Prospective evaluation of in vivo proton MR spectroscopy in differentiation of similar appearing intracranial cystic lesions


Abstract

Proton MR spectroscopy (PMRS) has been found to be useful in differentiating various cystic intracranial lesions. The purpose of the present study was to prospectively evaluate the spectral pattern of various cystic lesions of brain with similar imaging appearances and to determine the accuracy of this technique in the differential diagnosis of these lesions. Fifty-one patients with intracranial cystic lesions (21 abscesses, 20 gliomas, 3 hydatid cysts, 3 arachnoid cysts, 1 case each of glioependymal cyst, xanthogranuloma, infarction and acoustic neuroma) were evaluated with conventional MR imaging and in vivo PMRS. Ex vivo PMRS of the cystic contents aspirated at surgery in 31 cases was also done to confirm the in-vivo results. Preoperative diagnosis of the lesions was based on the results of in vivo PMRS. In vivo PMRS accurately predicted the pathology in 92% of the cases. We conclude that in-vivo PMRS complements imaging in better characterization of cystic intracranial mass lesions. © 2001 Elsevier Science Inc. All rights reserved.

Keywords: MR Spectroscopy; Cystic Lesions; Brain; MRI

1. Introduction

Cystic intracranial lesions include true cysts lined by epithelial, ependymal, or meningotheial cells, dermoid and epidermoid cysts, parasitic cysts (cysticercosis, hydatid cysts) or may be pseudocystic neoplastic or inflammatory lesions secondary to accumulation of necrotic, intercellular mixed or proteinaceous material [1–3]. It is not always possible to differentiate different cystic intracranial lesions on MR imaging findings. The management of these cystic lesions depends upon its nature and it varies from definite surgery (cystic glioma) to minimal invasion (abscesses, arachnoid cyst) [4,5]. Newer imaging techniques such as diffusion weighted imaging (DWI) and fluid attenuated inversion recovery imaging (FLAIR) have been applied to differentiate the cystic lesions [4–6]. DWI is considered useful in differentiating cystic gliomas from cerebral abscesses [5,6] and there are no reports of its use in differentiation in other types of cystic lesions. FLAIR imaging has also been used in the differentiation of cystic intracranial lesions. It has been shown that the maldevelopment/porencephalic cysts can be differentiated from neoplastic/inflammatory lesions [4]. However, FLAIR sequence was not found to be useful in separating neoplastic lesions from inflammatory/infective cystic lesions [4]. In vivo proton MR spectroscopy (MRS) has shown a high potential in the differentiation of neoplastic from non-neoplastic tissue [3,6–12]. Most of these earlier studies are of retrospective nature. The purpose of present study was to evaluate in prospective the accuracy of PMRS in differentiation of intracranial cystic lesions.

2. Patients and methods

Fifty-one patients (23 men and 28 women; mean age 32.6 years; range 8 to 50 years) having similar appearing
intracranial cystic lesions on conventional MR imaging formed the study group. The cystic lesions included 21 abscesses, 20 gliomas, 3 arachnoid cysts, 3 hydatid cysts and 1 case each of gliopendymal cyst, xanthogranuloma, infarction and acoustic neuroma. All the patients were subjected to conventional MR imaging including proton density (PD), T2 and T1 weighted sequences. In-vivo PMRS was done with a single voxel technique and was interpreted independently by two investigators (RKG, ASD) with out the knowledge of imaging except that the lesions were purely cystic. Ex vivo PMRS was interpreted independently by another author (RR) who was blinded of the imaging and in vivo PMRS data. The pre-operative diagnosis was based entirely on PMRS findings. Ex-vivo MRS of the fluid contents of cysts aspirated at surgery was also carried out in 31 patients. The final diagnosis was based on the results of histopathology, aspiration and culture of the contents for the organism (abscesses). The results of PMRS diagnosis were compared with final diagnosis to know the utility of in vivo PMRS in these cystic intracranial lesions. Spectral data were available from 50 age and sex matched healthy volunteers from the control data bank.

