

MAJOR PAPER

MR Spectroscopy to Distinguish between Supratentorial Intraventricular Subependymoma and Central Neurocytoma

Fumiaki Ueda^{1*}, Hiroyuki Aburano², Yasuji Ryu³, Yuichi Yoshie⁴,
Mitsutoshi Nakada⁵, Yutaka Hayashi⁵, Osamu Matsui¹, and Toshifumi Gabata²

Purpose: The purpose of this study was to discriminate supratentorial intraventricular subependymoma (SIS) from central neurocytoma (CNC) using magnetic resonance spectroscopy (MRS).

Methods: Single-voxel proton MRS using a 1.5T or 3T MR scanner from five SISs, five CNCs, and normal controls were evaluated. They were examined using a point-resolved spectroscopy. Automatically calculated ratios comparing choline (Cho), N-acetylaspartate (NAA), myoinositol (MI), and/or glycine (Gly) to creatine (Cr) were determined. Evaluation of Cr to unsuppressed water (USW) was also performed. Mann-Whitney *U* test was carried out to test the significance of differences in the metabolite ratios. Detectability of lactate (Lac) and alanine (Ala) was evaluated.

Results: Although a statistically significant difference ($P < 0.0001$) was observed in Cho/Cr among SIS, control spectra, and CNC, no statistical difference was noted between SIS and control spectra ($P = 0.11$). Statistically significant differences were observed in NAA/Cr between SIS and CNC ($P = 0.04$) or control spectra ($P < 0.0001$). A statistically significant difference was observed in MI and/or Gly to Cr between SIS and control spectra ($P = 0.03$), and CNC and control spectra ($P < 0.0006$). There were no statistical differences between SIS and CNC for MI and/or Gly to Cr ($P = 0.32$). Significant statistical differences were found between SIS and control spectra ($P < 0.0053$), control spectra and CNC ($P < 0.0016$), and SIS and CNC ($P < 0.0083$) for Cr to USW. Lac inverted doublets were confirmed in two SISs. Triplets of Lac and Ala were detected in four spectra of CNC.

Conclusion: The present study showed that MRS can be useful in discriminating SIS from CNC.

Keywords: *magnetic resonance spectroscopy, supratentorial intraventricular subependymoma, central neurocytoma*

Introduction

Supratentorial intraventricular subependymoma (SIS) and central neurocytoma (CNC) have affinities for the septum pellucidum or anterior portion of the lateral ventricle.¹ SIS is a histologically benign tumor that is often found incidentally at autopsy.¹ The typical imaging findings are homogeneous and non-enhancing lesions.² CNC has the appearance of a

heterogeneous, calcified, contrast-enhanced tumor. However, when a rather large SIS is discovered it may be heterogeneous, cystic, and calcified and may demonstrate slight enhancement making it difficult to distinguish from CNC.³ Even in cases with a suspected histologically benign tumor, large symptomatic masses should be treated surgically, and so pre-surgical differentiation between large SIS and CNC is not always necessary. However, if an asymptomatic tumor is discovered incidentally, clinicians should avoid unnecessary surgery and the follow-up strategy may change depending on the expected histology.

Our aim in this study was to assess the role of magnetic resonance spectroscopy (MRS) in the characterization of SIS and CNC.

Materials and Methods

Patients and normal control subjects

We performed MRS in pathologically confirmed five SISs and five CNCs. We retrospectively analyzed these MRS.

¹Department of Advanced Medical Imaging, Graduate School of Medical Science, Kanazawa University, 13-1 Takara-machi, Ishikawa 920-8641, Japan

²Department of Radiology, Kanazawa University, Ishikawa, Japan

³Department of Radiology, Tonami General Hospital, Toyama, Japan

⁴Department of Radiology, Toyama City Hospital, Toyama, Japan

⁵Department of Neurosurgery, Kanazawa University, Ishikawa, Japan

*Corresponding author, Phone: +81-76-265-2323, Fax: +81-76-234-4256, E-mail: fumiaki@staff.kanazawa-u.ac.jp

©2016 Japanese Society for Magnetic Resonance in Medicine

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives International License.

Received: February 3, 2015 | Accepted: October 28, 2015

As dictated by our institutional review board, consent was obtained from all patients. Resected specimens were evaluated by light microscopy. Hematoxylin and eosin staining and Ki-67 labeling indexes were evaluated in SIS. Hematoxylin and eosin staining and immunohistochemical examination for synaptophysin were performed in CNC. The Ki-67 labeling indexes of SIS were all <1%. According to the microscopic findings, a histological diagnosis of subependymoma corresponding to World Health Organization (WHO) grade I was made in all 5 cases. Strong staining for synaptophysin indicated a diagnosis of CNC in all 5 cases. Ten control MRSs were measured with a 1.5T scanner and other 10 control MRSs were measured using a 3T scanner. Clinical information and imaging findings obtained from both computed tomography (CT) and magnetic resonance imaging (MRI) are summarized in Table 1.

