IN VIVO PROTON MR SPECTROSCOPY IN DIAGNOSIS OF INTRACRANIAL CYSTIC LESIONS

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ABSTRACT

BACKGROUND

Magnetic resonance spectroscopy (MRS)¹ is a non-invasive diagnostic tool that has been used to detect biochemical environment and the concentration of the metabolites in various tissues, which correlate with physiologic and pathological processes.

Aims and Objectives: To determine the use of proton in vivo spectroscopy in diagnosing intracranial cystic lesions by providing additional metabolic information.

MATERIALS AND METHODS

This is a retrospective, descriptive, single institutional study with study population of 108 patients with intracranial cystic lesions. 1.5 Tesla Siemens system was used to perform MRI brain conventional sequences along with MR spectroscopy.

RESULTS

The pyogenic abscess showed amino acids, alanine, lactate, lipid and acetate peaks. Tuberculous abscess showed tall lipid with lactate peak and absent amino acids. Both neurocysticercosis and hydatid cysts showed succinate and lactate peaks with minimal acetate along with creatinine peak in NCC. Lactate was found in the benign non-neoplastic cysts studied including arachnoid cysts, porencephalic cysts, epidermoid cysts, craniopharyngioma and DNET. While choroid fissural cyst, choroid plexus cysts, ganglioglioma showed no specific metabolite. One colloid cyst studied showed increased NAA peak at 2.0 ppm. Among the malignant lesions, high-grade tumours showed lipid peak in addition to increased choline, lactate peaks, decreased creatinine and NAA peak. Metastatic lesions showed lipid and lactate peaks.

CONCLUSION

Magnetic resonance spectroscopy has a definitive complementary role in aiding the diagnosis of various intracranial cystic lesions.

KEY WORDS

Magnetic Resonance Spectroscopy, Pyogenic Abscess, Epidermoid, Neuroglial Cyst, Neurocysticercosis, Hydatid Cyst.

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BACKGROUND

Magnetic resonance spectroscopy (MRS)¹ is a non-invasive diagnostic tool that has been used to detect biochemical environment and the concentration of the metabolites in various tissues, which correlate with physiologic and pathological processes. Proton MRS is widely used for brain pathologies including tumours, strokes, seizure disorders, hypoxia, white matter diseases, stroke, multiple sclerosis, Alzheimer's disease, depression, etc. In Brain MR spectroscopy, spectrum² obtained shows the metabolites at specific ppm.

A variety of intracranial lesions including gliomas, metastases, craniopharyngiomas, abscesses, parasitic cysts (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 combined CT and MRI findings along with clinical information do not always characterise the lesions. MR spectroscopy may provide additional information in such cases.

Brain abscesses are localised pyogenic infection, which may mimic cystic tumours. Neurocysticercosis is intracranial parasitic infection by *Taenia solium*, which present as multiple lesions typically in the gray matter-white matter junction and deep sulci. Tuberculous abscess may be a focal manifestation, imaging features vary depending on the stage. Cerebral hydatid cysts (HC) are extremely rare, usually seen as unilocular cyst with ring enhancement which rarely calcifies.

Arachnoid cysts are CSF containing cysts lined by a layer of flattened mature arachnoid cells caused by maldevelopment of meninges. Choroid fissural cyst are shallow cysts noted in the fissure caused by maldevelopment of embryonic tela choroidea. Ependymal cysts are common benign cysts noted in the atrium of lateral ventricle. Porencephaly is congenital or acquired CSF filled cavities due to destructive process such as intraparenchymal haemorrhage, infection or surgery. The overall prevalence of porencephaly is 2.5% of congenital lesions in children. In MRI these are CSF dense lesion, which do not enhance or show diffusion restriction.

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Choroid plexus cysts are non-neoplastic, non-inflammatory cysts commonly located within the body of the plexus. These cystic lesions may be associated with aneuploidy, particularly trisomy 18. Neurenteric cysts are rare, benign, congenital endodermal lesions, more commonly located in the spine than in the brain (posterior fossa). Colloid cysts are endodermal derivative cysts, 50% of colloid cysts are hyperintense on T1-weighted images, hypointense on T2w images. Their rupture may lead to chemical meningitis.

