MAGNETIC RESONANCE SPECTROSCOPY (MRS) IN THE EVALUATION OF PEDIATRIC BRAIN TUMORS, PART II: CLINICAL ANALYSIS

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Over a 1-year period (1994-1995), 75 children with brain neoplasms were evaluated with a new automated magnetic resonance spectroscopy (MRS) software package called Proton Brain Exam/Single-Voxel (PROBE/SV) to determine the efficacy of this modality in children. The children ranged in age from newborn to 17 years and were comprised of 30 girls and 45 boys. The types of brain neoplasms consisted of 45 astrocytomas, 4 medulloblastomas, 2 ependymomas, 3 craniopharyngiomas, 3 germinomas, 1 pineoblastoma, 2 teratomas, 1 choroid plexus papilloma, 4 meningiomas, 2 astroblastomas, 3 rhabdoids, and 5 metastases from primary brain neoplasms. All children underwent magnetic resonance imaging (MRI) at the same setting as the MRS examination. The MRS examination was performed with the stimulated echo acquisition mode (STEAM) pulse sequence in all children, and occasionally the point resolved spectroscopy (PRESS) sequence also was used. Qualitative spectra were obtained in all children, and at times quantification data also were obtained.

We found that our spectra over the brain neoplasms were consistent with the MRS findings of brain neoplasms in the literature. There was markedly elevated choline with markedly decreased or absent N-acetylasparate and at times elevated lactate and lipid peaks. In children with meningiomas, there was also an elevated alanine peak. We found MRS to be extremely useful in 1) characterizing a brain mass as a neoplasm, 2) differentiating radiation necrosis and radiation-induced meningiomas from the recurrent primary tumor, 3) following treatment response of the primary neoplasm, 4) differentiating residual or recurrent primary neoplasm from postsurgical changes, and 5) identifying inactive neoplasms or neoplasms in remission. (*J Natl Med Assoc.* 1996;717-723.)

Key words • magnetic resonance spectroscopy (MRS) • children • brain tumors • brain neoplasms

Magnetic resonance spectroscopy (MRS) has been a research tool for more than 20 years, and a great deal of information has been accumulated in the research literature on the MRS spectrum for a wide variety of brain abnormalities.[1-6] Brain neoplasms demonstrate a MRS spectrum of markedly decreased or absent N-acetylasparate (NAA) with elevated choline (Cho) and at times elevated lactate (LAC) and lipid peaks.[3,7-10] With the use of MRS quantification, actual numerical values for the peaks of specific metabolites within the spectrum can be obtained.[11-14]

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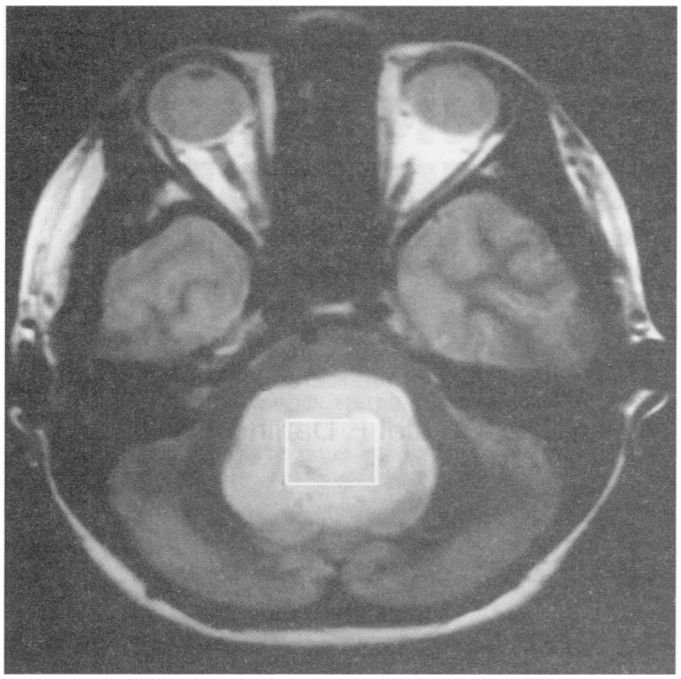

Figure 1A. MRI brain T2-weighted axial view. The voxel (white box) is placed over the center of a fourth ventricle grade 1 astrocytoma.

