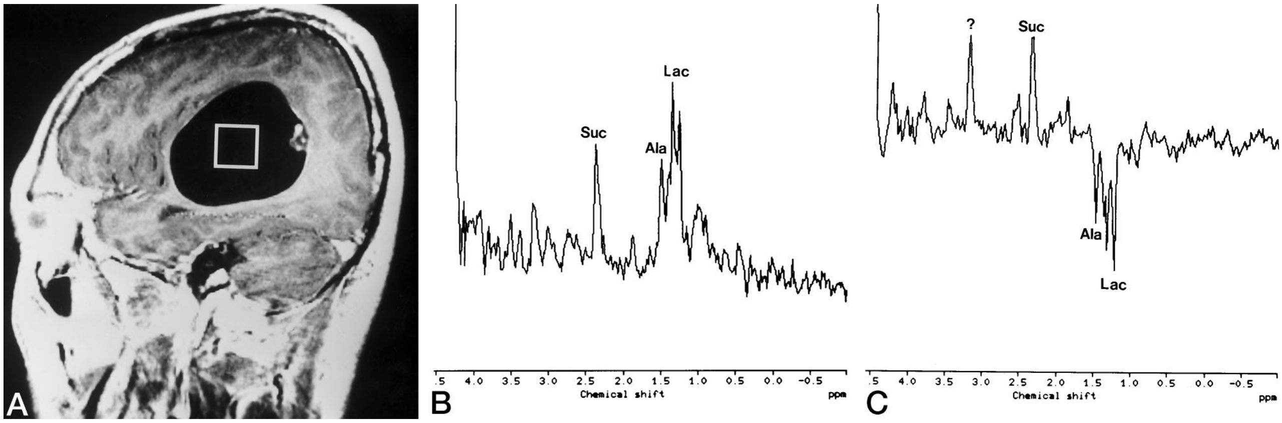

FIG 5. Pathologically proved cysticercosis.

A, Sagittal contrast-enhanced T1-weighted MR image (500/16) shows a large cystic mass with a small mural nodule (scolex) in the right temporal lobe. The VOI (*box*) of 2 × 2 × 2 cm^3 is entirely confined within the cyst.

B, Proton MR spectrum (2000/270) shows elevated lactate (*Lac*), alanine (*Ala*, 1.5 ppm), and succinate (*Suc*, 2.4 ppm) peaks.

C, Proton MR spectrum (2000/135) shows inversion of the lactate and alanine peaks. An unassigned peak (*?*) around 3.3 ppm is also seen.

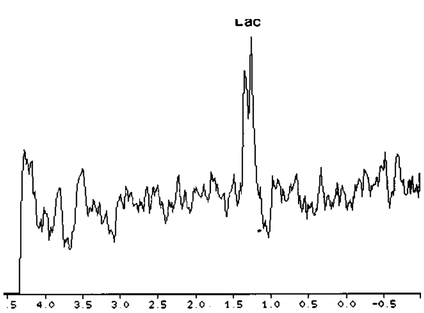

FIG 6. Proton MR spectrum (2000/270) from a large pathologically proved epidermoid cyst in the left cerebellopontine angle shows only a lactate (*Lac*, 1.3 ppm) peak. The VOI of 2 × 2 × 2 cm^3 was confined to the mass (not shown).

patients with cysticercosis, resonances were seen from lactate in three, from succinate in three, from alanine in two, from lipid in two, from acetate in one, and from an unassigned peak around 3.3 ppm (only at an echo time of 135) in one (Fig 5). All three patients with epidermoid cysts (Fig 6) had lactate signals of only low (+) or medium (++) peaks. One arachnoid cyst, one peritumoral meningioma cyst, and one porencephalic cyst showed no measurable resonances.

Discussion

All cystic tumors and inflammatory cysts (abscesses and cysticercosis) and some nonneoplastic cysts in our study commonly showed a lactate signal, indicating that lactate is a nonspecific metabolite that results from anaerobic energy generation (eg, glycolysis). All cystic and necrotic tumors except two (one glioma and one metastasis) exhibited only a lactate signal of variable peak height, regardless of histopathologic type and grading. In two cases, lactate and lipid signals were observed. As stated earlier, the lactate level was assessed by relative grading, not in absolute terms. It was based on the ratio of the integral of the lactate peak to the integral of the unsuppressed water peak. The ratio was as small as 10^{-5} to 10^{-3} (16). The wide overlap in the peak lactate heights of low- and high-grade tumors suggests that proton MR spectroscopy is of limited value in the diagnosis of cystic tumors and in the grading of malignant lesions, although high-grade tumors have a tendency toward higher lactate peaks. Our results are consistent with those of previous reports (8, 11). Although in one study (14), the presence of a Cho signal was reported in primary cystic neoplasms, we found no case of a cystic tumor showing a Cho peak.

In brain abscesses, the spectra showed elevation of acetate, succinate, and some amino acids, as well as lactate and lipid, which appear significantly different from the spectra of cystic or necrotic brain tumors. These results also agreed well with those of other studies (12–14). Increases in lactate, acetate, and succinate presumably originate from the enhanced glycolysis and fermentation of the organism (12, 14). Amino acids, including valine and leucine, are known to be the end products of proteolysis by enzymes released by neutrophils in pus (17). To our knowledge, detection of resonance peaks from acetate, succinate, and such amino acids as valine and leucine has not been reported in proton MR spectra of brain tumors.

Discrimination between amino acids (ie, valine or leucine at 0.9 ppm) and lipid (at 0.8 to 1.2 ppm) is important, because lipid signals may exist in both brain tumors and abscesses, whereas amino acids are not seen in proton MR spectra of brain tumors, suggesting that amino acids may be markers for brain abscesses. Therefore, if there are resonance peaks at around 0.9 to 1.5 ppm on proton MR spectra obtained with an echo time of 270, an additional spectrum obtained at an echo time of 135 would be necessary to discriminate lactate or amino acids signals from lipid signal. It is known that with an echo time of 135, phase inversion occurs as a result of J-coupling in lactate and amino acids, but not in lipid (14), which may be helpful, along with the presence or absence of acetate or succinate, in differentiating brain abscess from tumor. In our study, cysticercosis also revealed multiple peaks corresponding to the resonances from lactate, acetate, succinate, alanine, and unassigned metabolites. We could not find any studies on the chemical analysis and proton MR spectroscopic pattern of the cystic fluid of cysticercosis published in the English-language literature, although acetate, alanine, and lactate had been reported in hydatid cysts (15).

Epidermoid cysts are occasionally difficult to differentiate from other nonenhancing nonneoplastic cysts, such as arachnoid cysts, with MR imaging or CT. Proton MR spectroscopy may assist in distinguishing these cysts, as elevation of lactate is seen in the former but not in the latter.

Conclusion

Lactate is the most common metabolite observed in the contents of various intracranial cystic masses. Elevation of lactate alone and its peak height are of limited value in diagnosing cystic tumors or in predicting the pathologic grading of a malignant lesion. However, proton MR spectroscopic examination may be useful in differentiating cystic or necrotic brain tumors from inflammatory cystic masses (abscess and cysticercosis), because various metabolites, including acetate, succinate, and/or amino acids other than lactate, are frequently observed in brain abscesses and cysticercosis.

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