Case Study

The effect of white matter integrity on functional outcome in central pontine demyelination

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Abstract. [Purpose] Central pontine demyelination is a common osmotic demyelination syndrome. Typically, central pontine demyelination shows high signal intensity with demyelination in the mid-pons. Despite severe imaging findings, patients usually recover. This study investigated the integrity of the corticospinal tract (CST) and corticoreticular pathway (CRP) in patients at 12 months after the onset of central pontine demyelination. [Participants and Methods] This retrospective cross-sectional observational study assessed two patients with central pontine demyelination, who were ultimately able to walk without using an aid or orthosis and to use both hands but with mild residual symptoms. All participants underwent diffusion tensor imaging (DTI) at 12 months after onset. [Results] Both patients had mild ataxia at 12 months after onset. The integrity of the CST was restored in both cases, while the integrity of the CRP recovered partially. [Conclusion] The integrity of the CST and CRP at 12 months after the onset of central pontine demyelination was similar in both cases as well as the recovery status of the hand function and ambulation. These results may be useful in planning therapy for patients with central pontine demyelination.

Key words: Central pontine demyelination, Diffusion tensor imaging, Prognosis

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INTRODUCTION

Osmotic demyelination syndromes include central pontine and extrapontine myelinolysis1). In these syndromes, central pontine demyelination involves symmetrical myelin sheath disruption in areas where the white matter becomes exposed to osmotically active substances cleared from edematous grey matter, namely, the crossing pontocerebellar fibers within the pontine nuclei and other grey matter regions containing heavily myelinated fibers, such as the cerebellum and lateral geniculate body2). Clinical recovery from osmotic pontine demyelination can occur with correction of the electrolyte imbalance and underlying systemic disease2–4). More than half of patients with osmotic pontine demyelination have favorable outcomes3). The radiological findings of central pontine demyelination vary and include cortical and subcortical types5, 6). However, the integrity of the white matter in central pontine demyelination is not known. This case report describes two patients with central pontine demyelination who had severe quadriplegia and underwent rehabilitation; in the chronic stage, they both had mild ataxia.

PARTICIPANTS AND METHODS

This was a retrospective cross-sectional observational clinical trial. Two right-handed patients with osmotic central pontine demyelination were recruited from the Department of Rehabilitation Medicine, St. Vincent’s Hospital, Suwon, South Korea

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between January 2015 and December 2018. Considering the maturation of neurological recovery, completion of neurological recovery was defined as 6 months after onset. Demographic, clinical, and brain magnetic resonance imaging (MRI) data were obtained for both participants. Brain MRI diffusion tensor imaging (DTI) was performed around 12 months after onset, at the time of a functional evaluation. All participants received routine physical and occupational therapy for 1–2 hours per day, 5 days per week. The study protocol was reviewed and approved by the Institutional Review Board of The Catholic University, College of Medicine (Registry No. VC17ZESE0152); the board waived the need for informed consent.

The DTI was performed using a 3.0-T MRI (MAGNETOM® Verio, Siemens, Erlangen, Germany) equipped with a six-channel head coil. The data were acquired in the form of single-shot spin-echo echo-planar images, with axial slices covering the entire brain across 76 2.0-mm-thick interleaved slices (no gaps): repetition time (TR)/echo time (TE)=14,300/84 ms; field of view=224 × 224 mm²; matrix 224 × 224; voxel size 1 × 1 × 2 mm³; number of excitations=1. Diffusion-sensitizing gradients were applied in 64 non-collinear directions with a b-value of 1,000 ms/mm². The b=0 images were scanned before acquiring the diffusion-weighted images (65 volumes in total). DTI-Studio software (CMRM, Johns Hopkins Medical Institute, MD, USA) was used to reconstruct the corticospinal tract (CST) and corticoreticular pathway (CRP). Fiber tracking was based on fiber assignment continuous tracking (FACT) algorithm and a multiple regions of interest (ROIs) approach using DTI-Studio. ROIs were used for CST and CTR reconstruction. The initial ROI was placed on the pontomedullary junction portion of the CST, and the second on the anterior mid-pons portion of the CST (Fig. 1). To analyze the CRP, the seed ROI was placed on the reticular formation of the medulla and the target ROI on the midbrain tegmentum. The termination criteria were fractional anisotropy (FA) >0.2 and an angle change of <60 degrees.