MRI and MRS Techniques: All patients underwent MRI and PMRS in one session. MRI and single voxel PMRS was performed on a 2 Tesla whole body system (Magnetom, Siemens) operating at field strength of 1.5 Tesla using a circularly polarized head coil.

$T_1$-weighted (TR/TE = 600/15) and PD, T2 weighted, (TR/TE = 2200/12/80) axial images with interslice gap of 0.5 mm, 192 × 256 matrix were obtained. Post contrast T1 weighted axial imaging was done after injecting 0.1 mmol/Kg body weight of Gadolinium-DTPA. In vivo PMRS was performed on a lesion with a size more than 8 cm³. A volume of interest (VOI) of 4–8 mL within the confines of the lesion was selected for in-vivo MR spectroscopy. In some cases, the rim of the cystic lesion was also included in the VOI. Volume-selective spectroscopy was performed using STEAM localizing sequence with TE = 20 msec, SE sequence with TE = 135 msec or both in all the cases. The total time taken for imaging and spectroscopy ranged between 50–60 min.

Ex-vivo MRS: High resolution NMR spectroscopy of the aspirate fluid of the cystic lesions was performed in 31 cases. A 300 MHz NMR system (Bruker, Switzerland) with a multinuclear probe head and Z gradient was used with the following parameters: flip angle 90, relaxation delay 3 sec, spectral width 3.142 KHz, transients 128 with presaturation of water. In addition, SE Fourier transformed spectra were also recorded with TE = 80 msec and relaxation delay of 2 s to see the phase reversal of the J coupled multiplets.

The diagnosis of different intracranial cystic lesions was based on the combination of resonances of different metabolites, described in the literature [3,8,13]. The criteria for the diagnosis in these cystic lesions were:

- **Abscesses**: Lipid/lactate at 1.3 ppm and amino acids at 0.9 ppm in all with/without additional resonances of succinate, acetate, alanine and glycine.

- **Glioma**: lipid and or lactate with choline

- **Arachnoid cyst**: Presence of small resonance of lactate with very low signal to noise spectrum

- **Hydatid cyst**: Very large succinate with lactate, alanine, acetate with absence of amino acids

3. Results

All the cystic lesions appeared as hyperintense on T2 weighted images and hypointense on T1 weighted images with a well-defined rim.

Spectral quality was interpretable in 50 cases. In one case of acoustic neuroma, data set was of poor quality and was not included for analysis. The pathology was correctly recognized with PMRS data in 46/50 patients. The results are summarized in Table 1.

In all cases of glioma (n = 20) except one, choline (3.2ppm) and lipid/lactate resonances (1.3ppm) were observed. In remaining one case (Fig. 1), only lactate resonance was observed and the PMRS data were interpreted as inconclusive. In this patient, the ex vivo PMRS also did not show any choline containing compound. Resonances from cytosolic amino acids (0.9ppm) and lactate (1.3ppm) were
observed in all 21 cases of abscesses. Alanine (1.5ppm) \( (n = 11) \), acetate (1.9ppm) \( (n = 10) \), and succinate (2.4ppm) \( (n = 7) \) were also observed in some abscesses. Three cases of hydatid cysts demonstrated resonances from lactate, acetate and succinate. In one patient with a hydatid cyst (Fig. 2) with perifocal edema, choline and resonances at 3.3 and 3.4 ppm were also observed at STEAM 20 msec. The resonances at 3.3 ppm disappeared while a resonance at 3.4 ppm showed a reduction in signal on SE 135 msec. The ex vivo PMRS confirmed the resonances as mannitol. It was found from the treatment chart that the patient was on i.v. mannitol for intracranial tension reduction until the time of surgery. In three cases of arachnoid cysts only small lactate resonance was observed. In one patient with arachnoid cyst, serum enzyme linked immuno-sorbent assay (ELISA) test for hydatid cyst was positive (Fig. 3), however the diagnosis of arachnoid cyst was made as only lactate resonance was observed on PMRS. In one case the PMRS data were interpreted as inconclusive (Fig. 4) wherein a single resonance at 2.04 ppm which was previously unassigned in cystic lesion was observed. The ex-vivo spectroscopy assigned the resonance as N-acetyl group of compound and the pathology proved to be a glioependymal cyst. In remaining two cases, resonances from choline and lipid/lactate were only observed and were interpreted as representing glioma. However, histopathology proved the cases benign: an infarction and a xanthogranuloma (Fig. 5).