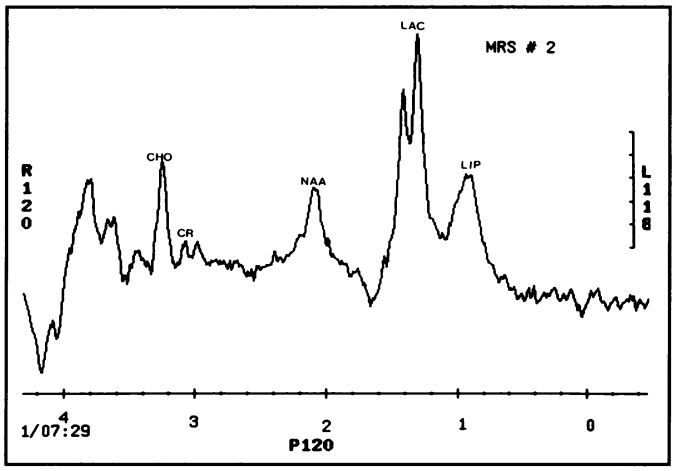

Figure 1B. MRS STEAM of the voxel in Figure 1A. The spectrum demonstrates elevated Cho, decreased NAA, and markedly elevated LAC and lipids.

Although a great deal of information on the MRS of brain neoplasms in adults has been obtained, there is relatively little information on the MRS of brain neoplasms in children.[15-18] Because we recently acquired the automated General Electric Medical Systems spectroscopy software package, Proton Brain Exam/Single Voxel (PROBE/SV), we decided to determine the efficacy of PROBE/SV in the evaluation of children with brain tumors.

MATERIALS AND METHODS

Over a 1-year period (from June 1994 to July 1995), 75 children with a confirmed histologic diagnosis of a brain neoplasm were evaluated. They ranged in age from 1 month to 17 years, and there were 30 girls and 45 boys. The types of brain neoplasms consisted of 45 astrocytomas, 4 medulloblastomas, 2 ependymomas, 3 craniopharyngiomas, 3 germinomas, 1 pineoblastoma, 2 teratomas, 1 choroid plexus papilloma, 4 meningiomas, 2 astroblastomas, 3 rhabdoids, and 5 metastases from primary brain neoplasms. All of the children were evaluated with the stimulated echo acquisition mode (STEAM) pulse sequence with a voxel ranging in size from 1 to 3 cm^3. At times, some of these children also had the point resolved spectroscopy (PRESS) pulse. Rarely, the PRESS pulse sequence was used to confirm the presence of lactate using teslas of 135 and 270 msec.

The MRS was performed after a routine MRI of the brain, which consisted of a sagittal T1-weighted, fast spin echo (FSE) axial T2-weighted, and axial T1-weighted images. After the MRS, a routine postgadolinium spoiled GRASS pulse sequence of the brain was obtained. Rarely, a postgadolinium MRS also was obtained. The FSE axial T2-weighted images were used to localize the area for placement of the MRS voxel. When quantification was performed from the MRS, which is called spectroscopy analysis/general electric (SA/GE), a Sun computer was used at an off-site location. When sedation was necessary the MRI examination, the sedation also was adequate for the MRS examination, and no additional sedation was required. All sedated children had their vital signs monitored throughout the MRI and MRS examinations.

The MRS examination consisted of the first spectrum with the voxel placed over the center of the brain tumor (Figure 1). If the tumor was large or necrotic in its center, a second spectrum was obtained over the periphery of the tumor (Figure 2). A spectrum was always obtained over normal white matter, usually at the left or right posteroparietal region. Each spectrum was acquired within 7 to 10 minutes. The total MRS study required 14 to 20 minutes if two spectra were obtained and 21 to 30 minutes if three spectra were obtained. If multiple neoplasms were present as in metastatic disease, then the voxels were placed over the larger lesions and additional spectra were obtained. In all children having follow-up MRS examinations, a routine brain MRI pre- and postcontrast was obtained.

