

Case Report

Callosal Disconnection Syndrome after Corpus Callosum Infarct: A Diffusion Tensor Tractography Study

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We report a patient who presented with callosal disconnection syndrome (CDS) and fiber disconnection on diffusion tensor tractography (DTT) after an infarct of the corpus callosum (CC). A 72-year-old woman presented with manifestations of CDS, including frontal alien hand syndrome (AHS), left agraphia, right hemiparesis, right somatosensory deficit, left neglect, and impaired visual recognition. DTT was performed for the evaluation of CC fibers, followed by comparison with DTT findings of normal subjects. DTT of the normal subject revealed bilateral extension of CC fibers to the frontal, parietal, and occipitotemporal cortices. By contrast, CC fibers of the patient revealed extensive disruption, with the exception of CC fibers passing through the anterior genu and the posterior splenium. The extensive disruption of CC fibers appears to explain the patient's various CDS symptoms. In brief, DTT could be useful for detection of CC lesions in patients with CDS. **Key Words:** Callosal disconnection syndrome—cerebral infarct—corpus callosum—diffusion tensor imaging—diffusion tensor tractography.

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The corpus callosum (CC) contains nerve fibers that connect both cerebral hemispheres and make an important contribution to interhemispheric transfer of cognitive, somatosensory, motor, executive, and visual information.^{1,2} Injury to CC fibers can result in impaired transfer of interhemispheric information and can cause heterogeneous neurologic manifestations, including alien hand syndrome (AHS), apraxia, tactile anomia, agraphia,

visual anomia, neglect, and alexia.³⁻⁶ A combination of these neurologic manifestations after an injury of CC fibers is defined as callosal disconnection syndrome (CDS).

In the past, conventional computed tomographic (CT) or magnetic resonance imaging (MRI) scans of the brain have been used for the identification of CC lesions in patients with CDS in association with various brain diseases, including cerebral infarct, cerebral hemorrhage, brain tumor, and multiple sclerosis.⁷⁻¹⁰ However, these modalities do not have the capacity for visualization of interhemispheric CC fiber connections. By contrast, the recently developed diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), allows for 3-dimensional visualization of the architecture and integrity of the CC.^{2,11-13} Therefore, DTT has been used to show injury to CC fibers in some brain pathologies, including diffuse axonal injury, CC lesions after surgery for removal of arteriovenous malformation, and cerebral hemorrhage.¹¹⁻¹³ However, little is known about injury of CC fibers in patients with cerebral infarct.

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We report on a case involving a patient who presented with CDS and CC fiber disconnection on DTT after infarct of the CC.

Methods

Case Presentation

A 72-year-old right-handed woman underwent conservative treatment for a cerebral infarct resulting from left anterior cerebral artery occlusion at the neurology department of a university hospital. The patient signed an informed consent statement. This study was conducted in compliance with the international Declaration of Helsinki. The institutional review board of our university hospital approved the study protocol (PCR-11-125). At the onset of cerebral infarct, she was alert but had right hemiparesis (4/5 in the upper extremity and 2/5 in the lower extremity on the Medical Research Council [MRC]).¹⁴ Two weeks after onset, she was transferred to the rehabilitation department of the same university hospital in order to undergo rehabilitation. An MRI scan of the brain performed 16 days after onset revealed infarct lesions confined to the anterior portion of the left cingulate gyrus and the CC, which extended from the posterior portion of the genu to the anterior portion of the splenium (Fig 1A).

On neurologic examination at 4 weeks after onset, the patient presented with AHS, which is characterized by autonomous complex movements of one hand against the patient's will.¹⁵ Three features of AHS were observed

in her right hand: (1) she would often, on impulse, reach toward and grasp objects within her sight using her right hand. For example, when we placed objects (e.g., spoon, pencil, and cell phone) in front of her, she would unintentionally use her right hand to grasp the object. We also noted that the patient unwillingly felt the clothes she was wearing with her right hand, and, when sitting in her wheelchair, her right hand continuously fumbled with the right armrest of the wheelchair. (2) Other observed behavior included compulsive manipulation of objects. For example, we observed the patient compulsively putting food into her mouth with a spoon using her right hand, even though her mouth was already filled with food. She was unable to refrain from these types of actions. (3) Finally, we observed that the patient often had difficulty with voluntary release of objects from her grasp. Intermanual conflict and denial of ownership of the upper limb were not observed.

Results of the line bisection test with the right and left hands indicated left neglect; displacement from the midpoint was 7.84 and 7.52 mm to the right (cutoff >6.33 mm), respectively.¹⁶ Left agraphia was also observed when the patient was asked to write dictated speech. The writing ability of the right hand was well preserved; however, writing with the left hand was slow and illegible, and proceeded from left to right in a mirror fashion. The patient had right hemiparesis. Her score on the MRC was 4 out of 5 for both the upper and lower right extremities. She also presented with right somatosensory deficit. Tactile and kinesthetic sensations of the right side