MRS

All the MRSs were performed using a 1.5T or 3T scanner (SIGNA; General Electric Healthcare, Milwaukee, Wisconsin, USA) with standard quadrature head coils. Automated MRS examination (proton brain examination; PROBE, GE acronym for automated MRS) was performed by volume-selective, inversion-recovery, water-suppressed, 90°-180°-180° point resolved spectroscopy with the following parameters: short echo time (TE), 1500/35/128 (repetition time [TR]/TE/number of excitations); long TE, 1500/144/128 obtained from voxels located within the tumor. Long TE MRS of each case was obtained from the same sampling voxel of short TE MRS. In one CNC, spectra were obtained from two different voxels both measured at short TE. Voxel size was chosen to maximize the partial volume of tumor in each single-volume study. In all cases, sampling voxels were localized to avoid contamination by normal brain tissue or cerebrospinal fluid in the lateral ventricle. The size of the sampling voxel varied from 10 × 10 × 10 mm³ to 30 × 30 × 30 mm³, depending on the dimensions of individual neoplasms.

Data analysis

Three neuroradiologists each with >10 years' experience (F.U., H.A., and Y.R.) analyzed both the imaging findings and the MR spectra of all the SIS and CNC cases and control patients. Evaluation was performed independently by two of the three neuroradiologists and when any discrepancies were noted, the evaluation was repeated with a third neuroradiologist until a consensus was reached. Normal MRS showed six major peak resonances at 1.33, 1.48, 2.02, 3.03, 3.22, and 3.56 ppm, which corresponded to lactate (Lac), alanine (Ala), N-acetylaspartate (NAA), creatine (Cr), choline (Cho), and myo-inositol (MI) and/or glycine (Gly), respectively. We present the normal MRS acquired from the occipital lobe of a 56-year-old female at TE = 35 msec, volume 8 cm³ (Fig. 1).

A doublet resonating at around 1.33 ppm, which inverted at TE = 144 ms, was defined as Lac. A triplet resonating at around 1.3–1.5 ppm was considered as Lac and Ala.

Automatic calculation of ratios comparing Cho, NAA, MI, and/or Gly to Cr were successfully performed by PROBE in all SIS and CNC cases. Because PROBE sequence provides the peak area values corresponding to unsuppressed water (USW) and that of Cr concentration using water peak values under the assumption that the water concentrations are constant, we further evaluated Cr to USW ratio. In one SIS case, MRS data were analyzed with a user-independent spectral fit program (LCModel; Stephen Provencher, Oakville Inc., Ontario, Canada).⁴ Twenty healthy volunteers (10 men and 10 women; mean age 31.4 ± 5.4 years) were included as a control group and MRS metabolic ratio was measured with 20 × 20 × 20 mm³ voxel size. MRS was measured from both the frontal and occipital lobes of each of the 10 cases. LCModel data were measured using a 3T machine and absolute concentrations of Cr concentration obtained from the LCModel from TE = 35 and 144 msec data were recorded.

Because of the heterogeneity of the MRS method, we used the spectroscopic ratio of short echo time acquired in a 1.5T machine for statistical analysis, and the average ratios of the metabolites were calculated from these results. We used JMP 10 statistical software program (SAS Institute Inc., Cary, NC, USA) for data analysis. Mann-Whitney *U* test was carried out to determine the significance of differences in metabolite ratios between SIS and CNC or SIS and control spectra. *P* < 0.05 was considered statistically significant. The average ratio of SIS and CNC was also calculated using 1.5T short TE MRS. The average ratio of control subjects was calculated using both frontal and occipital lobe MRS data. Detectability of Lac and Ala was evaluated by inversion of peaks at long echo time spectra and/or visual consideration of doublet or triplet.

Results

MR scanner magnetic strength, TE of MRS, and automatically calculated ratios of metabolites obtained from both PROBE and LCModel and detectability of Lac and Ala are summarized in Table 2. Absolute concentration of Cr from LCModel in SIS was 5.132 mmol/l measured at TE = 35 msec, and 6.791 mmol/l at TE = 135 msec.

Figs. 2–5 show the statistical differences for Cho/Cr, NAA/Cr, and MI and/or Gly to Cr, and Cr to USW between SIS and CNC or SIS and control spectra. A statistically significant difference was observed in Cho/Cr between SIS and CNC (*P* < 0.0001), and between CNC and control spectra (*P* < 0.0001). There were no statistical differences between SIS and control spectra for Cho/Cr (*P* = 0.11). The average ratio of Cho/Cr was 0.78 (±0.18) in SIS and 4.16 (±0.57) in CNC. Statistically significant differences were observed in NAA/Cr both between SIS and control spectra (*P* < 0.0001) or CNC (*P* = 0.04). The average ratio of NAA/Cr in SIS was 0.31 (±0.29) and 0.69 (±0.17) in CNC. A statistically significant difference was observed in MI and/or Gly to Cr between SIS and control spectra (*P* = 0.03),

Table 1. Patient information and imaging findings

Case	Age/ Sex	Symptom	Appearance of ventricles	Tumor Location	Size (cm)	Calcification	Signal intensity on T ₁ WI/T ₂ WI or FLAIR	Heterogeneity/ Cyst formation	Enhancement	Pathology
1	48/M	Coma	Obstruction of Foramen of Monro	rt LV	2.5 × 1.5	Absent	Hypointensity/ Hyperintensity	Homogeneous/ Absent	Absent	Subependymoma
2	41/M	Headache	Normal	rt LV	3 × 4	Present	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Subependymoma
3	65/M	Headache	Obstruction of Foramen of Monro	rt LV	1.5 × 2	Absent	Hypointensity/ Hyperintensity	Homogeneous/ Present	Absent	Subependymoma
4	27/F	Headache	Hydrocephalus	bil LV and third ventricle	10 × 7	Present	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Subependymoma
5	35/M	Nausea	Obstruction of Foramen of Monro	rt LV	2.5 × 1.5	Absent	Hypointensity/ Hyperintensity	Homogeneous/ Present	Absent	Subependymoma
6	18/M	Headache	Hydrocephalus	lt LV	5 × 4	Absent	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Neurocytoma
7	26/M	Vomiting	Hydrocephalus	lt LV	3 × 4	Present	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Neurocytoma
8	21/F	Headache	Hydrocephalus	lt LV	2.5 × 3	Present	Hypointensity/ Hyperintensity	Homogeneous/ Absent	Present	Neurocytoma
9	28/F	Headache	Hydrocephalus	bil LV and third ventricle	8 × 6	Present	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Neurocytoma
10	29/M	Headache	Hydrocephalus	lt LV	5 × 3	Present	Hypointensity/ Hyperintensity	Heterogeneous/ Present	Present	Neurocytoma

