Proton MR spectroscopy of brain tumors: The cause of wrong diagnosis and grading

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Learning objectives

To illustrate the cause of wrong diagnosis and grading in brain tumors on proton MR spectroscopy.

Background

Proton MR spectroscopy is very valuable in the diagnosis and grading of brain tumors. However, occasionally discrepant results to final diagnosis have occurred. In this exhibit, we will describe the cause of wrong diagnosis and grading in brain tumors. The examinations of 81 patients (68 tumors and 13 non-tumorous conditions), who performed brain MRS for 3 years at our hospital were retrospectively analyzed. Among them, wrongly diagnosed and graded cases were retrospectively reviewed.

Imaging findings OR Procedure details

<Results>
Among the total 81 patients, 1 patient with tumor (anaplastic oligoastrocytoma) was misdiagnosed as non-tumorous condition due to mislocated VOI. And 5 patients with non-tumorous conditions (1 infarction, 2 inflammations and 2 glioses) were misdiagnosed as tumors due to non-specific MRS patterns (slightly increased choline, decreased NAA, presence or not of lactate) and poor efforts to correlate with other imaging findings. Among the 68 patients with tumors, 2 patients with high grade tumors (1 anaplastic oligoastrocytoma and 1 glioblastoma) were misdiagnosed as low grade tumors, due to mislocated VOI and too small number of VOIs. And 13 patients with low grade tumors were misdiagnosed as high grade tumors, due to peculiar tumor histopathologies such as pilocytic astrocytomas (2), meningiomas (3), oligodendrogliomas (2) and non-specific MRS patterns (6).

<Discussion>

MRS ratios can be used to differentiate malignant and nonmalignant lesions from normal brain tissue. In general, high-grade astrocytoma have higher Cho/NAA and Cho/Cr ratios
compared with low-grade astrocytoma [1]. The use of the Cho/Cr ratio in the evaluation of neoplastic lesions has already been described in the literature as Cho is an important constituent of cell membranes with increases occurring when there are increases in cell synthesis and conversion to carcinogenic cells, while creatine is generally stable [2,3,4]. NAA is found in normal neurons and when altered, reductions occur both in tumors and in inflammatory lesions thereby indicating neuronal loss. The NAA/Cr ratio has discriminatory value when analyzed together with the Cho/Cr ratio increasing the specificity of the method [2,5]. MRS is an important useful method in the distinction of inflammatory brain lesions and high-degree tumors when the Cho/Cr ratio is greater than 1.97 and the NAA/Cr ratio is less than 1.12. And so this method is important in the planning of treatment and monitoring of the therapeutic efficiency [2].

In MRS studies evaluating gliomas, Meng Law et al. [6] reported that this method is useful in the differentiation of high- and low-grade glial tumors with the Cho/Cr ratio being higher than 1.56 in high-degree tumors. These data are sustained in studies by Fayed et al. [7] who demonstrated that a Cho/Cr ratio greater than 1.55 has a discriminatory power to differentiate between high- and low-grade glial tumors [7-9].

MRS has distinct limitations as a diagnostic tool. First and foremost, a sampling of only a single ROI is fraught with the problem that the voxel sampled may not represent the findings in other regions of the same lesion. This problem is analogous to a sampling error that can be seen with small stereotactic biopsies that sample only one region of a large mass lesion. This is less of a problem for smaller lesions, but can pose significant limitations in large lesions with variable regions of hypo-intensity and gadolinium enhancement on T1-weighted MRI scans. Second, a pattern of diminished NAA/Cr, elevated Cho/Cr and a lactate-lipid doublet may be seen in regions of tumor necrosis, infarction, or radiation necrosis. Many of these problems can be reduced by sampling from multiple regions or by the use of multi-voxel or spectroscopic imaging techniques. Sampling near bony structures or CSF pathways can reduce the signal quality and consequently the reliability of the spectra. Furthermore, individual and regional variations in metabolite concentrations in the brain, along with variations induced by previous or ongoing therapies, surgeries, or injuries can alter the spectral patterns. Each one of these factors must be taken into consideration when determining the value of a single voxel study as a clinical decision-making tool on a case-by-case basis [10].

Limitations of MRS at some histologies are also noted.

1) Meningioma

Many MRS studies consistently found that meningioma was characteristic of increased choline (Cho) [11-14]. Absolute Cho concentration, especially Cho concentration corrected according to intra-voxel cystic/necrotic parts, reflects cell density of meningioma [11].

2) Pilocytic astrocytoma
Kuesel at al. [15] reported a positive correlation between the lipid content and necrosis in high-grade astrocytomas, lipids have been recognized as potential indicators of malignancy. In addition, lactate is often identified within tumors, which may indicate necrosis and ischemia, or it may be the product of primary metabolic pathways involving lactate, such as anaerobic glycolysis.

