Clinical Case Report

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Aggravation of an injured dentato-rubro-thalamic tract in a patient with mild traumatic brain injury

A case report

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Abstract

Rationale: We report on a patient with mild traumatic brain injury (TBI) by follow-up diffusion tensor tractography (DTT), and observed for approximately nine monthsby serial diffusion tensor tractography (DTT).

Patient concerns: A 66-year-old male patient was injured in a car crash. Approximately four weeks after the crash, he developed a tremor in the right hand and leg. His symptoms worsened over time.

Diagnoses: Approximately six months after the crash, he developed a mild tremor in the left hand. Nine months after the crash, he manifested severe tremor in his right hand, mild resting and intentional tremor in his left hand and both legs, and mild trunkal ataxia.

Interventions: N/A.

Outcomes: On 3-week DTT, well reconstructed DRTTs were observed in both hemispheres, except for the thinned lower portion of the right DRTT. On 9-month DTT, the right lower DRTT had thinned compared with the 3-week DTT and showed a disruption at the upper portion. The left DRTT showed thinning in the lower portion and tearing in the upper portion compared with 3-week DTT.

Lessons: Aggravation of an injured DRTT was demonstrated in a patient with mild TBI, using serial DTT examination.

Abbreviations: DRTT = dentato-rubro-thalamic tract, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, ROI = region of interest, SARA = Scale for Assessment and Rating of Ataxia, TBI = traumatic brain injury.

Keywords: ataxia, dentato-rubro-thalamic tract, diffusion tensor tractography, mild traumatic brain injury, tremor

1. Introduction

Tremor, an unintentional and uncontrollable rhythmic movement, is a major clinical manifestation of movement disorders.[1] It is the most frequent movement disorder in patients with traumatic brain injury (TBI).[2] Injury of the dentato-rubro-thalamic tract (DRTT), a major efferent pathway from the deep cerebellar nuclei to the brainstem and thalamus, is suggested as a major pathogenetic mechanism of tremor.[3,4] Several studies reported injury of the DRTT in patients with tremor following various brain pathologies including TBI.[5–9] However, little is known about aggravation of an injured DRTT.

Most studies of the DRTT in the human brain used conventional brain MRI[4,10] and precise evaluation has been limited because of its long, narrow shape, multisynapse, low discrimination with adjacent neural structures, and decussation to the opposite hemisphere in the midbrain.[3] Introduction of diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), enabled 3-dimensional reconstruction and evaluation of the DRTT in the live human brain,[11,12] a patient with injury of the DRTT following mild TBI was recently reported,[9] however, it has not been clearly elucidated so far.

To demonstrate aggravation of injured DRTT over approximately 9 months, we report on a patient with mild TBI using serial DTT.

2. Case report

A 66-year-old male patient was injured in a car crash. While driving on a congested highway, his car was struck by a tow truck from behind. The patient lost consciousness for approximately 1 minute and experienced post-traumatic amnesia approximately 5 minutes from the time of the accident. The patient's Glasgow Coma Scale score was 15. No specific lesion was observed on the conventional brain MRI performed at 3 weeks after onset (Fig. 1A). Three weeks after the crash, he was admitted to the rehabilitation department of a university hospital. At the beginning of rehabilitation, Mini-Mental State Examination was 29 (full score: 30, cutoff score < 25). Neurological examination revealed mild motor weakness without spasticity and flaccidity and somatosensory impairment of the right upper and lower extremities (Manual Muscle Test; right upper extremity [good grade: movement against a resistance lower

