Aggravation of excessive daytime sleepiness concurrent with aggravation of an injured ascending reticular activating system in a patient with mild traumatic brain injury

A case report

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Abstract

Background: We report on a patient who developed aggravation of excessive daytime sleepiness (EDS) concurrent with aggravation of an injured ascending reticular activating system (ARAS) following mild traumatic brain injury (TBI), demonstrated by follow-up diffusion tensor tractographies (DTTs).

Methods: A 42-year-old male patient experienced head trauma resulting from flexion-hyperextension injury after collision with another vehicle from behind while stopped at an intersection. The patient lost consciousness for approximately 10 seconds and experienced no post-traumatic amnesia following the accident. The patient’s Glasgow Coma Scale score was 15. No specific lesion was observed on the conventional brain MRI performed at 10 weeks after onset. The patient complained of EDS after the head trauma and aggravation of EDS with passage of time. The Epworth Sleepiness Scale indicated abnormality with a score of 12 at 10 weeks after onset (cut-off: 10 points full mark: 24 score) and it was aggravated with a score of 18 at 16 months.

Results: On 10-week DTT, decreased neural connectivity of the intralaminar thalamic nucleus to the prefrontal cortex and basal forebrain was observed in both hemispheres. However, no significant abnormality was observed in the dorsal and ventral lower ARAS. On 16-month DTT, the upper portion of the left dorsal lower ARAS showed partial tearing and the ventral lower ARAS showed thinning (both sides) and partial tearing (right side).

Conclusions: Aggravation of EDS concurrent with aggravation of an injured ARAS was demonstrated in a patient with mild TBI using DTT.

Abbreviations: ARAS = ascending reticular activating system, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, EDS = excessive daytime sleepiness, ESS = Epworth Sleepiness Scale, ILN = intralaminar thalamic nucleus, ROI = region of interest, TBI = traumatic brain injury.

Keywords: ascending reticular activating system, diffusion tensor tractography, hypersomnia, mild traumatic brain injury

1. Introduction

Excessive daytime sleepiness (EDS) is a common sequela of traumatic brain injury (TBI).[1-4] Because EDS is related to poor daytime function, elucidation of its pathogenetic mechanism is important.[5-6] However, the pathogenesis of EDS has not been clearly elucidated so far. Since the recent development of diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), for the ascending reticular activating system (ARAS), several studies have demonstrated that injury of the ARAS was related to EDS in a few brain pathologies, including TBI, subarachnoid hemorrhage, and intracerebral hemorrhage[5-6]; however, it has not been clearly elucidated so far.

In the present study, we report on a patient who developed aggravation of EDS concurrent with aggravation of an injured ARAS following mild TBI, demonstrated by serial DTTs.

2. Case report

A 42-year-old male patient experienced head trauma resulting from flexion-hyperextension injury after collision with another vehicle from behind while stopping at an intersection in his vehicle. No previous medical history of neurological, physical, or psychiatric illness was noted before head trauma. The patient lost consciousness for approximately 10 seconds and experienced no post-traumatic amnesia at 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 10 weeks after the crash.
The patient complained of EDS after the head trauma and aggravation of EDS with the passage of time. As a result, he frequently felt difficulty in performing activities of daily life because of EDS; working or watching a movie. The Epworth Sleepiness Scale (ESS) indicated abnormality with a score of 12 at 10 weeks after onset (cut-off: 10 points full mark: 24 score), aggravated to a score of 18 at 16 months after onset (Table 1).[7]

For treatment, he underwent comprehensive rehabilitative treatment, including administration of neurotrophic drugs (modafinil: 200mg, ropinirole: 0.25mg, amantadine: 100mg, choline aldoscerate: 400mg, paroxetine HCl: 12.5mg, alprazolam: 0.25mg), physical and occupational therapy sessions 5 times per week (60 min/day). The patient signed an informed consent statement and the study protocol was approved by the Yeungnam University Hospital Institutional Review Board of a university hospital.

2.1. DTI

DTI data were acquired twice at 10 weeks and 16 months after the head trauma using a 1.5T Philips Gyroscan Interax with 32 non-collinear diffusion sensitizing gradients by single-shot echo-planar imaging. Imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm²; TR = 10,398 ms; TE = 72 ms; parallel imaging reduction factor = 2; echo-planar imaging factor = 59; b = 1000 s/mm²; and a slice thickness of 2.5 mm. The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRI) Software Library was used for analysis of DTI data. Affine multiscale 2-dimensional registration was used to correct the head motion effect and image distortion because of the eddy current. FMRI Diffusion Software with routines option (0.5 mm step lengths, 5000 streamline samples, curvature thresholds = 0.2) was used for fiber tracking. Three portions of the ARAS were reconstructed by selecting fibers passing through regions of interest (ROIs) as follows:[8-10] the dorsal lower ARAS, between the pontine reticular formation (ROI 1) and the intralaminar thalamic nucleus (ILN, ROI 2),[9] the ventral lower ARAS, between the pontine reticular formation (ROI 1) and the hypothalamus (ROI 2),[10] and the upper ARAS, in which the neural connectivity of the ILN (ROI 1) to the cerebral cortex was analyzed.[9]