Epidermoid cysts represent ectopic epidermal rest due to defect in neural tube closure during gastrulation. T2 bright lesions are partly suppressed by FLAIR, shows restricted diffusion which is diagnostic. DNET are low grade, cortical based mixed neuronal-glial tumour may be associated with cortical dysplasia. Ganglioglioma are well-differentiated neuroepithelial tumours with varying amounts of solid and cystic components. DNET and Ganglioglioma both are typically seen in temporal lobes presenting with seizures.

Here, we are assessing the usefulness of proton in vivo spectroscopy in providing additional information regarding various intracranial cystic lesions and differentiating them as infectious, congenital, benign and malignant lesions.

MATERIALS AND METHODS

This is a retrospective, descriptive, single institutional study conducted during the time period of December 2015 - December 2017. The selected population consists of 108 patients (56 males and 52 females).

Inclusion Criteria

Patients with intracranial cystic lesions, either incidentally or intentionally who came to our department for MRI brain study. Informed consent was obtained from the patients. In case of multiple lesions, lesion with largest cystic component was selected. Exclusion criteria- Lesions below the size of 5 mm were not taken up for study. Lesions very close to scalp were excluded due to contamination of value by scalp fat. Postoperative patients and post radiation were excluded from the study.

All participants were studied with a 1.5-T whole-body MR imager (Siemens Magnetom Aera, Germany) equipped with high-performance gradients using a manufacturer-supplied head coil. Routine sequences performed in all patients were sagittal T1-weighted (608/17/1 [TR/TE/excitations]), axial fast spin-echo T2-weighted (4450/98/1), coronal fast fluid-attenuated inversion recovery (FLAIR) (9000/90/1, TI 2.2 seconds), diffusion-weighted sequences and ADC. In general, all axial sequences used 5-mm thickness with intersection gap of 3 mm, a 305 × 448 matrix, the same imaging angle along the orbitomeatal line and a 200 mm field of view.

In all patients, proton MR spectroscopy was performed by using chemical shift imaging (CSI) sequence (2000/144 and 135/35 [TR/TE]), FOV 160 × 160 mm, sample volume size 27 × 27 × 20 mm; matrix size- 128 × 128 mm; section thickness- 5 mm. Multivoxel grid was placed in cyst or cystic component in case of necrotic lesions.

Care was taken not to include bony regions or haemorrhagic portions to exclude contamination of spectroscopic values. Typical acquisition time per spectral acquisition was 3 mts 10 s. The spectra were assessed independently by two experienced Radiologists. Concordance

between their findings was taken as a positive indicator that the spectrum was diagnostic for the pathology under consideration.

Following that based on the MR findings few patients were further subjected to IV contrast of gadolinium at a dose of 0.1 mmol/kg.

The diagnosis of brain abscess was confirmed by either microscopic examination of aspirated fluid or histopathological examination of surgically excised material. Histologic diagnosis was confirmed in all patients with epidermoid cysts, tumours and metastases from specimen obtained by surgical resection. The diagnosis of benign non-surgical cyst was confirmed by imaging follow-up after 6 months while neurocysticercosis, hydatid cysts and tuberculous abscesses by post-treatment follow-up after 6 months.

RESULTS

The abscesses (n= 5) showed amino acid (valine, leucine, isoleucine), lactate, lipid, acetate and alanine peaks. All 14 neurocysticercosis cases showed lactate, succinate and creatinine peaks. Of the 4 tuberculous abscesses all showed lipid peak, while only 2 of them showed lactate peak. The two hydatid cysts showed lipid, lactate, succinate and alanine peak.