bil, bilateral; CNC, central neurocytoma; F, female; FLAIR, fluid attenuated inversion recovery; M, male; lt, left; LV, lateral ventricle; rt, right; T₁WI, T₁-weighted image; T₂WI, T₂-weighted image.

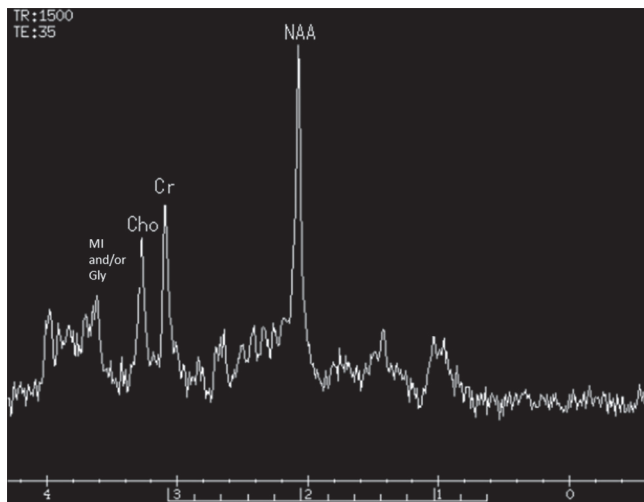


Fig 1. Automated proton brain examination (PROBE) originally acquired from a 56-year-old healthy volunteer female occipital lobe PROBE acquired at TE = 35 msec volume 8 cm³. Normal MRS shows right side up configuration of each myoinositol (MI) and/or glycine (Gly), choline (Cho), creatine (Cr), and N-acetylaspartate (NAA) peaks. Neither lactate nor alanine was detected. The concentration of Cho decreased from anterior brain to posterior, Cr decreased in white matter from anterior to posterior, and increased in gray matter from anterior to posterior. NAA increased from anterior to posterior in gray matter. Trend of MI and/or Gly is not apparent.

Table 2. MR spectroscopic data of supratentorial intraventricular subependymomas, central neurocytomas, and control groups

Case	Magnet (tesla)	TE (ms)	Cho to Cr	NAA to Cr	MI and/or Gly to Cr	Cr/Unsuppressed water	Lactate peak	Alanine peak
1	1.5	35	0.51	0.08	0.65	0.00025	Not detectable	Not detectable
2	1.5	35	0.84	0.27	0.70	0.00037	Not detectable	Not detectable
3	1.5	35	0.90	0.74	1.71	0.00032	Not detectable	Not detectable
4	1.5	35	0.86	0.15	0.77	0.00040	Detectable	Not detectable
		144	1.13	0.18	0.27	0.00037	Detectable	Not detectable
5	3	35	0.98 (0.3)	0.61 (0.48)	1.31 (2.13)	0.00026	Detectable (0.16)	Not detectable (0)
		144	1.15 (0.39)	0.41 (0.50)	0.68 (1.46)	0.00038	Detectable (0.50)	Not detectable (0)
6	1.5	35	4.29	0.59	1.71	0.00013	Detectable	Detectable
7	1.5	35	3.51	0.54	0.72	0.00022	Not detectable	Not detectable
8	1.5	35	4.88	0.74	1.07	0.00028	Detectable	Detectable
9	1.5	35	3.64	0.64	1.13	0.00015	Detectable	Detectable
		35	4.46	0.98	1.96	0.00014	Detectable	Detectable
10	3	35	3.21	0.48	1.28	0.00012	Not detectable	Not detectable
		144	5.23	0.88	0.94	0.00023	Not detectable	Not detectable
Control group	1.5	35	0.67 ± 0.07	1.59 ± 0.09	0.57 ± 0.08	0.00048 ± 0.00015 (NA)	Not detectable	Not detectable
		144	0.86 ± 0.07	1.72 ± 0.09	0.57 ± 0.11	0.00021 ± 0.00021 (NA)	Not detectable	Not detectable
Control group	3	35	0.76 ± 0.11 (0.35 ± 0.08)	1.71 ± 0.09 (1.98 ± 0.15)	0.54 ± 0.09 (0.67 ± 0.16)	0.00053 ± 0.00056 (NA)	Not detectable (0)	Not detectable (0)
		144	0.91 ± 0.07 (0.45 ± 0.05)	1.64 ± 0.11 (1.68 ± 0.11)	0.58 ± 0.03 (0.77 ± 0.11)	0.00037 ± 0.00041 (NA)	Not detectable (0)	Not detectable (0)