On 10-week DTI, decreased neural connectivity of the ILN to the prefrontal cortex and basal forebrain was observed in both hemispheres. However, no significant abnormality was observed in the dorsal and ventral lower ARAS. By contrast, on 16-month DTI, the upper portion of the left dorsal lower ARAS showed partial tearing and the ventral lower ARAS showed thinning (both sides) and partial tearing (right side) (Fig. 1).

3. Discussion

According to the international classification of sleep disorders by the American Academy of Sleep Medicine, this patient’s diagnosis was posttraumatic EDS because he developed EDS after head trauma and experienced frequent daily sleep episodes.[11] The degree of EDS increased from 12 (ESS score) at 10 weeks to 18 (ESS score) at 16 months after onset. Although only decreased neural connectivity in the prefrontal cortex and basal forebrain was observed on 10-week DTI, aggravation of the left dorsal lower ARAS and both ventral lower ARAS was observed on 16-month DTI. As a result, it appeared that EDS in this patient was at least in part attributable to injury of the ARAS caused by traumatic axonal injury because no specific lesion was observed on the conventional brain MRI.[12] Considering recent studies reporting that injury of the ventral lower ARAS is closely related to hypersomnia, it appeared that the injury of the ventral lower ARAS was the most important contributor to aggravation of EDS in this patient, although injuries of the upper ARAS and lower dorsal lower ARAS were also observed.[3-6, 8-9] In addition, the aggravation of EDS and delayed appearance of injury of the dorsal and ventral lower ARAS in this patient suggest that the traumatic axonal injury might partially result from secondary injury. In this condition, axons were not damaged at the time of injury, but undergo axonal injury by a sequential process of impaired axoplasmic transport, continued axonal swelling, and subsequent disconnection.[13]

Since the introduction of DTI, several studies using DTI have demonstrated the association of hypersomnia and injury of the ARAS.[3-6] In 2015, Jang et al.[3] reported on a patient with narcolepsy who showed injury of the ventral lower ARAS following mild TBI. Subsequently, a study demonstrated recovery from hypersomnia with recovery of injured dorsal and ventral (more recovery than the dorsal lower ARAS) lower ARAS in a patient with subarachnoid hemorrhage.[4] Recently, Jang et al reported on patients with hypersomnia and injury of the dorsal and ventral (more injury than the lower dorsal ARAS) lower ARAS in patients with pontine hemorrhage (1 patient) and mild TBI (2 patients), respectively.[5, 6] These studies suggest that injury of the ARAS could be a probable cause for the hypersomnia in patients with brain injury particularly TBI. In addition, analysis of the ARAS using DTI might contribute to understanding the prognosis of EDS. To the best of our knowledge, this is the first study to demonstrate an association between aggravation of EDS and worsening injury of the lower ARAS in patients with brain injury. However, the limitations of this study should be considered. First, because it is a case report, this study is limited; therefore, conduct of further studies comprising a large number of patients is necessary. Second, because regions of fiber complexity and crossing can prevent full reflection of the underlying fiber architecture, DTI may underestimate the neural fiber tracts.[14] Third, we were not able to measure the degree of EDS using an objective measure such as the Multiple Sleep Latency Test.[15] Therefore, conduct of further studies including an objective measure such as the Multiple Sleep Latency Test should be encouraged.

In conclusion, aggravation of EDS concurrent with aggravation of an injured ARAS was demonstrated in a patient with mild TBI using DTI. These results suggest that evaluation of the ARAS

| Table 1 |
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| **Epworth Sleepiness Scale for the patient.** |
| **No** | **Situation** | **Score (0–3)** |
| **10 wk** | **16 mo** |
| 1 | Sitting and reading | 2 | 2 |
| 2 | Watching TV | 2 | 2 |
| 3 | Sitting, inactive in a public place (e.g., a theater or a meeting) | 2 | 3 |
| 4 | As a passenger in a car for an hour without a break | 1 | 2 |
| 5 | Lying down to rest in the afternoon when circumstances permit | 2 | 3 |
| 6 | Sitting and talking to someone | 0 | 2 |
| 7 | Sitting quietly after lunch without alcohol | 2 | 3 |
| 8 | In a car, while stopped for a few minutes in traffic | 1 | 1 |
| **Total** | | 12 | 18 |
using follow-up DTTs might be useful for patients who show change of EDS following brain injury particularly TBI.

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