Benign non-neoplastic cysts studied including 21 arachnoid cysts, 2 choroid fissural cyst and 2 choroid plexus showed non-specific signals. 12 porencephalic cysts studied showed mild lactate peaks and no other specific peak. 6 epidermoid cysts were studied- all showed mild lactate peak and no other specific peaks. Cystic component in 2 craniopharyngiomas showed lactate peak. Among 6 DNETS studied, two showed minimal lactate peaks and four others showed no specific signals. The 2 ganglioglioma studied minimal lactate with absent Cr, Choline peaks. One colloid cyst studied showed NAA peak at 2.0 ppm.

Among the 29 neoplastic lesions with necrotic components, 13 low-grade tumours all showed increased choline peak, decreased creatinine, NAA peak along with lactate peak. The 10 high-grade neoplasms including gliomas, medulloblastoma showed increased choline, decreased creatinine, NAA peaks along with lipid and lactate peaks. The 6 cystic metastatic lesions showed lipid, lactate peaks.

RESULTS

Age	Number of Patients
<5	7
5-10	15
11-20	19
21-30	11
31-40	13
41-50	17
51-60	8
61-70	12
>71	6

Table 1a. Age Distribution

		Frequency	Percent
	Pyogenic abscess	5	4.6
	TB abscess	4	3.7
	NCC	14	13.0
	Hydatid	2	1.9
	Arachnoid cyst	21	19.4
	Epidermoid	6	5.6
	Porencephalic	12	11.1
	CH plexus	2	1.9
	CH fissure	2	1.9
	Ganglioglioma	2	1.9
	DNET	6	5.6
	Craniopharyngioma	2	1.9
	Colloid	1	.9
	Low grade	13	12.0
	High grade	10	9.3
	Metastasis	6	5.6
	Total	108	100.0

Table 1b. Intracranial Cysts

CYST	Total No.	MRS Findings
Brain abscess	5	Lactate- 5 (100%) Branched chain Amino acids- 5 (100%) Alanine- 5 (100%) Acetate- 5 (100%) Succinate- 1 (20%)
Tuberculous abscess	4	Lipid- 4 (100%) Lactate- 2 (50%)
Neurocysticercosis	14	Lactate- 14 (100%) Succinate- 14 (100%) Choline- 14 (100%) Acetate- 3 (21.4%), NAA, Cr- 9 (64.3%)
Hydatid cyst	2	Lactate- 2 (100%), Alanine- 1 (50%) Succinate- 2 (100%), Acetate- 1 (50%)
Arachnoid cyst	21	Lactate- 16 (76.2%) No specific metabolites- 5
Porencephalic cyst	12	Lactate- 12 (100%)
Epidermoid cyst	6	Lactate- 6 (100%)
Choroid fissural cyst	2	No specific metabolites
Choroid plexus cyst	2	No specific metabolites
Ganglioglioma	2	No specific metabolites
DNET	6	Lactate- 2 (33.3%) No specific metabolites- 4
Craniopharyngioma	2	Lactate- 2 (100%)
Colloid cyst	1	NAA- 1 (100%)
Low-grade glioma	13	Increased Choline- 13 (100%) Reduced NAA, Creatinine- 13 (100%) Lactate- 13 (100%) Lipid- 2 (15.4%)
High-grade glioma	10	Increased Choline- 10 (100%) Reduced NAA, Creatinine- 10 (100%) Lactate- 10 (100%) Lipid- 10 (100%)
Metastasis	6	Lactate- 6 (100%), Lipid- 6 (100%) Increased Choline- 2 (33.3%)