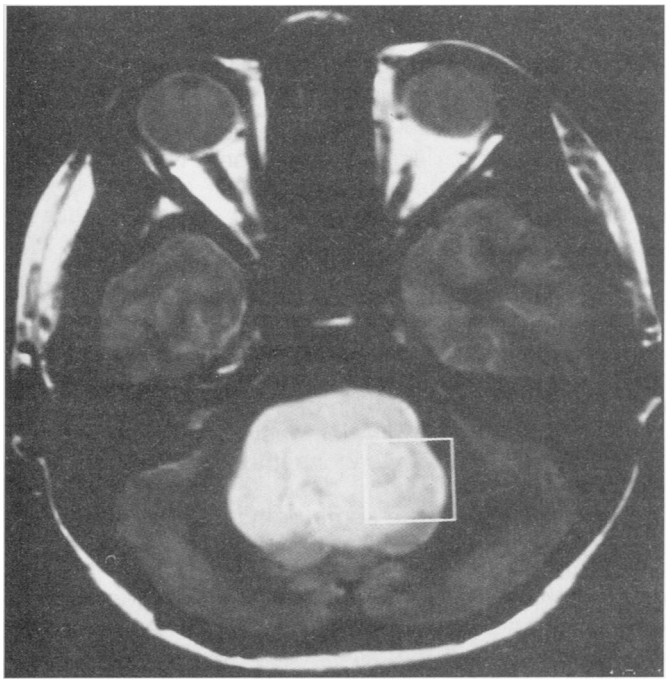

Figure 2A. MRI brain T2-weighted axial view. The voxel overlies the peripheral aspect of a fourth ventricle grade 1 astrocytoma.

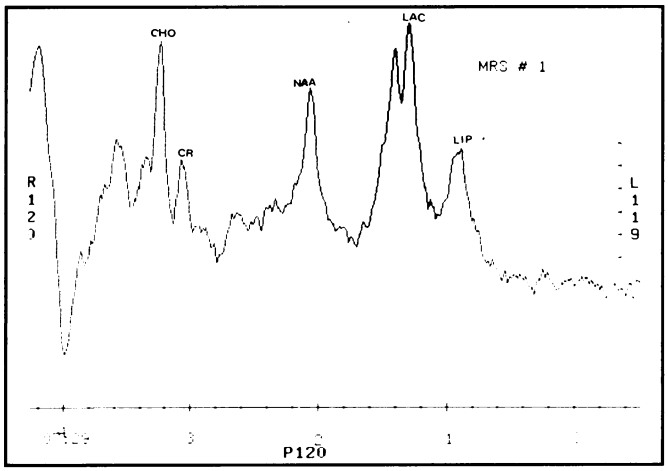

Figure 2B. MRS STEAM of the voxel in Figure 2A. The spectrum demonstrates elevated Cho, decreased NAA, and markedly elevated LAC and lipids.

