Clinical Case Report

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Sustained disconnection in sensorimotor pathways results in poor motor function outcome in a term infant after severe white matter injury

A case report

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Abstract

Introduction: We report a case of an infant with severe white matter injury (WMI), which was serially evaluated using diffusion tensor imaging (DTI).

Case presentation: A male infant showed decreased muscle tone and weak breathing. A brain magnetic resonance imaging (MRI) 10 days after birth (first study) revealed diffuse microhemorrhages and encephalomalacia. DTI revealed lack of reconstruction of corticospinal tract (CSTs), minimal reconstruction of medial lemniscus, and related thalamocortical pathways (MLs) from the brain stem to the internal capsule level on the left side. The spinothalamic tract and related thalamocortical pathways (STTs) were reconstructed from the brain stem to the internal capsule level bilaterally. The second study one year later showed the absence of reconstruction of CSTs, but reconstruction of MLs and STTS from the brain stem to above the internal capsule showed increased visualization. The third study 3 years later still showed the absence of CSTs reconstruction and MLs and STTs showed no changes from the second study. During this 3-year observation period, the patient showed minimal motor development, and was unable to walk independently, although Gross Motor Function Measure (GMFM) scores were slightly increased.

Lessons: Sustained disconnection of major sensorimotor pathways after WMI confirmed by DTI was used to predict motor function outcome.

Abbreviations: CSTs = corticospinal tract, DTI = diffusion tensor imaging, FA = fractional anisotropy, GMFM = Gross Motor Function Measure, MLs = medial lemniscus and its related thalamocortical pathways, STTs = spinothalamic tract and its related thalamocortical pathways, WMI = white matter injury.

Keywords: corticospinal tract, development, diffusion tensor imaging, gross motor function measurement, medial lemniscus, spinothalamic tract, thalamocortical pathway

1. Introduction

White matter injury (WMI), which is usually known to occur in preterm infants, is one of the most frequent causes of cerebral palsy. The injury results in functional deterioration in many preterm births, and studies have been conducted to ascertain the structural manifestation and prognosis of WMI. Diffusion tensor imaging (DTI) has been widely used to identify and visualize the integrity of microstructures in WMI [1] and facilitates the prediction of the neurodevelopmental outcome in preterm infants.[2]

In this case report, we performed 3-year follow-up DTI tractography a near term infant with severe WMI, and examined the sustained disconnection in sensorimotor pathways including corticospinal tracts (CSTs), medial lemniscus, and related thalamocortical pathways (MLs), and the spinothalamic tract and related thalamocortical pathways (STTs). We evaluated the gross motor function with Gross Motor Function Measure (GMFM) to know the motor function prognosis. The study protocol was approved by the institutional review board of the Chung-Ant University Hospital. Informed consent was confirmed by the Institutional Review Board (IRB).

2. Case report

A male infant was born by normal spontaneous vaginal delivery. The subject was in the 38th week of pregnancy according to physical examination. The exact period was unknown as the subject's mother failed to initially recognize her pregnancy, nor did she seek any medical care during her pregnancy. The subject's mother denied any history of medication. She acknowledged and was concerned about her frequent consumption of alcohol (3–4 times a week) during her pregnancy. The patient's initial Apgar scores were 3 in 1 minutes and 5 in 5 minutes. Because the infant

