Measurement of the apparent diffusion coefficient in paediatric mitochondrial encephalopathy cases and a comparison of parenchymal changes associated with the disease using follow-up diffusion coefficient measurements☆

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ABSTRACT

Objectives: To reveal the contribution of MRI and diffusion-weighted imaging (DWI) to the diagnosis of mitochondrial encephalopathy (ME) and to evaluate the parenchymal changes associated with this disease in the involved parenchymal areas using the apparent diffusion coefficient (ADC) parameter.

Methods: Ten patients who had undergone MRI and DWI analysis with a pre-diagnosis of neurometabolic disease, and who were subsequently diagnosed with ME in laboratory and/or genetic studies, were included in our study. ADC values were compared with a control group composed of 20 patients of similar age with normal brains. Evaluations involved measurements made in 20 different areas determined on the ADC map. The dominance or contribution of ADC coefficient measurements to the conventional sequences was compared with the controls.

Results: In the first examination, an increase in both diffusion and ADC values was detected in six cases and diffusion restriction and a decrease in ADC values in three patients. While an increase in both diffusion and ADC values was demonstrated in four cases, there was diffusion restriction and a decrease in ADC values in three cases in the control examinations.

Conclusions: DWI provides information that complements conventional MRI sequences in the diagnosis of ME.

1. Introduction

MRI has limited specificity in detecting brain lesions associated with childhood metabolic diseases [1,2]. Diffusion weighted imaging (DWI) provides unique information regarding tissue activity which cannot be obtained from conventional MRI sequences [2]. In our study, we aimed to evaluate the contribution of MRI and DWI carried out in our department to the diagnosis of 10 paediatric patients with mitochondrial encephalopathy (ME), and to investigate the parenchymal changes associated with this disease in the involved parenchymal areas using the apparent diffusion coefficient (ADC) parameter. With this purpose in mind, ADC values were compared with control groups; evaluations involved measurements made in 20 different areas determined on the ADC map in the patient group, and the dominance or contribution of ADC coefficient measurement in relation to the conventional sequences were compared with the control group.

2. Methods

Approval for this study was obtained from our ethical review board. Ten patients who had undergone MRI and DWI analysis with a pre-diagnosis of neurometabolic disease in our MRI unit, and who were subsequently diagnosed with ME in laboratory and/or genetic studies in the clinic were included in our study. Findings that established this diagnosis in patients were high lactate levels in blood or cerebrospinal fluid, radiological studies or postmortem examination of basal ganglia, or the involvement of the brainstem; diagnosis can additionally be established by means of muscle biopsy in some patients.

Table 1
Age distribution, periods for obtaining control examinations, significant neurological findings, genders of the patients and the diagnosis methods.

Case no.	Age	Period of examination	Gender	Onset finding	Lactic acidosis (serum-CSF)	Muscle biopsy	Additional neurological findings	Result
1	2 years	4 years	F	Progressive dystonia	Available	Normal	Ophthalmoplegia, mental retardation, ataxia	Dystonia, mental retardation
2	2 months	4 years	F	Progressive dystonia-seizures	Available	Normal	Moderate mental retardation	Dystonia, mental retardation
3	2 years	N/A	F	Acute metabolic encephalopathy	Available	Normal	Moderate mental retardation	Ex due to Metabolic decompensated attack
4	3 years	1 year	M	Psychomotor retardation	Available	Normal	Ptosis, sensorineural hearing loss, microcephaly	Progressive psychomotor retardation
5	4 years	1 year	M	Psychomotor retardation	Available	Normal	Ptosis, sensorineural hearing loss, microcephaly	Progressive psychomotor retardation
6	1 month	N/A	M	Acute metabolic encephalopathy	Available	Abnormal	Moderate mental retardation	Ex due to metabolic decompensated attack
7	3.5 years	N/A	M	Acute metabolic encephalopathy	Available	Abnormal	Ophthalmoplegia	Ex due to metabolic decompensated attack
8	3 years	1 year	F	Psychomotor retardation, convulsion	Available	Not done	Ophthalmoplegia	Mental retardation
9	8 years	1 year	M	Sensorimotor polyneuropathy	Available	Normal	Ophthalmoplegia, mental retardation, ataxia	Progressive psychomotor retardation
10	12 years	1 year	M	Psychomotor retardation, convulsion	Available	Normal	Epilepsy, cataract, microphthalmia	Progressive psychomotor retardation

CSF, cerebrospinal fluid.

