WALKER-WARBURG SYNDROME: DIFFUSION MR IMAGING

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SUMMARY
A 5-month-old boy with Walker-Warburg syndrome is reported. On MR imaging a characteristic pontomesencephalic kink was evident. Collicular fusion, hydrocephalus, callosal dysgenesis, cobblestone lissencephaly, small cerebellar cysts, pontine and cerebellar hypoplasia, and bilateral subretinal hemorrhages were noted. ADC (apparent diffusion coefficient) maps of an echoplanar diffusion MR imaging sequence revealed an elevated diffusion pattern throughout the cerebral white matter, manifested with prominently high ADC values, ranging from 1.82 to 2.45×10⁻³ mm²/s. This corresponded to prominent hypomyelination. On the other hand, ADC values of the lissencephalic cortex were normal, ranging from 0.95 to 0.97×10⁻³ mm²/s. In addition, ADC values from the hypoplastic cerebellar hemispheres, and from the hypoplastic pons were normal.

Key words: Congenital muscular dystrophy, Walker-Warburg syndrome, Diffusion MR imaging.

INTRODUCTION
Walker-Warburg syndrome represents one of the congenital muscular dystrophies, which is associated with brain and eye anomalies. There are typical MR imaging changes in the syndrome, which have been previously reported [1-8]. These mainly include hypomyelination of the white matter, cobblestone lissencephaly, callosal dysgenesis, and hydrocephalus. Pontine hypogenesis with a kink at the mesencephalic-pontine junction is a characteristic finding [1-8]. This paper reports MR imaging and diffusion MR imaging findings in the syndrome.

CASE REPORT
The present patient is a 5-month-old boy. He had severe hypotonia, and generalized seizures since the very first days of life. At admission severe psychomotor retardation, chronic retinal detachment, and hemorrhage were noted. Muscle biopsy revealed dystrophic changes. Chromosome analysis, and blood biochemistry (including creatine kinase) were normal.

On MR imaging examination performed on a 1.5 T MR unit, (Magnetom Vision, Siemens, Erlangen, Germany) a characteristic pontomesencephalic kink was evident associated with pontine, and cerebellar hypoplasia. In addition, collicular fusion, hydrocephalus, callosal dysgenesis, cobblestone lissencephaly, small cerebellar cysts, and bilateral subretinal hemorrhages were noted. There were cauliflower-like gyri located medial to the temporal horns of the lateral ventricles (figure 1a-1d). A diffusion MR imaging sequence were added to the imaging protocol.

Diffusion MR imaging was obtained using the single-shot, spin-echo, echo-planar trace sequence. The acquisition time was 22 sec with TR=5700 msec, and TE=139 msec. Matrix was 96×128, and FOV was 240. The b=1000s/mm² images revealed diffuse hypointensity of the white matter relative to the gray matter which consisted of diffuse cobblestone lissencephaly (figure 2a). On ADC (apparent diffusion coefficient) maps, the abnormal white matter had prominently high signal, and high ADC values, ranging from 1.82×10⁻³ mm²/s to 2.45×10⁻³ mm²/s. ADC values of the lissencephalic cortex were normal, ranging from 0.95×10⁻³ mm²/s to 0.97×10⁻³ mm²/s (figure 2b). In addition, ADC values from the hypoplastic cerebellar hemispheres (0.94 and 0.93×10⁻³ mm²/s), and from the hypoplastic pons (0.88×10⁻³ mm²/s) were normal.

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Congenital muscular dystrophies associated with brain changes comprise four main groups: 1. Pure congenital muscular dystrophy (with merosin-positive, and merosin-negative subgroups); 2. Fukuyama type congenital muscular dystrophy; 3. Muscle-eye-brain disease; and 4. Walker-Warburg syndrome. These disorders develop due to deficiency of a group of proteins in the skeletal muscle including merosin (laminin α2), laminin 1, laminin 2, and laminin β2, as these proteins are also critical for the development of the central nervous system [1-8]. In pure congenital muscular dystrophy main imaging finding is widespread delayed myelination or hypomyelination of the white matter. Pons and cerebellum may exhibit mild atrophy. Fukuyama type congenital muscular dystrophy, primarily seen in Japan, is mainly associated with delayed myelination of the white matter, frontal polymicrogyria, occipital cobblestone lissencephaly, hypoplasia of the brainstem, and cerebellum, dysplasia of the folia with subcortical cysts, and collicular fusion. Muscle-eye-brain disease, primarily seen in Finland, manifests with delayed myelination of the white matter, cobblestone lissencephaly, hypoplasia of the corpus callosum, pons, and cerebellum, and cerebellar cysts. Impaired visual fixation is present from birth. On the other hand, imaging features of Walker-Warburg syndrome include prominent hypomyelination of the white matter, cobblestone lissencephaly, callosal dysgenesis, and hydrocephalus. Pontine hypogenesis...
with a kink at the mesencephalic-pontine junction is a characteristic finding. Collicular fusion, cerebellar hypoplasia is present. Occipital cephalocele may be seen. Congenital microphthalmos, glaucoma, vitreous and subretinal hemorrhages may be noted [1-8].

In the present case, most of the abovementioned changes for Walker-Warburg syndrome was present (figure 1), identifying condition as this syndrome. It is cited that cerebellar subcortical cysts are usually confined to Fukuyama, and muscle-eye-brain disease, however, this patient with Walker-Warburg syndrome had such cysts [1]. Also, a cauliflower-like gyral pattern at the medial temporal regions was a noteworthy finding. With respect to the contribution of diffusion MR imaging, a prominently elevated diffusion pattern was evident throughout the cerebral white matter, which corresponded to prominent hypomyelination (figure 2). This finding was especially seen on the ADC maps, compared to the b = 1000 s/mm² images. ADC maps provided mathematical information on diffusion coefficients that the elevated diffusion of hypomyelinated cerebral white matter ranged from 1.82×10⁻³mm²/s to 2.45×10⁻³mm²/s. It was noteworthy that ADC values of the diffuse lissencephalic cortex were normal, ranging from 0.95×10⁻³mm²/s to 0.97×10⁻³mm²/s. In addition, ADC maps revealed that the ADC values from the hypoplastic cerebellar hemispheres (excluding the regions with subcortical cysts) were normal (0.94 and 0.93×10⁻³mm²/s). Also, ADC values from the hypoplastic pons were normal (0.88×10⁻³mm²/s). Although, major changes in Walker-Warburg syndrome are at the supratentorial region, presence of subcortical cysts, and a relatively normal myelination pattern of the cerebellum, as especially noted on the ADC maps, appear to be new findings in the syndrome.

REFERENCES