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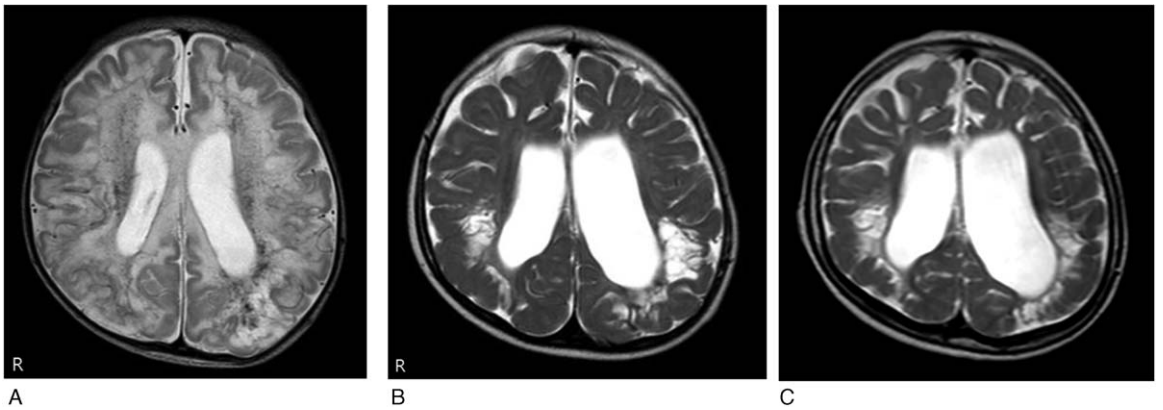

Figure 1. Initial Brain MRI showed severe, diffuse microhemorrhages in the periventricular region, centrum semiovale, precentral and postcentral gyri, and macrohemorrhages in the bilateral parietal and occipital lobes (A), which led to diffuse encephalomalacia involving whole white matter in second (B) and third (C) brain MRIs, suggesting long-term sequelae of hypoxic WMI.

showed decreased muscle tone and weak breathing, a brain MRI was administered 10 days after birth. The MRI showed diffuse microhemorrhages in the periventricular region, centrum semiovale, precentral and postcentral gyri, and macrohemorrhages in the bilateral parietal and occipital lobes (Fig. 1A). The brain stem and cerebellum were relatively spared. DTI tractography revealed absence of reconstruction of CSTs and minimal reconstruction of MLs from the brain stem to the internal capsule on the left side (Fig. 2A). The STTs were reconstructed from the brain stem to the internal capsule bilaterally (Fig. 2C). We evaluated the subject's development in an outpatient clinic 5 months after birth, and found bilateral Moro reflex, bilateral Babinski's reflex, bilateral Galant reflex, and bilateral asymmetric tonic neck reflex. During postural reflex, traction, and Landau reaction were below the 6-week level. In the GMFM, the subject scored 15.7% in the Lying and Rolling dimension (Table 1).

The patient received a course of comprehensive rehabilitation lasting about 1 year and follow-up developmental examination at about 1 year of age. Although the GMFM score increased slightly from the previous score (Table 1), the subject was only partially able to control his head in the prone position. The subject was unable to crawl or stand, and the muscle tone was still severely decreased. Furthermore, the subject's communication ability appeared to be severely compromised because the subject failed to verbalize any recognizable words and exhibited no response to verbal and visual stimulation. Follow-up (the second) brain MRI with DTI was performed at this point (one year after birth), which showed diffuse encephalomalacia involving whole white matter (Fig. 1B). DTI tractography showed that CSTs were not reconstructed, and MLs showed increased visualization, and reconstruction from the brain stem to above the internal capsule level on the left side with increased fiber density (Fig. 2B), although it failed to reach the level of the cerebral cortex. STTs also showed increased visualization, and reconstruction from the brain stem to above the internal capsule level bilaterally (Fig. 2D), without extending to the cortex.

Follow-up physical examination was conducted when the subject was 3-years old, and GMFM scores showed a slight increase (Table 1). The subject intermittently lifted his head in a sitting position and occasionally rolled over with assistance. At this juncture, however, the subject was unable to independently crawl or stand. The muscle tone was still relatively decreased. Moreover, the subject was only able to focus on moving objects occasionally, with rudimentary speech and unrecognizable words. The third brain magnetic resonance imaging (MRI) showed diffuse cerebromalacia accompanied with atrophic changes, suggesting long-term sequelae of hypoxic WMI (Fig. 1C). DTI tractography showed absence of CSTs reconstruc-