The examinations were performed under oral sedation with chloral hydrate (50–75 mg/kg). All patients were examined using a 1.5-T magnetic resonance unit (Intera Achieva and Gyroscan Intera, Philips Medical Systems, Best, The Netherlands) equipped with a standard head coil. The duration of the entire MRI examination was 20–25 min per patient. After routine magnetic resonance imaging with spin echo T1-weighted sagittal, dual-echo turbo spin echo T2-axial, sagittal and fluid-attenuated inversion-recovery axial sequences, transverse single-shot echo planar diffusion-weighted imaging (TR/TE: 5200/105 ms; field of view: 240 mm; matrix: 128×128; section thickness: 5 mm; intersection gap: 1.5 mm) were performed.

Control MRI and DWI analysis was carried out for 1–4 years on 7 of the 10 patients included in our study. Control analysis of the other three patients could not be performed because they died. ADC measurements were undertaken on both of the two hemispheres at 20 individual white-grey matter points; these were identified prior to measurement in all patients in both the control and patient groups. The anatomical locations at which the ADC measurements were made were as follows: frontal-parietal-occipital white matter; frontal-parietal-occipital grey matter; caudate nucleus; globus pallidus; putamen; thalamus; internal capsule anterior-posterior limb; mesencephalon anterior-posterior section; dentate nucleus; pons anterior-posterior section; bulbus; cerebellar white matter; and periventricular cerebral white matter. ADC measurements were undertaken using two separate standard measurement circles (region of interest: ROI) with areas of 25.2 and 56.5 mm^2. This ROI for the $b = 0$ data was placed on the point to be measured on the images and it was automatically transferred to the same point on the ADC map by the system.

All conventional and diffusion MR images were evaluated by two radiologists, one of whom was experienced in paediatric radiology. In the evaluations, parenchymal signal intensity changes, lesion localisations, diffusion characteristics on DWI and diffusiveness of the lesions were considered; whether or not additional lesions were identified was also considered. The signal characteristics of DWIs were visually evaluated and ADC values were measured using the standard ROI from 20 separate measurement points, identified prior to measurement in all patients in both the control and patient groups. All patients were compared with the control group which was composed of 20 patients of similar age and gender who had normal brain MRI-DWI analyses.

In both of the examinations, the comparison of patient ages was performed using the Mann–Whitney U test, and the comparison of genders was performed using the Fisher exact test (chi-square); the selection of the control group was found to be appropriate. ADC values obtained in statistical comparison of axial single-shot echo planar imaging (EPI) DW-MRI were compared with the control group using the Mann–Whitney U test.

3. Results

Of the cases in our study, four were girls and six were boys. Their ages varied between 1 month and 13 years, and the average age was calculated at 47.7 months. Control MRI and DWI examinations were undertaken on seven of the patients at 1–4 years after the first examination. Control examinations of the three remaining patients could not be carried out because they had died. Age distribution, periods over which control examinations were conducted, significant neurological findings, patient gender and the diagnostic methods are shown in Table 1.

Increased diffusion and ADC values were evident at the first examination in six (cases 3, 6, 7–10) out of the 10 patients included in the current study. Diffusion restriction and a decrease in ADC values were identified in three patients (cases 1, 4 and 5). In control examinations, while there was an increase in diffusion and ADC values in four patients (cases 1, 8–10), diffusion restriction and a decrease in ADC values was found in three patients (cases 2, 4 and 5).

Diffusion restriction detected using DWI and a decrease in ADC values was apparent at the first examination in three patients (cases 1, 4 and 5). An increase in ADC values was noted in one patient (case 1) in the control examination performed 4 years later (Fig. 1). In the other two patients (cases 4 and 5), while there was a slight increase