Data are metabolite peak area ratio measured by proton brain examination (PROBE). Data in parentheses are metabolite concentration rate obtained from LCModel analysis. Cho, choline; Cr, creatine; Gly, glycine; MI, mioinositol; NA, not available; NAA, N-acetyl aspartate.

and CNC and control spectra ($P < 0.0006$). There were no statistical difference between SIS and CNC in MI and/or Gly to Cr ($P = 0.32$). The average ratio of MI and/or Gly to Cr of SIS was 0.95 (± 0.50) and 1.32 (± 0.51) in CNC. Statistically significant differences were observed in Cr/USW both between SIS and control spectra ($P < 0.0053$) or CNC

($P < 0.0016$), and between CNC and SIS ($P < 0.0083$). The average ratio of Cr/USW in SIS was 0.000337 (± 0.000066) and 0.000484 (± 0.0006) in CNC. Lac inverted doublets were confirmed in two SIS (Figs. 6, 7). Triplets of Lac and Ala were detected in four spectra of CNC by visual inspection (Fig. 8).

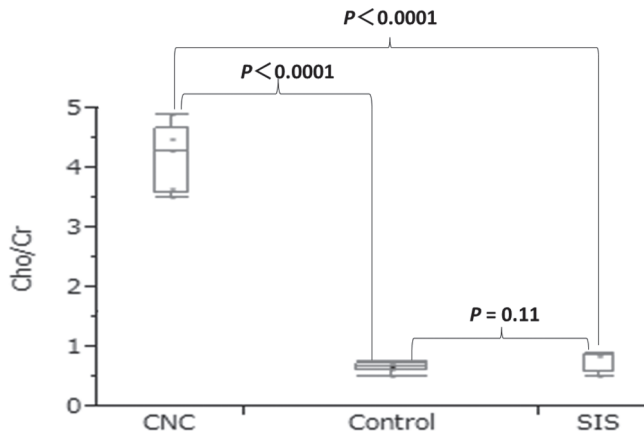


Fig 2. Metabolic ratio of choline (Cho) to creatine (Cr) obtained from supratentorial intraventricular subependymoma (SIS), central neurocytoma (CNC), and normal control.

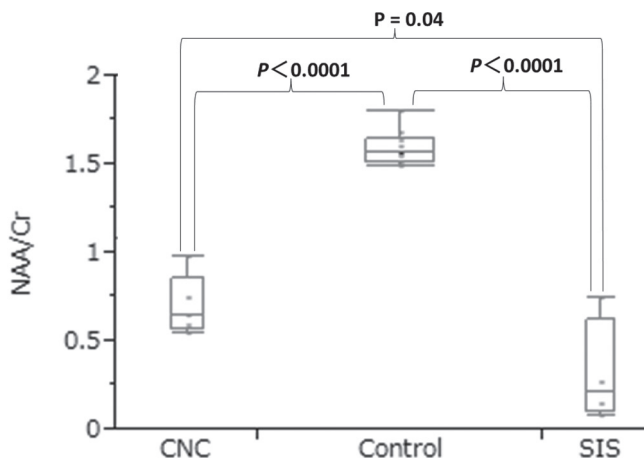


Fig 3. Metabolic ratio of N-acetylaspartate (NAA) to creatine (Cr) obtained from supratentorial intraventricular subependymoma (SIS), central neurocytoma (CNC), and normal control.

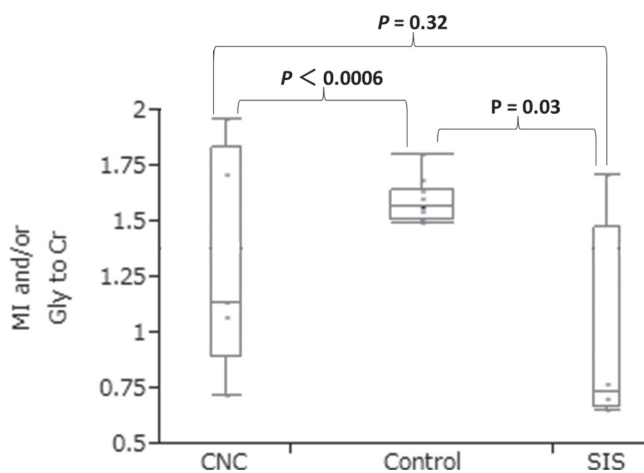


Fig 4. Metabolic ratio of myoinositol (MI) and/or glycine (Gly) to creatine (Cr) obtained from supratentorial intraventricular subependymoma (SIS), central neurocytoma (CNC), and normal control.

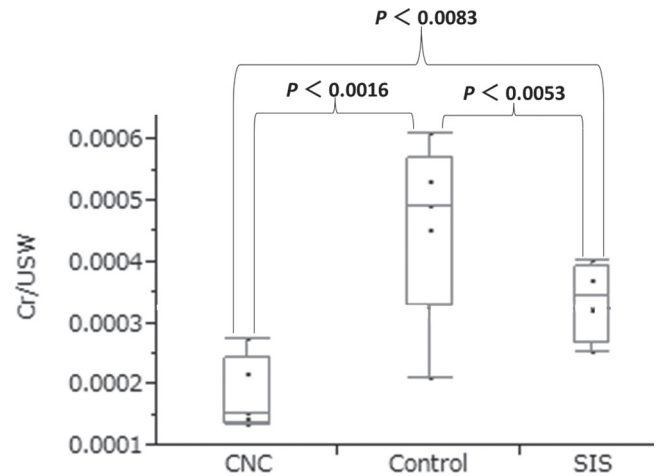


Fig 5. Metabolic ratio of creatine (Cr) to unsuppressed water (USW) obtained from supratentorial intraventricular subependymoma (SIS), central neurocytoma (CNC), and normal control.