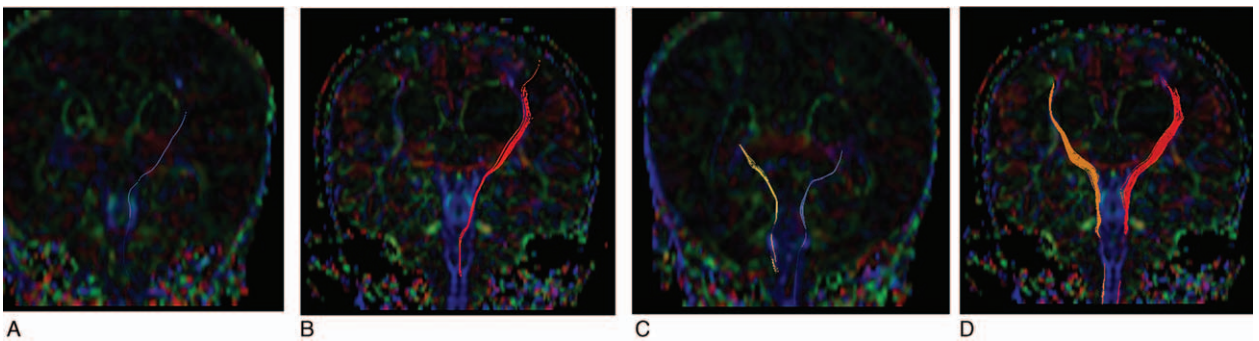

Figure 2. DTI tractography. No CSTs are shown because no trajectory was reconstructed in the whole follow-up studies. MLs in the first study (A) were only reconstructed from brain stem to internal capsule level on the left side only. MLs were reconstructed from the brain stem to above the internal capsule level on the left side with increased fiber density in the second study (B). It showed no change in the third study (not shown). STTs in the first study (C) were reconstructed minimally from the brain stem to the internal capsule bilaterally, and increased visualization in the second study (D), which were reconstructed from the brain stem to above the internal capsule level bilaterally, without extending to the cortex. No changes were detected in the third study (not shown).

Table 1

Gross Motor Function Measure (GMFM) results.

Dimension	5 Months after birth		1 Year after birth		3 Years after birth	
	Calculation of dimension	% Scores	Calculation of dimension	% Scores	Calculation of Dimension	% Scores
Lying and rolling	8/51	15.7	12/51	23	26/51	51
Sitting	0/60	0	5/60	8	12/60	20
Crawling and kneeling	N/T	N/T	N/T	N/T	2/42	5
Standing	N/T	N/T	N/T	N/T	N/T	N/T
Walking, running, and jumping	N/T	N/T	N/T	N/T	N/T	N/T

N/T = Not tested (Unable to be tested).

tion, and MLs and STTs showed no specific changes, which indicate sustained disconnection from the cerebral cortex.

3. Discussion

DTI has been used not only to verify the structural prognosis of WMI [3] but also to predict the functional outcome after a specific therapeutic strategy in WMI patients.[4] Previous studies reported the correlation of fractional anisotropy (FA) in corpus callosum with CSTs involving cognitive and motor performance.[4] In another study, CST injuries were related to reduced thalamic volume in preterm infants with cystic periventricular leukomalacia.[5] As documented in this study, white matter injury during perinatal period affected the white matter as well as induced the atrophy of the cerebral cortex and thalamus. Conventional MRI study could show the severity of WMI, but it is not to know the connectivity of major pathways in white matter. In our patient, severe WMI was mediated via sustained disconnection in the sensorimotor pathways including CSTs, MLs, and SSTs, which was confirmed by DTI tractography. Limited and poorly developed motor functions were also observed in the 3-year follow-up period. In another study, whole white matter connectivity was related to functional improvement in cerebral palsy during therapy,[6] although the initial structural deficits showed an important impact. We suggest that prognosis should be based on not only whole brain connectivity or FA but also functional connectivity of CSTs, MLs, and SSTs in the early stages after WMI using DTI tractography. In our patient, the initial disconnection was sustained until at least 3 years of age, along with poor motor skills. Prompt prediction of outcomes facilitates individual rehabilitation tailored to address the patients' needs rapidly.

Author contributions

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Writing – original draft: Sunhan Son, Si Hyun Kang.
Writing – review & editing: Si Hyun Kang, Don-Kyu Kim, Kyung Mook Seo.

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