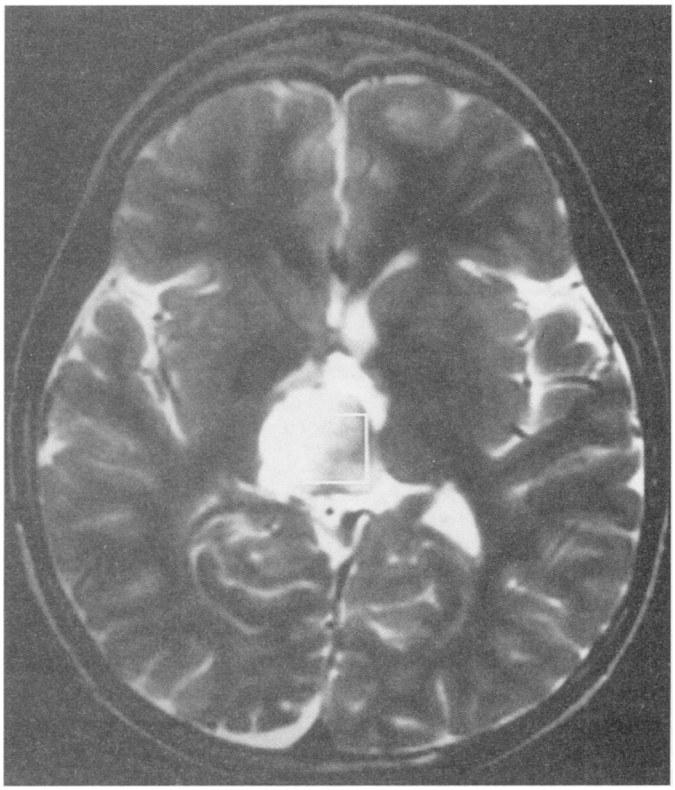

Figure 3A. MRI brain T2-weighted axial view. The voxel overlies a pineoblastoma.

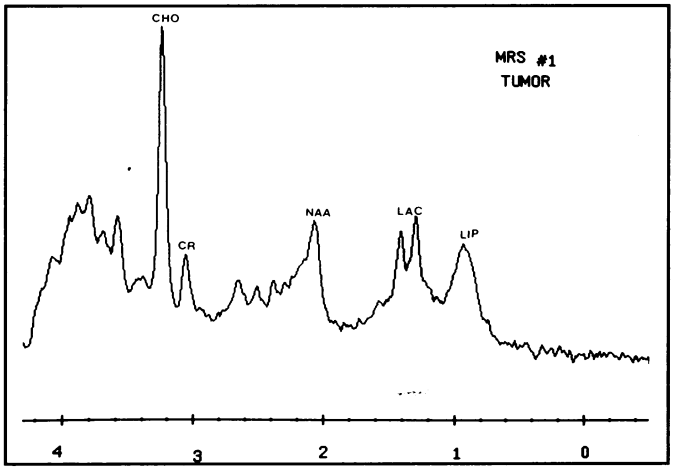

Figure 3B. MRS STEAM of the voxel in Figure 3A. The spectrum demonstrates markedly elevated Cho, decreased NAA, and elevated LAC and elevated lipids.

RESULTS AND DISCUSSION

The initial MRS spectra in all of our brain neoplasms whether benign (grade 1 astrocytoma) or malignant (grade 4 astrocytomas, medulloblastoma, anaplastic astrocytoma, etc) demonstrated elevated Cho and decreased NAA (Figures 1 and 2).[3] The Cr peak varied from decreased, increased, absent, or normal. There was no correlation with the Cr peaks and brain tumors.[3] However, in the more malignant brain neoplasms independent of cell types, markedly elevated Cho, absent or markedly decreased NAA, and elevated LAC and lipid peaks were noted (Figure 3). These findings correlated

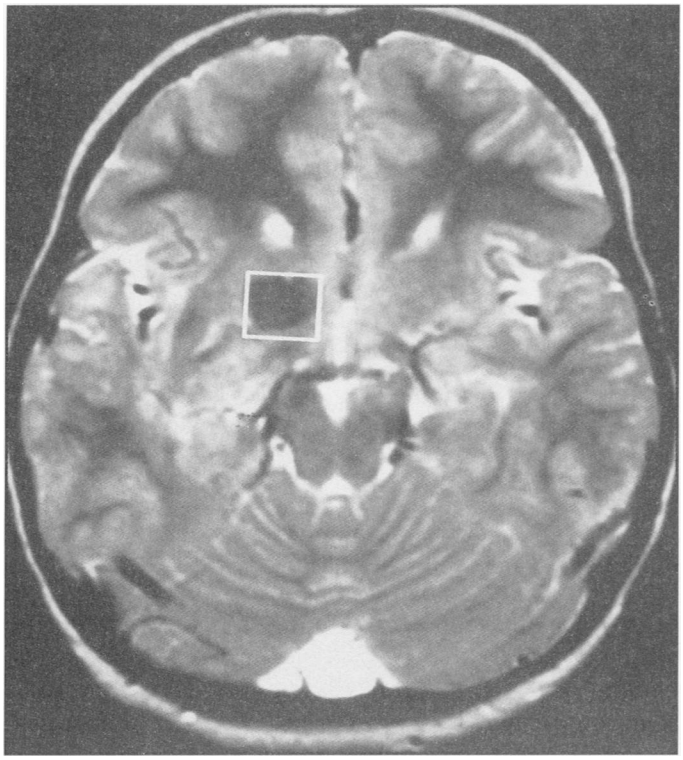

Figure 4A. MRI brain T2-weighted axial view. The voxel (1cm^3) overlies a calcified lesion on the right side of thalamus.