Discussion

SIS is a benign, slow-growing tumor that occurs most commonly in middle-aged and elderly men.² Most symptomatic patients with SIS present with signs of cerebrospinal fluid obstruction.² SIS is often found incidentally at autopsy.¹ SIS is defined as a WHO grade I tumor, which means low proliferative potential and potential curability with surgical resection alone. The tumor location of SIS overlaps with that of CNC. CNC is defined as a WHO grade II tumor that can be derived from bipotential precursor cells of the periventricular germinal matrix capable of both neuronal and glial differentiation. CNC is thought to originate from rather neuronally committed stem cells.

Previous reports regarding SIS showed a Cho/Cr ratio slightly higher than 1.0 on *in vivo* long TE MRS.⁵ Ragel et al. reported one SIS showing a Cho/Cr ratio of 1.0 on *in vivo* long TE MRS, and mentioned that normal Cho/Cr is <1.2 in their institution.⁶ Although the tumor location was not mentioned, Tugnoli et al. studied the spectra of two subependymomas by *in vitro* high-resolution MRS, and reported a low Cho/Cr ratio (<1).⁷ The Cho/Cr is lower in short TE MRS than in long TE. Alteration of the Cho/Cr depending on TE can be explained by the longer T_2 relaxation time of Cho compared to that of Cr. The Cr concentration is high in mature astrocytes and oligodendrocytes and so the presence of Cr is considered as an astroglial rather than a neuronal marker. Neoplastic cells synthesize lower levels of Cr. The high Cho/Cr is thought to be a malignant feature, which increases in parallel with the histological grade. Although the histological grade of CNC is defined as WHO grade II, previous reports of *in vivo* MRS of CNC showed a prominent Cho peak with small Cr resonance.^{8,9} We tried to calculate Cr concentration using water peak values supplied by PROBE under the assumption that the intra voxel water concentrations would be constant, and revealed significant differences between SIS and CNC. That means that MRS of our SIS