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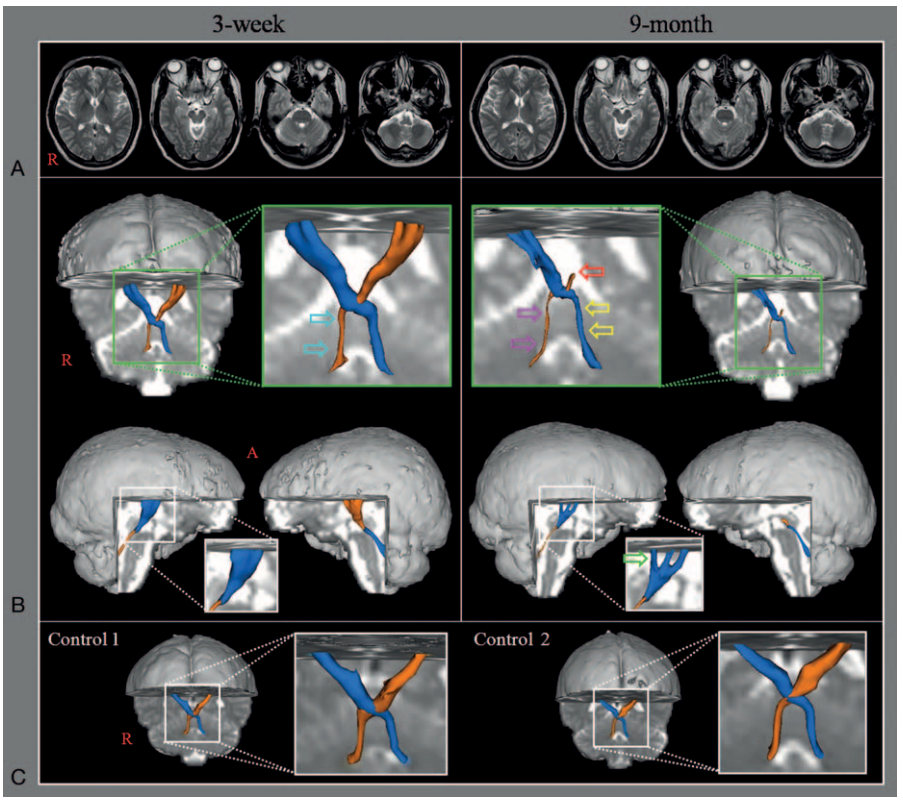

Figure 1. (A) T2-weighted brain MR images at 3 wk and 9 mo after onset show no abnormality. (B) Results of diffusion tensor tractography (DTT) for the dentato-rubro-thalamic tract (DRTT). On 3-wk DTT, well-reconstructed DRTTs are observed in both hemispheres, except for the thinned lower portion of the right DRTT (sky-blue arrows). On 9-mo DTT, the right DRTT has become thinner in the lower portion (purple arrows) compared with 3-wk DTT and shows a disruption (red arrow) at the upper portion. In addition, the left DRTT also shows thinning (yellow arrows) in the lower portion and tearing (green arrow) at the upper portion. (C) Results of DTT for the DRTT in 2 normal control subjects (control 1: 61-y-old male, control 2: 64-y-old male).

than resistance overcome by the healthy side] and right lower extremity [fair grade: movement against gravity], Nottingham Sensory Assessment; tactile sensation—right upper extremity [6; full score, 10], right lower extremity [4; full score, 10]; kinesthetic sensation—the right upper extremity [8; full score, 12], right lower extremity [8; full score, 12]). He reported central pain in the right upper and lower extremities (tingling sensation with allodynia), visual analogue scale score (6; full score, 10), memory impairment (Memory Assessment Scale; global memory: 68 [2 percentile], short-term memory: 53 [1 percentile], verbal memory: 53 [1 percentile], and visual memory: 98 [45 percentile]), and visual disturbance. He received comprehensive rehabilitative therapy including movement therapy and neuromuscular electrical stimulation on the right finger and knee extensor muscles. Movement therapy was conducted for 30 minutes, 5 times per week in our physical and occupational therapy department. Although we tried medications for weakness and central pain, his severe drug allergies prevented this treatment. Approximately 4 weeks after the crash, he began to show a resting and intentional tremor in the right hand and leg, and developed a mild truncal ataxia. His symptoms worsened with time. Approximately 6 months after the crash, he developed mild resting and intentional tremor in the left hand. Nine months after the crash, he manifested severe resting and intentional tremor on his right hand, mild resting and intentional tremor in his left hand and both legs, and mild truncal ataxia. The Scale for Assessment and Rating of Ataxia (SARA, full mark: 40 points) indicated aggravation from 2 points at 3 weeks after onset to 26 points at 9 months after onset. Eight age- and sex-matched normal control subjects (mean age: 62.9 ± 5.0 years, range: 60–71 years) with no history of neurological disease were recruited for this study. The patient provided written informed consent, and the study protocol including data deposition was approved by the Yeungnam University Hospital Institutional Research Board.