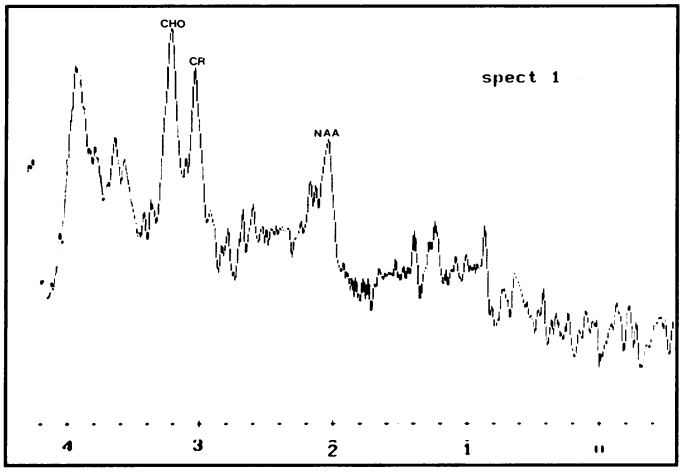

Figure 4B. MRS STEAM of the voxel in Figure 4A. The spectrum demonstrates elevated Cho and decreased NAA compatible with a neoplasm. The lesion was biopsied, and the histology was grade 1 astrocytoma.

with the MRS findings in the literature with respect to brain neoplasms.[3,6,9,10,16-18]

Absent or markedly decreased NAA in neoplasms is due to the lack of NAA in the cells from which neoplasms develop.[3] Gliomas develop from astrocytes, meningiomas from connective tissue (meninges), medulloblastomas from posterior medullary velum, and ependymoma from ependymal cells. Because NAA is present only in neurons and axons, neoplasms either replace or destroy the neurons and axons, thereby accounting for the decreasing NAA.[3] Choline is present in cell membranes.[3] In neoplasms, the choline is increased from proliferation of neoplastic cells and destruction of neurons and axons releasing the osmolyte, choline. Lactate elevation is related to the high rate of anaerobic glycolysis in neoplasms, which results in increased pyruvate and is converted to lactate.[3] Elevated LAC can be seen in any part of active neoplasms but is seen more commonly in the anoxic necrotic parts, which are usually the center or cystic component of these neoplasms. Elevated lipids, 0.9 to 1.3 ppm, can be seen in untreated neoplasms or in treatment-responsive necrosis.[3] Neoplasms that are invading or destroying myelinated white matter will demonstrate lipid peak elevation because of the breakdown of

TABLE. THE PRIMARY ROLE OF MAGNETIC RESONANCE SPECTROSCOPY (MRS) IN THE EVALUATION OF BRAIN NEOPLASMS

- Characterize a brain mass as a neoplasm
  - Elevated Cho, decreased or absent NAA, at times increased lactate and lipids
- Rule out radiation necrosis and radiation-induced meningioma from recurrence of the primary brain neoplasm
  - Radiation necrosis: all metabolites absent except LAC may be elevated
  - Meningioma: elevated Cho, decreased NAA, elevated alanine, at times elevated lactate and lipid
- Follow treatment response of neoplasms
  - Cho will demonstrate decreasing peaks on successive MRS examinations if tumor is responding to treatment
  - Cho will remain the same or increase on successive MR examinations if tumor is not responding to treatment
- Differentiate residual neoplasms from postsurgical changes and scar
  - Residual neoplasm: elevated Cho, decreased NAA, at times elevated LAC/lipid
  - Postsurgical changes: all metabolites are decreased and Cho is not elevated
- Identify inactive neoplasms or neoplasms in remission
  - Decreasing Cho, decreased NAA with stable MRS spectra over several months

Abbreviations: NAA=N-acetylasparate, Cho=choline, and LAC=lactate.