RESULTS

A 40-year-old man (Case 1) with diabetes mellitus, hypertension, and chronic alcoholic hepatitis presented to the emergency room with sudden memory impairment with no trauma. He was treated for hepatic encephalopathy and hyponatremia (serum sodium 105 mEq/L). While correcting the sodium (daily 2–7 mEq/L), he became increasingly drowsy. A 57-year-old man (Case 2) with poor oral intake, hypertension, and chronic alcoholic hepatitis presented to the emergency room with generalized weakness of all limbs with no trauma. He was treated for hyponatremia (serum sodium 107 mEq/L), anemia, and thrombocytopenia in the Department of Internal Medicine. After the acute treatment, quadriplegia was noted. Their finding of MRI showed central pontine demyelination. In the early stage, on manual muscle testing (MMT), they had proximal limb weakness greater than distal weakness, graded poor and fair (Case 1) and graded poor+ and fair+ (Case 2) respectively. They had no restrictions in range of motion (ROM). Main problems of those were postural instability due to trunk and proximal muscle weakness and ataxic movements.

They got rehabilitation programs including physical therapy and occupational therapy, 30 min per session, 2–3 sessions a day, five times a week. In particular, physiotherapy focused on core stabilization, proximal gross muscle strengthening, and trunk and limb coordination training. They underwent sit-to-stand, assisted-standing, and sitting and standing balance training. They started gait training with moderate assistance at 5 weeks after onset and progressed to gait training with supervised use of sand bags on both ankles. Case 1 underwent body-weight-supported treadmill training (BWSTT) for 30 minutes, beginning with a 40% decrease in weight to full weight acceptance, and with an average speed ranging from 0.3 to 0.5 m/s. After rehabilitation for 12 weeks, he ambulated without a walking aid or orthosis. Case 2 started BWSTT for 20 minutes beginning with a 40% decrease in weight to full weight acceptance, with average speed ranging from 0.2 to 0.4 m/s. After rehabilitation for 20 weeks, he ambulated with a cane, without an orthosis. One year after onset, they had regained most of his functional abilities for gait and hand function. However, they still complained of ataxia and sensory changes in the lower limbs. Follow-up MRI showed large central high signal intensities in the pons. The white matter integrity evaluated by DTI showed a relatively well-preserved CST compared with the CRP (Figs. 1 and 2).

DISCUSSION

Studies have demonstrated the clinical usefulness of DTI for evaluating function in two patients with central pontine demyelination. The integrity of the white matter, i.e., the CST and CRP, in central pontine demyelination may be an important factor of good functional recovery. The relationship between DTI CST images and hand function has been evaluated several times. Most reports have shown that damage to the CST is useful for predicting the restoration of motor function in patients with stroke. Consistent with previous studies, the CST integrity reflected the functional status of the central pontine demyelination in our patients.

Central pontine demyelination follows a biphasic course with initial seizures or encephalopathy that may improve gradually, but which are then followed by severe deterioration manifesting as dysarthria, dysphagia, oculomotor dysfunction, and variable degrees of quadriaparesis. The typical radiological findings on brain MRI are hyperintense lesions in the central pons or associated extrapontine structures on T2-weighted and fluid-attenuated inversion recovery sequences, with corresponding hypointensity on T1-weighted sequences. It is very difficult to predict the prognosis of central pontine
demyelination. Conventional MRI does not match the clinical findings. Therefore, we used DTI to predict the outcome and explain the central pontine demyelination.

The CRP is an extrapyramidal motor pathway that innervates the proximal muscles of the extremities and the axial muscles; it plays roles in postural control and locomotor function. The CRP originates mainly from the premotor cortex (PMC). Associations of the PMC lesions with proximal muscle weakness, gait recovery, and postural control have been reported. Both of our patients had proximal weakness and balance problems during rehabilitation.

The CST integrity is reflected in the recovery of upper limb motor function, while the CRP integrity is reflected in the recovery of lower limb motor function. Both of our patients with central pontine demyelination fully recovered their hand function, while lower limb ataxia remained. These findings are consistent with previous studies. However, our patients’ problems cannot be fully explained using only the CST and CRP findings. In early DTI images, they had normal CST integrity, but disconnection of the CRP; it is possible that the CST takes over CRP functions during recovery.

A few limitations of our study should be noted. First, we used a cross-sectional design; we did not collect tensor images in the early stage, so the changes in DTI over time were not investigated. Second, we evaluated only two patients because of the rarity of central pontine demyelination. To overcome this methodological limitation, further larger-scale study is needed to confirm the role of DTI in patients with central pontine demyelination.

In conclusion, the integrity of the CST and CRP was consistent with clinical recovery in patients with central pontine demyelination. These results will be useful for predicting functional restoration of the hand and gait in the acute phase in patients with central pontine demyelination, and will contribute to our understanding of the functional prognosis of central pontine demyelination.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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