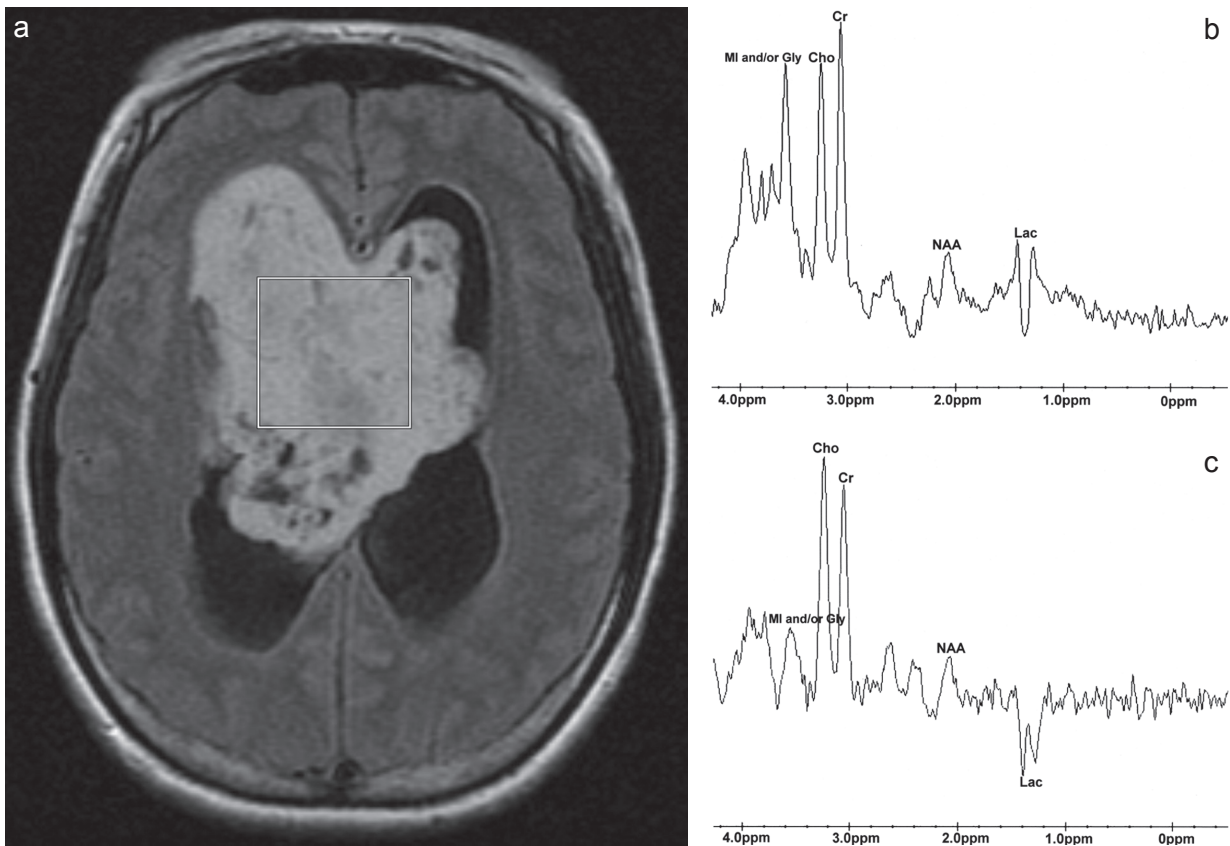


Fig 6. Case 4: Supratentorial intraventricular subependymoma (SIS). A 27-year-old woman with a history of progressive headache, urinary incontinence, memory disturbance, and unsteady gait. SIS originated from the septum pellucidum and extended becoming attached to the inner walls of the bilateral lateral ventricles. **(a)** Axial fluid attenuated inversion recovery image showing a large septum pellucidum tumor attached to the inner wall of both bilateral lateral ventricles. Voxel indicates the position of magnetic resonance (MR) spectroscopy. **(b)** MR spectroscopy obtained at echo time (TE) = 35 ms shows a prominent creatine (Cr) peak and a slightly smaller peak of choline (Cho). There is a large myoinositol (MI) and/or glycine (Gly) peak. Doublet peaks of lactate (Lac) and a small N-acetylaspartate peak are seen. **(c)** MR spectroscopy obtained at TE = 144 ms from the same voxel location indicates an inverted Lac doublet. The Cho peak is only slightly larger than the Cr peak. A resonance peak at 3.56 ppm suggesting MI and/or Gly with a predominantly MI component is observed.

showed a not so prominent Cho peak but the variation of Cr affects the ratios of all other metabolites. This is one of the marked differences from CNC, which is in agreement with previously reported MRS results.

The peak in the vicinity of 3.56 ppm is thought to be produced by MI and/or Gly. MI is an important osmolyte in neuroglial cells and accumulates intracellularly after cell shrinkage to maintain cell volume homeostasis. Various CNS lesions, such as hamartoma, subcortical, and subependymal tubers of tuberous sclerosis, subependymoma, ependymoma, neurinoma, and gliomatosis cerebri are associated with increased MI levels in the brain. The correlation between MI level and astrocytoma grade showed lower MI levels in anaplastic astrocytomas and glioblastoma multiforme compared with low-grade astrocytomas.¹⁰ High levels of MI in subependymoma tissue were reported in an *in vitro* study.⁷ The Gly singlet is overlapped by the larger signal of MI in short TE MRS. MI signals decay rapidly with increasing TE

because of the rapid J-coupling effect, and the singlet peak resonating at 3.56 ppm in long TE MRS represents mainly Gly. The current consensus is that histological upgrading of glioma results in an increase in Gly and decrease in MI.^{11,12} In CNC, the peak at 3.56 ppm was assigned to Gly based on the results of high-resolution studies of surgically excised tumor tissues.⁹ We performed both MRS at 35 and 144 msec in only one case of CNC with the peak reduction rate at long TE smaller than that of SIS. Although our SIS and CNC showed peaks of MI and/or Gly, two SIS cases, the large peak resonances at 3.56 ppm at short TE MRS became definitely smaller in long TE MRS but remained as a single peak. So we consider that both metabolites are present in SIS. Hattingen et al. investigated Gly and MI concentrations in low- and high-grade gliomas based on MRS with short and long echo times, and showed that the comparison of both short TE and long TE MRS should facilitate discrimination between MI and Gly.¹¹ Therefore, the peak is thought to be composed