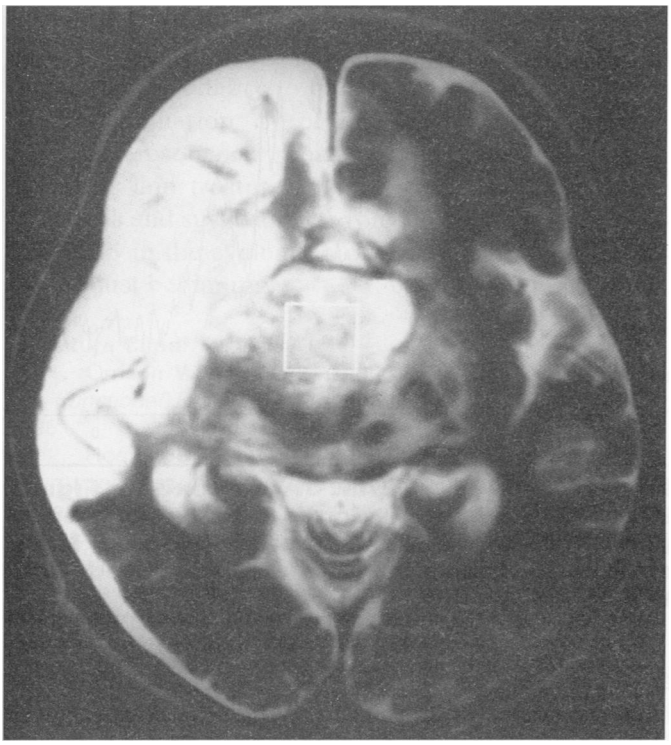

Figure 5A. MRI brain T2-weighted axial view. The voxel (1.5cm^3) overlies a suprasellar mass.

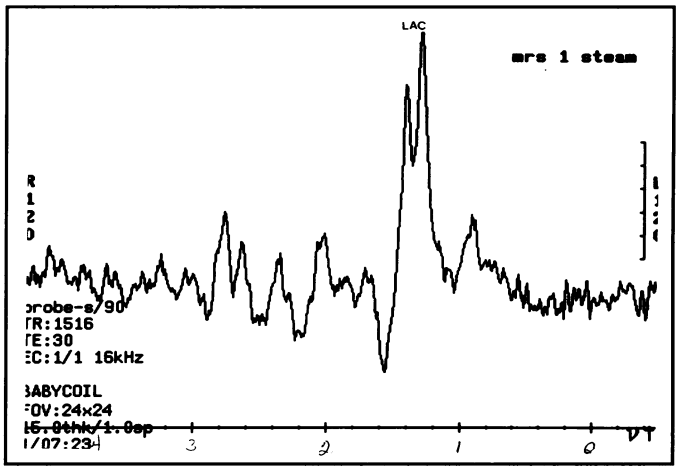

Figure 5B. MRS STEAM of the voxel in Figure 5A. The spectrum demonstrates only elevated LAC. All other peaks are artifactural (noise only), indicating radiation necrosis of the tumor.

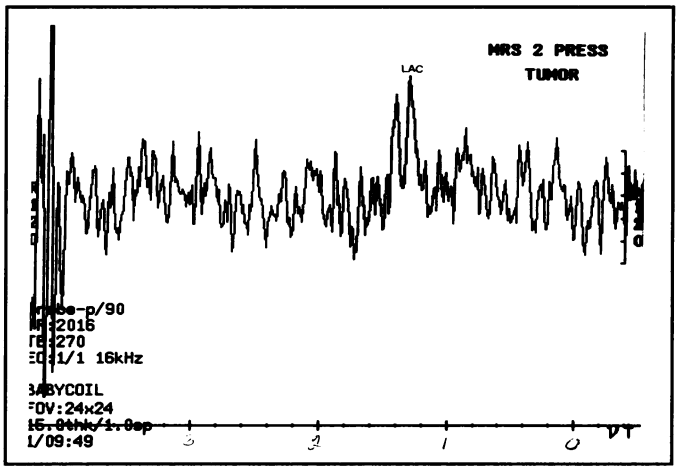

Figure 5C. MRS PRESS of the voxel in Figure 5A. The spectrum demonstrates radiation necrosis of the tumor with no evidence of metabolites except LAC.

myelin, which is a lipid.