Table 2. Spectral Patterns in various Cysts analysed in the Table Below

Metabolite Peak	Number	Lesions
Lactate	90 (83%)	Pyogenic abscess- 5 (100%) Tuberculous abscess- 2 (50%) Neurocysticercosis- 14 (100%) Hydatid cyst- 2 (100%) Arachnoid cyst- 16 (63.8%) Porencephalic cyst- 12 (100%) Epidermoid cyst- 6 (100%) DNET- 2 (33.3%) Low-grade glioma- 13 (100%) High-grade glioma- 10 (100%) Metastasis- 6 (100%)
Lipid	22 (20.4%)	Tuberculous abscess- 4 (100%) High-grade glioma- 10 (100%) Low-grade glioma- 2 (15.4%) Metastasis- 6 (100%)
Branched amino acids	5 (4.6%)	Pyogenic abscess- 5 (100%)
Succinate	17 (15.7%)	Pyogenic abscess- 1 (20%) Neurocysticercosis- 14 (100%) Hydatid cyst- 2 (100%)
Acetate	9 (8.3%)	Pyogenic abscess- 5 (100%) Neurocysticercosis- 3 (21.4%) Hydatid cyst- 1 (50%)
Choline	34 (31.5%)	Low-grade glioma- 13 (100%) High-grade glioma- 10 (100%) Metastasis- 2 (33.3%) NCC- 9 (64.3%)
Creatinine	14 (100%)	Neurocysticercosis- 14 (100%)
NAA	10 (9.3%)	Colloid cyst- 1 (100%) Neurocysticercosis (64.3%)
Alanine	13 (12%)	Pyogenic amino acids- 5 (100%) Neurocysticercosis- 7 (50%) Hydatid cyst- 1(50%)
Table 3. Analysis and Frequency of Metabolite Peaks found in various Cysts illustrated in Table Below		

DIAGNOSIS	Cho*	Cr	NAA	Suc	Acet	Alan	AA Val, Leu, Ileu	Gly	Lactate	Lipid		Lip	AA	Ur	BB
Brain abscess	-	-	-	+/-	+	+	+	-	++	-			↑		
Neurocysticercosis	+/-	+	+/-	++	+/-	+	-	-	+++	-					
Tuberculoma	-	-	-	-	-	-	-	-	+/-	+++	+				
Hydatid	-	-	-	+++	+/-	+/-	-	-	++	-					
Arachnoid cyst, Choroid plexus cyst, Choroid fissural cyst,	-	-	-	-	-	-	-	-	+/-	-					
Epidermoid	-	-	-	-	-	-	-	-	+	-				↑	
Porencephalic cyst	-	-	-	-	-	-	-	-	+	-		=-			↑↑
Colloid cyst	-	-	+	-	-	-	-	-	-	-		↑			
Ganglioglioma	-	-	-	-	-	-	-	-	+/-	-					
DNET	-	-	-	-	-	-	-	-	+/-	-					
Low-grade tumours	↑	↓	↓	-	-	-	-	-	+	-					
High-grade tumours	↑	↓	↓	-	-	-	-	-	+	+					
Metastasis	-	-	-	-	-	-	-	-	+	+					
DNET	=	=	=						+						
Neuroglial cysts	-	-	+					-							
Table 4. Based on the Findings and Analysis, the Spectral Pattern of the Intracranial Cystic Lesion Illustrated															

Cho- choline, Cr- creatinine, NAA- Acetylaspartate, Suc- succinate, Acet- Acetate, Ala- Alanine, AA- Aminoacids, Gly- Glycine

DISCUSSION

The MRI images and spectroscopic patterns of the 108 patients with intracranial cystic lesions included in our study were analysed and spectral peaks of specific metabolites were identified.

All the pyogenic abscesses in our study showed cytosolic branched chain amino acid, lactate, alanine, acetate and one of them showed succinate peak. The amino acids were explained by the presence of large amounts of neutrophils and pus, which on cell lysis secrete proteolytic enzymes, which result in the amino acid content. In the previous studies by RK Gupta² et al, pyogenic abscesses showed amino acid, lactate and alanine peaks. Similarly, in study by Luthra³ et al, pyogenic abscesses showed amino acid, lactate, lipid,

acetate and succinate peaks. While Hyun Chang⁴ et al, demonstrated amino acids, lactate, acetate and succinate peaks. Poptani⁵ et al demonstrated amino acids, lactate and acetate peaks in the pyogenic abscesses.