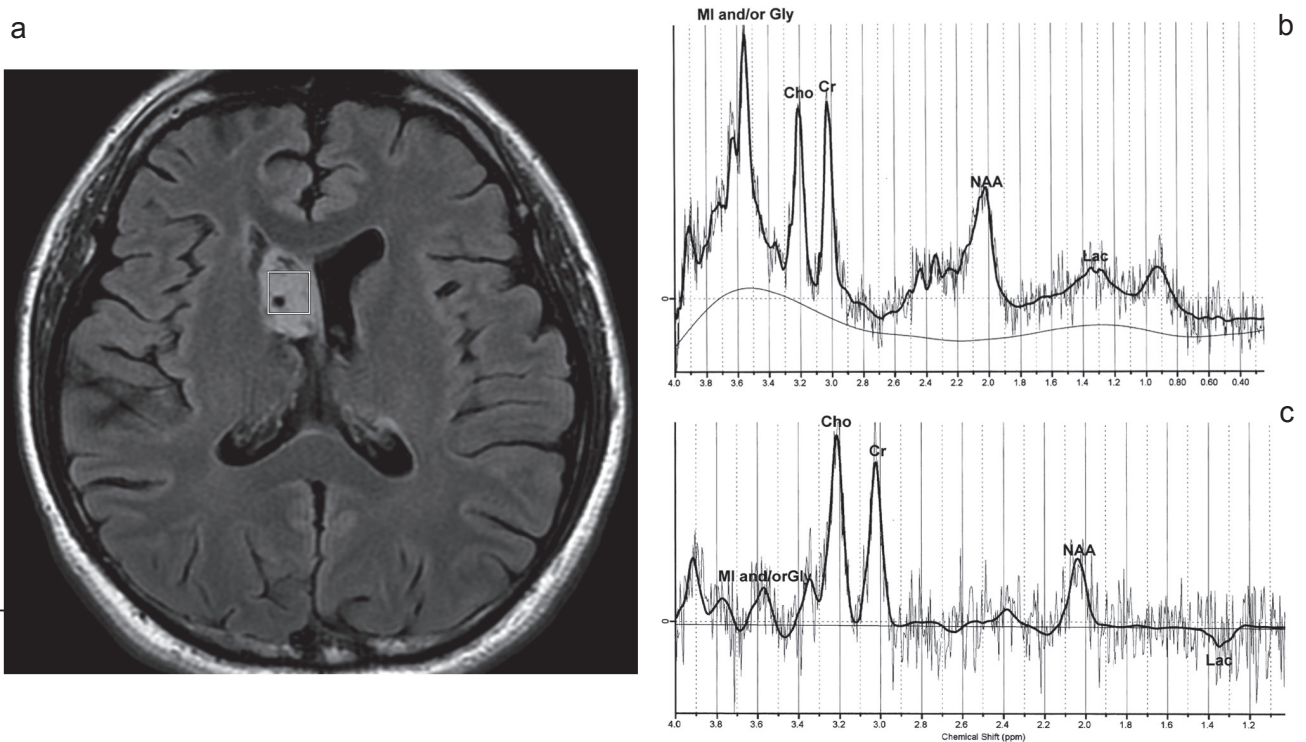


Fig 7. Case 5: Supratentorial intraventricular subependymoma (SIS). A 35-year-old man complaining of nausea. SIS originated from the right lateral ventricular wall near the foramen of Monro. (a) Axial fluid attenuated inversion recovery image showing a tumor in the right lateral ventricle near the foramen of Monro. The voxel shows the sampling position for MR spectroscopy. (b) MR spectroscopy at echo time (TE) = 35 ms analyzed automatically by LCModel shows a prominent creatine (Cr) peak and a choline (Cho) peak of equivalent size, large peak of myoinositol (MI) and/or glycine (Gly), and reduced N-acetylaspartate. A lactate (Lac) doublet is observed. (c) MR spectroscopy at TE = 144 ms analyzed automatically by LCModel spectra in the same voxel shows an inverted Lac peak. The Cho peak is only slightly larger than the Cr peak. A resonance peak at 3.56 ppm suggesting MI and/or Gly is observed.

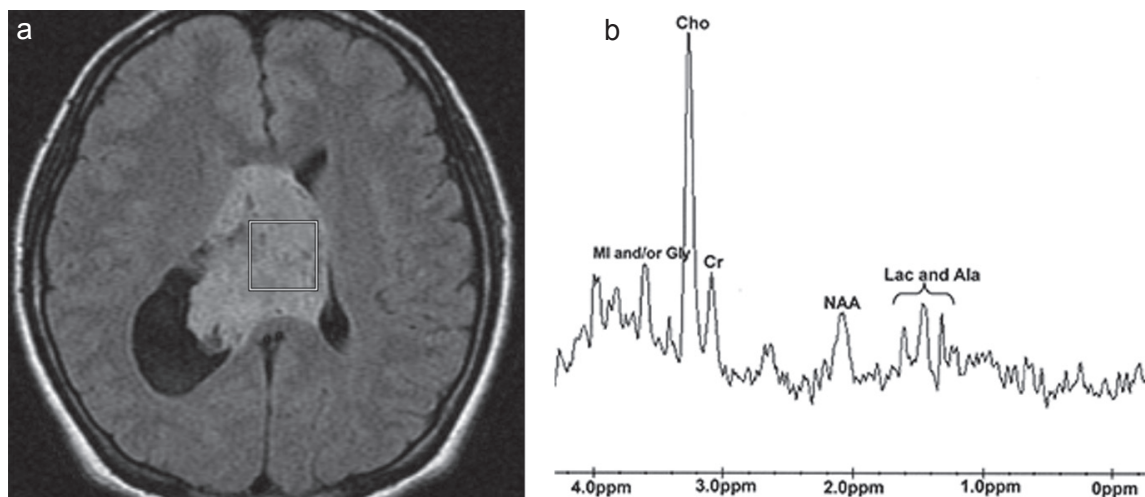


Fig 8. Case 9: Central neurocytoma (CNC). A 28-year-old woman with a history of chronic headache. CNC originated from the septum pellucidum and extended to the inner wall of the left lateral ventricle. (a) Axial fluid attenuated inversion recovery image showing a tumor originating from the septum pellucidum attached to both inner walls of the bilateral lateral ventricles. Voxel shows the sampling position for MR spectroscopy. (b) MR spectroscopy obtained at echo time of 35 ms showing a prominent peak of choline and a small N-acetylaspartate peak. The creatine (Cr) peak is small. The myoinositol and/or glycine peak is equivalent to the Cr peak. The triplet alanine and lactate peak is detectable at around 1.3–1.5 ppm.

partly of Gly. In addition, the reduction rate of this peak height was very high in the long TE study in SIS, and so the metabolite resonating at 3.56 ppm in SIS was thought to be composed of a massive amount of MI. The presence of a large MI peak might contribute to the differential diagnosis of SIS and CNC using short and long TE MRS.

Lac is a product of anaerobic tissue metabolism that resonates at around 1.33 ppm and consists of two distinct resonant peaks called a “doublet.” The Lac doublet is characterized by inversion at TE of 144 ms. Lac peaks have been reported in both SIS and CNC.^{5,8} An Ala peak, with or without a Lac peak, was reported in CNC in previous *in vivo* MRS studies.^{13,14} The Ala peak was reported in intraventricular tumors, not only in CNC and meningioma but also in other intraventricular tumors, such as ependymomas and primitive neuroectodermal tumors.¹⁵ The Ala peak at 1.48 ppm originally resonates as a doublet because of J-coupling modulation, but sometimes the spectra show a triplet because the peak overlaps with the Lac doublet in CNC.¹³ To our knowledge, there has been no reports of previous *in vivo* studies on the prominence of the Ala peak in SIS. In addition, moreover Tugnoli et al. reported no Ala peak in two subependymomas *in vitro*.⁷ Therefore, the positive Ala peak may negate SIS.