The primary role of MRS in the evaluation of brain neoplasms is outlined below and summarized in the Table. It must be emphasized that MRS is used as an adjunct to MRI. All children must have a routine MRI consisting of at least three pulse sequences (T1-weighted, T2-weighted ,and T1-weighted postgadolinium) with their MRS examination.

- *Magnetic resonance spectroscopy has helped characterize a brain mass on the MRI as a neoplasm.* Although on a routine MRI brain study, the mass demonstrated may have all of the MRI findings of a neoplasm, the MRS can provide objective chemical evidence of tumor, and in children in whom the MRI findings are not unique to tumor, MRS can provide objective chemical evidence (Figure 4).
- *Magnetic resonance spectroscopy has been extremely useful in differentiating radiation necrosis from radiation-induced meningioma, radiation-induced sarcoma, or recurrent tumor.* Radiation necrosis on MRS shows absence or marked decrease in all metabolites except at times when there may be elevated lactate (Figure 5). Meningiomas, whether de novo or radiation induced, demonstrate an MRS spectrum with elevated Cho, decreased or absent NAA, elevated alanine, and at times elevated LAC and lipid more than 90% of the time (Figure 6). Alanine is considered an MRS marker for meningioma and typically is demonstrated as elevated in more than 90% of meningiomas (Figure 6). However, the MRS spectrum cannot differentiate between recurrent neoplasm and a radiation-induced sarcoma. Both demonstrate similar spectra with elevated Cho, decreased NAA, and at times elevated lactate and lipid.
- *Magnetic resonance spectroscopy has its greatest usefulness in following treatment response of brain neoplasms.* An extremely difficult problem in evaluating children with brain neoplasms is determining if the neo-

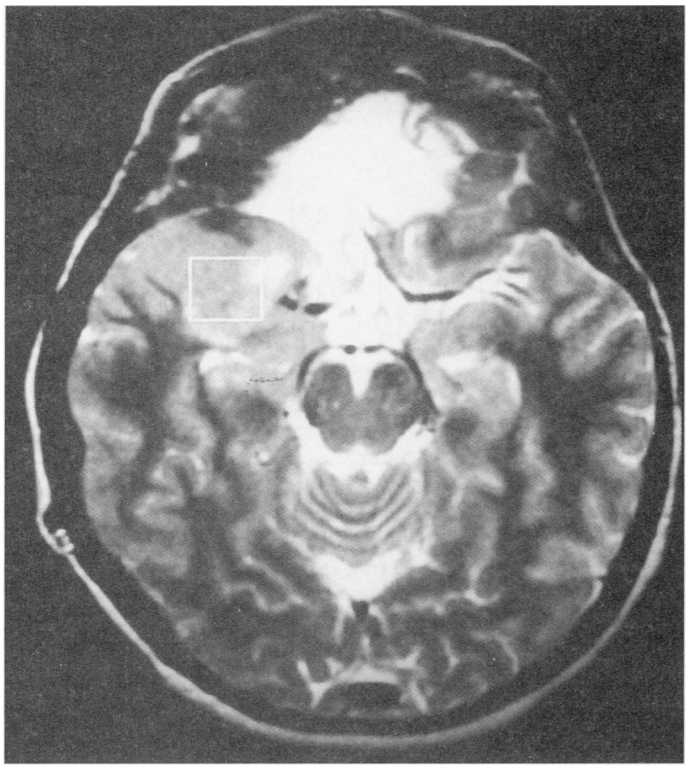

Figure 6A. MRI brain T2-weighted axial view. The voxel is over a right middle cranial fossa meningioma.