Pilocytic astrocytomas, despite the benign histology of the tumor, which generally lacks necrosis, have high lactate concentrations from as yet unknown biochemical mechanisms. The presence of lactate within pilocytic tumors could be explained by several mechanisms, such as the abnormal number or dysfunction of mitochondria, which would interfere with the process of oxidative phosphorylation and electron transport, alterations in proportional oxygen delivery, and oxygen extraction or usage by tumor or anaerobic glycolysis by tumor cells [16].

Whether the Cho peak itself is actually elevated in pilocytic astrocytomas has also recently come into question. According to Lazareff et al [17], in a spectroscopic imaging study of pilocytic tumors, the Cho signal in the tumor itself may not be elevated relative to the Cho signal from contralateral normal tissue.

3) Oligodendroglioma

In the study of MRS of low-grade versus high-grade oligodendrogliomas, some low grade oligodendrogliomas showed elevated Cho/Cr values. There are two possible explanations for these findings. According to the WHO classification of tumors, low-grade oligodendroglioma and oligoastrocytoma are defined by the absence of endothelial proliferation and necrosis but can have moderately elevated cell density and therefore elevated choline levels [18]. An alternative explanation is that because these tumors were managed with only partial resection, areas of more cellular and anaplastic tumoral tissues may not have been submitted for histologic analysis [19].
Fig. 1: A 31-year-old man with tumor (anaplastic oligoastrocytoma, WHO grade III) was misdiagnosed as non-tumorous condition (necrosis) due to mislocated VOI at necrotic portion. A and B, Contrast enhancing mass lesion is noted in the right temporal lobe (A: FLAIR image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the mass shows marked elevation of lactate/lipid and decreased NAA without significant increase of choline, interpreting as necrosis.
**Fig. 2:** A 50-year-old male with non-tumorous condition (inflammation) was misdiagnosed as tumor due to non-specific MRS pattern. A and B, ill defined enhancing lesion is noted in the left temporal lobe with extensive brain edema (A: T2-weighted image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the mass shows slightly increased choline and lactate with decreased NAA, interpreting as tumor. Lactate inversion at long TE is needed for correct diagnosis.
Fig. 3: 5 years ago, tumor removal state of astrocytoma in the R parasagittal region. A 49-year-old female with non-tumorous condition (gliosis with focal calcification) was misdiagnosed as tumor due to non-specific MRS pattern. A and B, T2 high signal intensity mass is noted in the right rolandic region with suspicious subtle enhancement (A: T2-weighted image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the mass shows increased choline and lactate with decreased NAA, interpretating as residual or recurrent tumor. Choline level and choline/NAA ratio are needed for correct diagnosis.
Fig. 4: A 52-year-old male with high grade tumor (glioblastoma, WHO grade IV) was misdiagnosed as low grade tumor due to nonspecific MRS pattern and too small number of VOIs. A and B, T2 high signal intensity lesion is noted in the right hippocampus and anterior temporal lobe without definite contrast enhancement (A: T2-weighted image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the mass shows slightly increased choline, interpreting as low grade tumor.
Fig. 5: A 7-year-old female with low grade tumor (pilocytic astrocytoma, WHO grade I) was misdiagnosed as high grade tumor due to peculiar tumor histopathology of pilocytic astrocytoma. A, B and C, Lobulated T2 high signal intensity mass is noted in the suprasellar and intrasellar region with well enhancement and scattered microcystic portion (A and B: T2-weighted image, C: postcontrast T1-weighted image). D and E, MR spectroscopy of the mass shows markedly increased choline and lactate with decreased NAA, interpreting as high grade tumor.
Fig. 6: A 26-year-old male with low grade tumor (oligodendroglioma, WHO grade II) was misdiagnosed as high grade tumor due to peculiar tumor histopathology of oligodendroglioma. A, B and C, Focal cystic encephalomalacic change is noted in the right frontal lobe with peripheral enhancing portion (A: T2-weighted image, B: FLAIR image, C: postcontrast T1-weighted image). D and E, MR spectroscopy of the lesion shows markedly increased choline and lactate with decreased NAA, interpreting as high grade tumor.
Fig. 7: A 44-year-old female with low grade tumor (meningioma, WHO grade I) was misdiagnosed as high grade tumor due to nonspecific MRS pattern. A and B, T2 isosignal intensity lesion is noted in the L cerebellar region. This lesion show well enhancement with internal cystic portion (A: T2-weighted image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the lesion shows markedly increased choline and lactate with decreased NAA, interpreting as high grade tumor.
**Fig. 8:** A 48-year-old male with low grade tumor (fibrillary astrocytoma, WHO grade II) was misdiagnosed as high grade tumor due to nonspecific MRS pattern. A and B, Subtle enhancing mass with cystic portion is noted in the right rolandic region (A: T2-weighted image, B: postcontrast T1-weighted image). C and D, MR spectroscopy of the lesion shows increased choline and lactate, interpreting as high grade tumor.
Conclusion

Knowledge of the cause of wrong diagnosis and grading in brain tumors on proton MR spectroscopy would be helpful for clinical diagnosis and grading of brain tumors.

Personal Information

References


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