2.1. Diffusion tensor tractography

DTI was acquired twice (at 3 weeks and 9 months) using a 6-channel head coil on a 1.5T Philips Gyroscan Intera (Philips, Ltd, Best, the Netherlands) with single-shot echo-planar imaging. For each of the 32 non-collinear diffusion sensitizing gradients, 70 contiguous slices were acquired parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix $= 96 \times 96$; reconstructed to matrix $= 192 \times 192$; field of view $= 240 \times 240\,mm^2$; repetition time $=$ 10,398 ms; echo time $= 72$ ms; parallel imaging reduction factor $= 2$; echo-planar imaging factor $= 59$; b $= 1000\,s/mm^2$; and a slice thickness of 2.5 mm. Prior to the fiber tracking, eddy current correction was applied to correct the head motion effect and image distortion using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Diffusion Software. Fiber tracking used probabilistic tractography with default tractography option in the FMRIB Diffusion Software (5000 streamline samples, 0.5 mm step lengths, curvature thresholds $= 0.2$). For reconstruction of the DRTT, the seed

region of interest (ROI) was placed at the dentate nucleus behind the floor of the fourth ventricle on the coronal image.[11] Two target ROIs were placed on the portion of the superior cerebellar peduncle on the color map with the coronal image and the contralateral red nucleus of the upper midbrain on the axial image.[11] A threshold of 2 streamlines was applied for the results of fiber tracking. The tract volume of the DRTT was measured by counting voxels. Tract volume in DTT parameter value showing a deviation of more than 2 standard deviations from normal control values were defined as injury.

On 3-week DTT, well-reconstructed DRTTs were observed in both hemispheres, except for the thinned lower portion of the right DRTT. On 9-month DTT, the right DRTT had become thinner in the lower portion compared with 3-week DTT, and a disruption was observed at the upper portion. Thinning of the left DRTT in the lower portion and tearing in the upper portion were observed compared with 3-week DTT (Fig. 1B and C). Compared with normal controls (652.8 ± 76.5 voxels), the right DRTT (465 voxels) tract volume on 3-week DTT was significantly less. On the 9-month DTT, the DRTT in both hemispheres (right: 52 voxels and left: 476 voxels) revealed significantly less tract volume compared with normal controls. Tract volume decreased in both DRTTs on 9-month DTT (right: 52 voxels and left: 476 voxels) compared with the 3-week DTT (right: 465 voxels and left: 639 voxels).

3. Discussion

In this study, the DRTT was observed over time in both hemispheres in a patient with mild TBI using serial DTT. On 3-week DTT, DRTTs were well reconstructed, except for the thinned lower portion of the right DRTT. However, on 9-month DTT, both lower portions of the DRTTs had become thinner and the upper portions of the DRTT showed abnormalities: disruption (the right DRTT) and tearing (the left DRTT). Mild injury of the right DRTT was observed on 3-week DTT and injures of both DRTTs (more severe injury in the right DRTT) were observed on 9-month DTT. These changes suggest that the aggravation of both injured DRTTs developed during the period from 3 weeks to 9 months after onset. However, clinical symptoms related to the DRTT (tremor) began on the right side at 4 weeks after the crash, worsened and spread to the left side over time. The tremor in this patient can be partially ascribed to injury of the DRTT caused by traumatic axonal injury because the conventional brain MRI did not show any specific lesion.[13] In addition, the delayed onset (4 weeks after head trauma) and gradual aggravation of the tremor in this patient suggests that the traumatic axonal injury might be mainly ascribed to secondary injury. In this condition axons were not damaged by direct shear/strain injury at the time of head trauma, but axonal injury developed by progressively impaired axoplasmic transport, continued axonal swelling, and disconnection.[14] No specific causes for the neurological manifestations, including Parkinson disease were observed by a neurologist and a neurosurgeon. Furthermore, the patient presented with only tremor and ataxia, but without rigidity and bradykinesia which are main symptoms of Parkinson disease.[15,16]

Several studies using DTT have described injured DRTT with movement disorder in patients with stroke, brain tumor, and TBI.[5–9] Only 1 study has reported injury of the DRTT from TBI.[9] In 2015, Kwon and Jang demonstrated injury of the DRTT (thinning) on DTT in a patient who showed delayed onset (2 weeks after head trauma) and aggravation of tremor and ataxia following mild TBI. To the best of our knowledge, this is the first study to demonstrate aggravation of an injured DRTT in a patient with TBI using serial DTT. Limitations of this study should be considered. First, because it is based on a case report, this study is limited. Second, DTT can show both false positive and negative results throughout the white matter of brain due to the crossing fiber and partial volume effects.[17] Third, the patient was managed only at the department of rehabilitation, so more comprehensive assessment of the patient's neurological state following TBI could have been obtained by collaborating with the neurology staff.

In conclusion, aggravation of an injured DRTT was demonstrated in a patient with mild TBI, using serial DTT. Our results suggest the need to evaluate the DRTT in patients who develop delayed onset of a movement disorder after TBI, even though no definite brain lesion is observed on conventional brain MRI. Further studies involving large numbers of subjects on the anterograde axonal degeneration of injured DRTTs following the initial injury should be encouraged.

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