In study conducted by Lai PH⁶ et al, he differentiated aetiology of the pyogenic abscess by MR spectroscopy by absence of succinate peaks in aerobes and facultative aerobic bacteria. In case of aerobic metabolism, pyruvate from glycolysis may enter into the citric acid cycle and in facultative anaerobes in the presence of oxygen. Thus, although succinate is one of the intermediate metabolites of the citric acid cycle, succinate does not accumulate and gets transformed into the next intermediate form. This event results in the absence of succinate in these abscesses. Monika Garg⁷ et al, RK Gupta² et al also differentiated aerobes showed amino acids, lactate, lipid and alanine. Glycine from anaerobes showed acetate, minimal succinate peaks in addition to it.

In contrast to pyogenic abscesses, tubercular abscesses all showed tall lipid peak, while only 2 of them showed lactate peak. There was no evidence of amino acid, acetate, succinate, alanine peaks in contrast to pyogenic abscess. This is in accordance with previous studies conducted by Luthra⁴ et al, RK Gupta² et al. The presence of lipid peak can be explained by the lipid rich mycolic acid present in the tuberculous cell wall.

The neurocysticercosis cysts we studied all showed lactate, succinate and creatinine peaks, while 3 showed very minimal acetate peaks. 7 of them showed alanine peaks. In previous study by Rakesh Gupta² et al, neurocysticercosis cysts showed resonances in lactate, cytosolic amino acids, succinate, alanine with minimal acetate showing acetate: succinate ratio < 1 along with NAA, choline and creatinine. This ratio will be seen reversed in the case of pyogenic abscesses. In our study very minimal acetate was visible in 3 of them, while all the cysts showed significant succinate peaks. At 1.3 ppm, there was significant overlap between lactate, amino acids and alanine signals. The individual signals could not be differentiated clearly.

All neurocysticercosis cysts showed choline peak, while 9 of them showed NAA, creatinine peaks. The presence of NAA, choline and creatinine may be attributed to the solid parenchymal tissue contaminating the voxel. This contamination interfered with creatinine peak, which is the differentiating feature of large neurocysticercosis cyst from hydatid cyst. According to previous literature, Chang et al,⁴ Creatinine is seen in viable cysts because of the muscle fibres noted in the bladder and scolex of the cyst. The creatinine peak can be explained by diffusion of creatinine molecule into cysts from surrounding parenchyma and creatinine present in the bladder wall of cysticercosis.

The hydatid cysts we studied showed lactate and tall succinate peak. One of them showed alanine and minimal acetate. Creatinine and Cytosolic amino acids were not detectable and acetate: succinate ratio was less than 1. In a study by Monika⁷ et al and Garg⁸ et al stated that there was absence of creatinine in hydatid cyst in contrast to neurocysticercosis cyst. Further, they postulated that fertile hydatid cysts show presence of malate and fumarate. Gupta² et al demonstrated similar findings and he also demonstrated malate peak at 4.3 ppm and fumarate peak at 6.5 ppm in

fertile hydatid cysts. However, this finding was not demonstrated in our study.

According to Gupta K² et al, succinate and acetate can be found in both parasitic pyogenic abscesses, while in pyogenic abscesses showed acetate: succinate > 1 and in parasitic abscesses ratio is reversed. Succinate is more specific in parasite, preferentially in cestodes.

The epidermoid cysts we included in our study showed lactate peak. Poptani⁵ et al and Lal et al⁹ showed lactate peak consistent in all epidermoid cysts. In case of arachnoid cysts, Lai⁹ et al showed minimal lactate peak, while study conducted by Bhuyan⁹ et al and Chang et al⁴ showed no specific metabolite peak. In the 21 arachnoid cysts we studied, we found 16 cysts with lactate peaks, while others showed no specific metabolite peak in the spectroscopy. Similarly, few DNETS and 2 craniopharyngiomas showed minimal lactate peak in the cystic component of the lesion.