In-vivo PMRS correctly identified the pathology in 46/50 (92%) cases in which good quality spectra were obtained. In two cases (4%) MR spectroscopy suggested glioma but
Fig. 2. Hydatid cyst. T2W axial image (a) showing a large, well defined, rounded cystic area with hypointense rim and perifocal edema in the right temporo-parietal region. Coronal T1W image (b) shows the cyst to be well defined with mass effect and midline shift. In vivo PMRS from the inset in (b) with STEAM 20 ms(c) shows the resonances of lactate (L) at 1.3ppm, alanine (AL) at 1.5ppm, succinate (S) at 2.4ppm, Choline (C) at 3.22ppm and mannitol (M) at 3.35 and 3.45ppm. SE 135 ms sequence (d) shows phase reversal of lactate and alanine. Note the reduction of the signal seen at 3.35 and 3.45ppm. Ex-vivo PMRS (e and f) confirms the resonances at 3.35 and 3.45ppm are due to mannitol. Patient was on i.v. mannitol infusion until the end of surgery.
histopathology confirmed it to be benign lesions. In the remaining two (4%) cases, the spectral data were inconclusive. Among these two cases one was benign and one malignant lesion.

4. Discussion

In vivo PMRS is a non-invasive technique to obtain the metabolite profile of normal and abnormal brain. It is widely used as a diagnostic tool in characterization of intracranial mass lesions [3,7,8,11,12,14,15]. Few retrospective studies have shown the utility of this technique in characterization of intracranial cystic lesions [3,8]. The characterization of intracranial cystic lesions in these studies was based on the presence of specific metabolite resonances or a specific combination of known metabolites [3,8,13].

Abscesses characteristically demonstrate resonances from cytosolic amino acids (leucine, isoleucine and valine at 0.9ppm), lactate (1.3ppm), alanine (1.5ppm) and acetate (1.92ppm) with absence of N-acetylaspartate (NAA), Choline (Cho) and Creatine (Cr), which can easily differentiate it from a neoplastic lesion [3,8,10–12]. Recently, it has been shown that the inversion of resonances in the chemical shift range 0.9–1.1ppm is indicative of an abscess with a specificity rate close to 100% [15]. In the present series, all the 21 cases of abscesses showed resonance at 0.9 ppm. In two cases, abscesses also demonstrated hemorrhage in the wall, simulating hemorrhagic cystic neoplasm. PMRS showed the characteristic resonance at 0.9ppm and the lesions were correctly diagnosed as abscesses, even in the presence of hemorrhage.

Neoplasm of the brain characteristically demonstrates increase in choline compounds and lactate with decrease in NAA [12,14,15]. Presence of choline signal in a cystic neoplasm of brain has been reported [3] although a recent series [8] has reported no such finding. In the present series, all except one case of cystic glioma demonstrated choline resonance on in vivo PMRS and were confirmed on ex-vivo PMRS. It is also likely that the voxel may contain the wall of the lesion that may be responsible for the presence of choline in the cystic lesions. In one patient with glioblastoma multiforme, even ex-vivo PMRS did not demonstrate choline signal suggesting that the nonvisualization of the choline resonance was simply not due the sensitivity constraints of the in-vivo PMRS. The non-demonstration of choline in this patient was probably due to resorption of free choline from the wall of cystic glioma.