Both SIS and CNC showed small NAA peaks. When we determine the MRS measurement voxel, we always avoid normal tissue contamination, but when an especially small sampling volume is required like in the case 5, it is difficult to exclude contamination from normal CSF of the lateral ventricle. But we consider that contamination from the lateral ventricular wall would not occur, and that we think in CNC neuronal immaturity is responsible for the small NAA.⁸

There were some limitations in this study. First of all, although histologically benign, when rapid growth and clinical deterioration of subependymoma are identified, prompt surgical intervention is recommended,¹⁶ and so the clinical impact of pre-surgical differentiation of subependymoma from CNC may be controversial. This is a retrospective study, and the magnetic field strength and MRS scan protocol were not uniform throughout the study period. And with regard to the sampling voxel, an especially small sampling volume may be required like in case 3, making it difficult to exclude contamination from the normal CSF of lateral ventricle. But we consider that contamination from the lateral ventricular wall is unlikely to be occurred. Long TE study was performed in only two SIS and one CNC case, and so conclusive evidence of Ala deficiency was not obtained. Moreover long TE and 3T data of both tumors for statistical analysis had to be excluded to avoid data heterogeneity. The number of cases was small, and so the results must remain preliminary until more such cases can be studied.

Conclusion

MRS may be a useful noninvasive tool for discrimination of SIS from CNC. The present study adds data available to clinicians in planning treatment and/or follow-up.

References

1. Koeller KK, Sandberg GD. Armed Forces Institute of Pathology. From the archives of the AFIP. Cerebral intraventricular neoplasms: radiologic-pathologic correlation. *Radiographics* 2002; 22:1473–1505.
2. Chiechi MV, Smirniotopoulos JG, Jones RV. Intracranial subependymomas: CT and MR imaging features in 24 cases. *AJR Am J Roentgenol* 1995; 165:1245–1250.
3. Yamasaki T, Kikuchi H, Yamashita J, Goto Y, Yamabe. Subependymoma of the septum pellucidum radiologically indistinguishable from cavernous angioma—case report. *Neurol Med Chir (Tokyo)* 1989; 29:1020–1025.
4. Provencher SW. Automatic quantitation of localized *in vivo* ¹H spectra with LCModel. *NMR Biomed* 2001; 14:260–264.
5. Kawaguchi T, Kumabe T, Shimizu H, Watanabe M, Tominaga T. ²⁰¹Tl-SPECT and ¹H-MRS study of benign lateral ventricle tumors: differential diagnosis of subependymoma. *Neurosurg Rev* 2005; 28:96–103.
6. Ragel BT, Osborn AG, Whang K, et al. Subependymomas: an analysis of clinical and imaging features. *Neurosurgery* 2006; 58:881–890.
7. Tugnoli V, Tosi MR, Barbarella G, et al. Magnetic resonance spectroscopy study of low grade extra and intracerebral human neoplasms. *Oncol Rep* 1998; 5: 1199–1203.
8. Kim DG, Choe WJ, Chang KH, et al. *In vivo* proton magnetic resonance spectroscopy of central neurocytomas. *Neurosurgery* 2000; 46:329–334; discussion 333–334.
9. Jayasundar R, Shah T, Vaishya S, Singh VP, Sarkar C. *In vivo* and *in vitro* MR spectroscopic profile of central neurocytomas. *J Magn Reson Imaging* 2003; 17: 256–260.
10. Castillo M, Smith K, Kwock L. Correlation of myo-inositol levels and grading of cerebral astrocytomas. *AJNR Am J Neuroradiol* 2000; 21:1645–1649.
11. Hattingen E, Lanfermann H, Quick J, Franz K, Zanella FE, Pilatus U. ¹H MR spectroscopic imaging with short and long echo time to discriminate glycine in glial tumours. *MAGMA* 2009; 22:33–41.
12. Davies NP, Wilson M, Natarajan K, et al. Non-invasive detection of glycine as a biomarker of malignancy in childhood brain tumours using *in-vivo* ¹H MRS at 1.5 tesla confirmed by *ex-vivo* high-resolution magic-angle spinning NMR. *NMR Biomed* 2010; 23:80–87.
13. Shah T, Jayasundar R, Singh VP, Sarkar C. *In vivo* MRS study of intraventricular tumors. *J Magn Reson Imaging* 2011; 34:1053–1059.
14. Chuang MT, Lin WC, Tsai HY, Liu GC, Hu SW, Chiang IC. 3-T proton magnetic resonance spectroscopy of central neurocytoma: 3 case reports and review of the literature. *J Comput Assist Tomogr* 2005; 29:683–688.
15. Majós C, Aguilera C, Cos M, et al. *In vivo* proton magnetic resonance spectroscopy of intraventricular tumours of the brain. *Eur Radiol* 2009; 19:2049–2059.
16. Laxton AW, Shannon P, Nag S, Farb RI, Bernstein M. Rapid expansion of a previously asymptomatic subependymoma. Case report. *J Neurosurg* 2005; 103:1084–1087.