In study conducted by Hyun Chang⁴ et al, porencephalic cysts showed no specific metabolite peak. In our study, MR spectroscopy shows varying levels of lactate in the porencephalic cysts. Other non-specific cysts like choroid fissural cyst, choroid plexus and ganglioglioma showed no specific metabolite peak.

According to Hingwala¹⁰ and Periakaruppan¹¹ et al, a large peak was found at 2.0 ppm is found in the place of NAA in neurenteric cysts which was not present in other benign or developmental cysts. One neurenteric cyst we studied showed rise in NAA peak with no other significant finding.

Total of 29 neoplastic lesions are included in our study. Among them, 13 low-grade tumours showed reduced NAA, increased choline and lactate peaks with only 2 showing lipid peak. 10 cases of high-grade glioma showed increased choline peak, reduced NAA, Cr along with lipid and lactate component. In previous studies like Lai et al, Chang⁴ et al and Rakesh Gupta² et al presence of lactate/ lipids (1.33 ppm) and elevated choline (3.2 ppm) signals suggest malignant tumours. In most gliomas and metastases, only a lactate resonance was observed with a higher lactate peak along with lipids in high-grade gliomas and metastasis. In the 10 high-grade gliomas we studied including 2 medulloblastomas, all of them showed similar findings.

According to Poptani⁵ et al, cystic metastasis lesions showed lipid, lactate peaks with absence of NAA, Choline-Creatinine peaks. This is also observed in the 6 cystic metastatic lesions taken up in our study. 2 of the metastases also showed moderate increase in choline peak.

Lactate was the most common metabolite found in these cysts- 90 in 108 cysts included in our study rendering it as non-specific finding.

In concluding our study many of the cysts like arachnoid cyst, colloid cyst and porencephalic cyst can be diagnosed by imaging appearance alone. Similarly, the diagnosis of infective abscesses and epidermoid cysts can be clinched by diffusion restriction. This study provides additional information in differentiating pyogenic abscess from tuberculous abscess by presence of aminoacids in pyogenic abscess and tall lipid peak in tuberculous abscess. Further, it gives a clue about the aetiological agent of the pyogenic abscesses, either aerobic or anaerobic agent by the absence of succinate peak in aerobic bacteria. Another significant advantage of this study is differentiating large

neurocysticercosis cyst from other parasitic cysts like hydatid cyst by presence of creatinine. The presence of NAA peak at 2.02 ppm is an unique finding of neuroglial cyst and differentiates it from other benign cysts like arachnoid cyst and porencephalic cyst. The presence of lipid in addition to lactate, choline peak and reduced NAA and creatinine indicates an aggressive high-grade malignant lesion.

Limitation in our study includes small sample size of cyst including hydatid and neuroglial cyst. This needs to be studied further with a larger number of sample. Around nine of the neurocysticercosis cysts showed NAA, Choline, Creatinine peaks likely due to parenchymal tissue contamination. This creates confusion in the creatinine peak value, which is also the content in the neurocysticercosis cyst wall and needs to be confirmed further with tissue biopsy.

CONCLUSION

Magnetic resonance spectroscopy has a definitive complementary role in aiding the diagnosis of various intracranial cystic lesions.

Summary

108 patients with intracranial cysts were analysed in our study with in vivo proton multivoxel spectroscopy which provided additional metabolic information about them. Diagnosis was confirmed by histopathological examination and aspiration and culture in few cases. Lactate is found in most of the cysts, a non-specific finding. Abscesses can be further divided into aerobic, anaerobic and tuberculous by their specific peaks and treated with appropriate antibiotics. Hydatid and neurocysticercosis can be differentiated. Colloid cyst can be differentiated by presence of NAA peak from other benign cysts. High-grade tumours can be differentiated from low-grade tumours by presence of lipid and higher choline peak.

Abbreviations

MRS– Magnetic resonance spectroscopy, MRI– Magnetic resonance imaging, TE– Time to echo, TR– Time to repeat, Cho– Choline, Cr– Creatinine, NAA– N-Acetylaspartate.

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