Arachnoid cysts are difficult to be differentiated from a large hydatid cyst and a gliopendymal cyst based on conventional MR imaging features alone [12,16]. Arachnoid cysts in the present series demonstrated a very small lac doublet and absence of resonances from NAA, Cr, and Cho at STEAM 20 msec. In one patient with arachnoid cyst, serum ELISA test was positive for hydatid cyst. However, the PMRS did not show any other resonances apart from lactate and was correctly diagnosed as arachnoid cyst in
Fig. 4. Glioependymal cyst. T2W axial image (a) shows a large cystic mass in the frontal region in midline with mass effect. Post contrast T1W image (b) shows no obvious enhancement. In vivo PMRS with SE 135 ms shows a resonance (N) at 2.04ppm (c). Ex vivo PMRS (d & e) shows a singlet at 2.04ppm assigned as N-acetyl group of compound. Histopathology (f) from the wall of the cyst shows flat cuboidal epithelium resting on a layer of astroglial stroma.
prospective. Earlier reports of PMRS in arachnoid cysts have also shown similar results [3,8].

Glioependymal cysts are lined by a single layer of ciliated epithelium supported by a delicate connective tissue or glial membrane [16]. These cysts are found both in intraxial and extraxial locations have smooth unilocular appearance and are difficult to differentiate from other cystic lesion especially arachnoid cysts when located in the extraxial location [17]. In the present series, one case of glioependymal cyst was studied. The cyst was extra ventricular, intraxial mass located in frontal region with a well-defined rim. PMRS showed a single resonance at 2.04 ppm that was previously not observed in a cystic lesion. Since there was no experience of PMRS in glioependymal cysts (of the investigators) in house or in the literature, the study was regarded as inconclusive. Ex-vivo spectroscopy confirmed the resonance as N-acetyl group of compounds. The presence of glial tissue in the ependymal lining may be responsible for the N-acetyl group of compound in this cyst.

Three cases of intracranial hydatid cysts in the present series showed lactate, acetate and succinate as reported earlier in literature [13]. One patient with hydatid cyst and pericystic edema showed presence of choline and mannitol on PMRS. The laminated membranes of hydatid cysts are known to be composed of choline containing compounds [18]. Degeneration of the cyst secondary to host response may have resulted in release of free choline and its accumulation in the cyst fluid. In vitro, secondary hydatid cysts have been found to absorb water, electrolytes, mebendazole, cholesterol and certain proteins [19]. It appears that secondary to degeneration, mannitol may have accumulated in the cyst fluid because of increased permeability of the membranes. There is only one report of in vivo MRS of neurocysticercosis in literature [8], which also showed presence of lactate, alanine and succinate similar to hydatid cyst reported earlier [13].

In two benign conditions, infarction and xanthogranuloma, PMRS contributed to a false diagnosis of a malignant lesion. Xanthogranuloma is composed of dense accumulation of xanthoma cells, which are characterized by intracellular accumulation of lipid droplets, predominantly occurring within histiocytes or macrophages [20]. In case of infarct, the area of necrosis is surrounded by an inflammatory response comprising of macrophages and cellular infiltrates. The presence of choline resonance in both these conditions is probably due to inclusion of the wall of these lesions in VOI, which are comprised of dense accumulation of inflammatory cells. Krouwer et al. [21] have reported increase in choline resonance in six patients with non-neoplastic lesions with a dense inflammatory infiltrate. These results suggest that some lesions that prove to be inflammatory, demyelinating, or vascular in nature may demonstrate MR spectroscopic data suggestive of a neoplastic process.

Overall, PMRS accurately diagnosed the pathology of cystic lesions in 46/50 cases (92%). In two cases, PMRS did not contribute to the diagnosis and in two cases, falsely
diagnosed benign lesions as malignant. In conclusion, PMRS may compliment imaging in preoperatively diagnosing the cystic lesions of the brain and influence the overall management of these lesions.

References