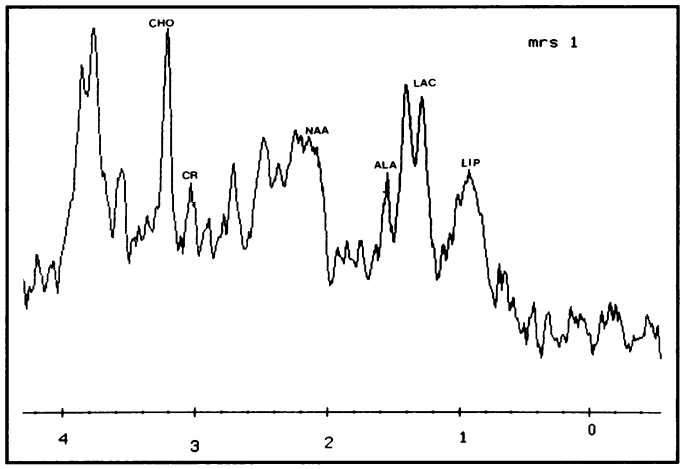

Figure 6B. MRS STEAM of the voxel in Figure 6A. The spectrum demonstrates a meningioma with elevated Cho, decreased NAA, elevated alanine (ALA), and elevated LAC and lipids.

plasm is responding to the chemotherapy or radiation therapy. Before clinical MRS, children had to be followed with routine MRI studies to determine if there was any change in the neoplasm size or MRI characteristics such as the development of necrosis. In the past, a change in size may have required a 3- to 12-month follow-up. In addition, in some neoplasms such as brain stem gliomas, an early change in the neoplasm after therapy such as an increase in size or the development of necrotic areas may represent either the tumor responding to treatment or the neoplasm out of control and not responding to treatment. Magnetic resonance spectroscopy can answer these two questions. If the neoplasm is responding to treatment, then the Cho will be decreasing. If the neoplasm is not responding to treatment, the Cho will be increasing. A baseline MRS always is obtained before treatment, and the changes in the Cho on the MRS after treatment will determine if the treatment is effective. A change in the Cho on a MRS can be seen as early as 2 weeks after beginning treatment.

- *Magnetic resonance spectroscopy can aid in differentiating residual tumor from postsurgical changes and scar formation.* After recent surgery for the removal of a brain neoplasm, it may be difficult to determine if we are dealing with postsurgical changes or residual tumor in the surgical bed. Even with early postsurgical changes, the adjacent tissue may demonstrate enhancement due to surgical manipulation and swelling. The tumor bed with postsurgical changes and without residual tumor will demonstrate decreased metabolites, including choline.
- *Magnetic resonance spectroscopy also allows for identification of inactive neoplasm.* Residual neoplasm may become inactive or go into remission. In these children, the choline decreases and then sequential MRS will demonstrate stable low levels of choline over several months, while the MRI shows no change in size, signal intensity, and enhancement.

Although MRS is extremely useful in evaluating children with brain neoplasm, in less than 5%, there may be overlapping spectra of brain neoplasms with some forms of multiple sclerosis, acquired immunodeficiency syndrome (AIDS) masses, and infarction.[3,19-21] Therefore, MRS studies (spectra and quantification data) must be interpreted in conjunction with the MRI examination and the clinical history and symptoms of the patient.

In more than 95% of our children, we were able to obtain diagnostic spectra on the first MRS examination. In the 5% of children in whom an initial MRS spectrum could not be obtained or the initial MRS spectrum was nondiagnostic, the reasons were recent hemorrhage within the neoplasm-producing magnetic susceptibility interference; air, fat, or bone adjacent to or within the voxel preventing shimming of the gradients; and inadequate water suppression.

CONCLUSION

Magnetic resonance spectroscopy is an excellent noninvasive modality to be used as an adjunct to MRI in the evaluation of children with brain tumors. Magnetic resonance spectroscopy allows for earlier diagnosis and treatment, which in turn will improve prognosis and survival. The role and usefulness of clinical MRS in the evaluation of brain pathology in children is just beginning.

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