The Usefulness of Proton MRS in Monitoring Ketogenic Diet Therapy in Mitochondrial Encephalopathy

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Introduction

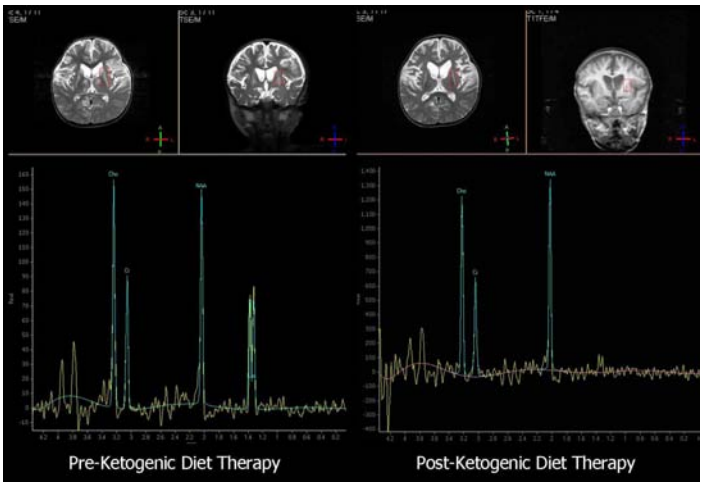
Mitochondrial encephalopathy (ME) is a heterogeneous group of clinical syndromes associated with abnormalities of mitochondrial energy metabolism. The impaired energy production results from the overall dysfunction of mitochondrial respiratory chain, composed of five enzymatic complexes embedded in the inner mitochondrial membrane. There is no specific treatment for ME and only conservative care is performed. One of the challenging trials is ketogenic diet therapy, and some favorable results are reported. The purpose of this study is to evaluate the changes of metabolic spectrum in ME by use of MR spectroscopy and establish the way of monitoring the course of disease by neuroimaging studies.

Methods

Six patients (M:F=3:3, 1 ~ 9 years, Mean age = 3.3 years) diagnosed to have ME by muscle biopsy were prospectively studied by MR spectroscopy before and 6 ~ 8 months after ketogenic diet therapy. Four patients were diagnosed to enzyme I deficiency, the other two were enzyme II and IV deficiency. Enzyme IV deficiency patient was confirmed as Leigh disease. Localized proton MR spectroscopy was performed with Philips Achieva 3.0T scanner by using a single-voxel point-resolved spectroscopy sequence. A 2 x 2 x 2 cm voxels were placed in the left basal ganglia and frontal white matter. Two acquisitions were obtained by using the same voxel location with TE = 40 and TE = 288, keeping all other parameters constant (with TR = 2000, and 128 averaged scans). The spectroscopic data were processed on an independent Philips (Best, Netherland) workstation by using dedicated software. The existence and changes of lactate peak, choline/Cr and NAA/Cr peak were analyzed. Along with the interpretation of MRS findings, morphologic findings on conventional T2 weighted imaging were also performed.

Results

All patients showed abnormal findings on T2WI. Diffuse cortical atrophy and ventriculomegaly were universal findings of ME. Signal increase and atrophy of deep gray nuclei is more apparent in Leigh disease although 2 of enzyme I deficiency also showed such findings. During ketogenic diet therapy, no remarkable interval change was seen on T2WI, i.e. progression of atrophy was not observed. However, all patients showed marked symptom improvement, decreased attack of seizure, improved neurologic function. On pre-treatment MRS, 5 patients showed lactate peak. Complete resolution of lactate was seen in two patients and the rest of them showed marked reduction of lactate fraction (Figure). Four of them showed serial NAA/Cr increase and Cho/Cr decrease. The patient who did not show lactate on pre-treatment MRS also showed serial increase of NAA/Cr and decrease of Cho/Cr.



Conclusion

MRS is a useful indicator for the efficacy of ketogenic diet therapy in ME although conventional MR imaging cannot depict morphologic changes. Decreased lactate peak and recovery of NAA fraction are well correlated with the improvement of clinical symptoms.

References

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