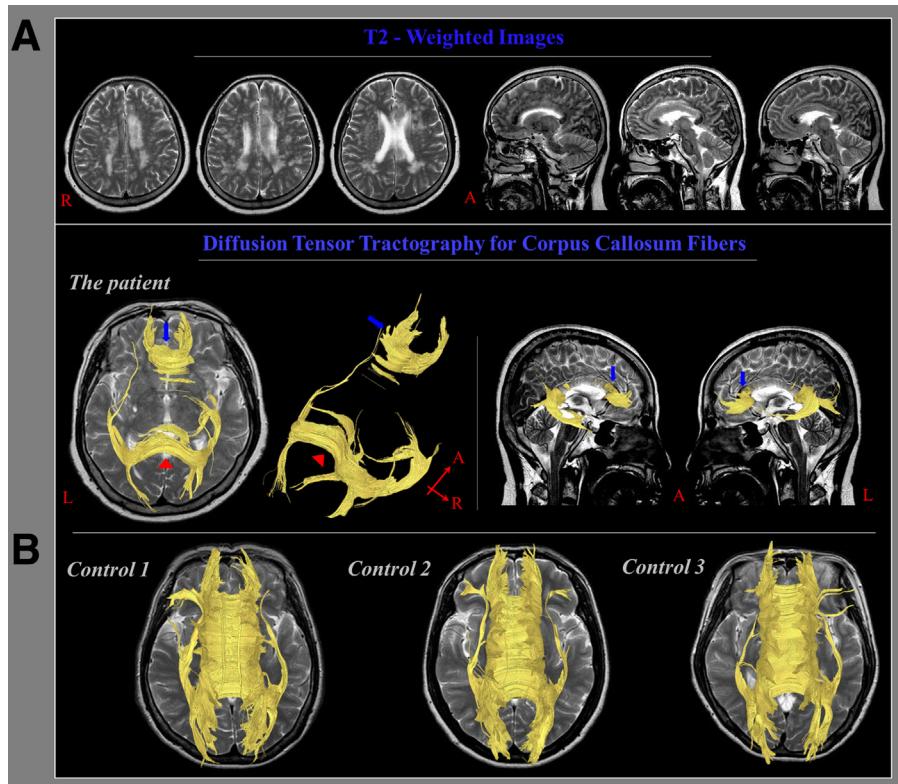


Figure 1. (A) *T*₂-weighted magnetic resonance images at 16 days after infarct. (B) Diffusion tensor tractography of the corpus callosum. Reconstructed corpus callosum fibers in the patient and age-matched controls.

revealed impairment, with scores of 16 (normal 20) and 18 (normal 24) on the Nottingham Sensory Assessment, respectively.¹⁷ Finally, the patient had impaired visual recognition, with .1 percentile on the Seoul neuropsychological screening battery (cutoff <6.68 percentile)¹⁸; however, the other domains, including verbal immediate recall (19.22 percentile), visual immediate recall (10.75 percentile), verbal delayed recall (7.08 percentile), visual delayed recall (9.18 percentile), and verbal recognition (20.61 percentile) did not show significant impairment. Results of tests for ideomotor,¹⁹ ideational apraxia,²⁰ tactile anomia, visual anomia,²¹ and alexia did not indicate significant abnormality. In addition, she did not have problems with language, such as aphasia or dysarthria.

Diffusion Tensor Tractography

We acquired DTI data of the patient 16 days after onset. We also conducted a comparison of DTI data acquired from 3 normal subjects (control 1 was a 72-year-old woman, control 2 was a 74-year-old man, and control 3 was a 72-year-old woman) with data from our patient (Fig 1B). The normal subjects had no history of neurologic or psychiatric disease. A sensitivity encoding head coil on a 1.5-T Philips Gyroscan Intera (Hoffmann-LaRoche Ltd, Best, The Netherlands) with single-shot echo-planar imaging and navigator echo was used for acquisition of DTI data. Imaging parameters were as follows: acquisition matrix 96×96 ; reconstructed to matrix 192×192 matrix; field of view 240×240 mm 2 ; TR 10,726 ms; TE 76 ms; parallel imaging reduction factor (SENSE factor) 2; EPI factor 49; $b = 1000$ s/mm 2 ; NEX = 1; and a slice thickness of 2.5 mm (acquired isotropic voxel size $2.5 \times 2.5 \times 2.5$ mm 3). The fiber assignment continuous tracking algorithm implemented within the DTI task card software (Philips Extended MR WorkSpace 2.6.3) was used in performance of fiber tracking.²² Regions of interest (ROIs) were selected on sagittal fractional anisotropy color maps throughout the entire CC. A fractional anisotropy (FA) threshold of <.3 and a direction threshold of >45° were used in performance of fiber tracking. Fiber tracts passing through the ROIs were designated as tracts of interest. FA values and tract numbers of depicted CC fibers were determined. The FA value is the mean of the individual values obtained from all the voxels, which are included in CC fibers. The tract number represents the total number of finally depicted tracts.

Results

In all of the normal subjects, CC fibers extended bilaterally to the frontal, parietal, and occipitotemporal cortices. However, those in our patient had extensive disruption, with the exception of CC fibers passing through the anterior genu (arrow in Fig 1B) and the posterior splenium (arrowhead in Fig 1B), which were connected bilaterally to the frontal and occipital cortices, respectively. We also

observed small CC fibers in the rostral midbody and isthmus of the CC; however, these were not connected to the cerebral cortices. In addition, the FA value and tract number were lower in the CC fibers of the patient than in those of the normal subjects (patient FA .488, tract number 4322; control 1 FA .504, tract number 17,847; control 2 FA .534, tract number 19,137; control 3 FA .509, tract number 17,711; Fig 1).

Discussion

Our patient presented with various neurologic manifestations, including right AHS, left agraphia, right hemiparesis, right somatosensory deficit, left neglect, and impaired visual recognition. A MRI scan of the brain revealed that the lesions were confined to the CC and its adjacent structures (a part of the left anterior cingulate gyrus); therefore, we believe that the majority of neurologic manifestations in this patient could be attributed to the CC lesions. AHS is recognized as a common neurologic manifestation of CDS. Feinberg et al²³ proposed 2 types of AHS: frontal and callosal. Frontal AHS, which affects the dominant hand, is characterized by forced grasping of objects and impulsive reaching and groping movements toward nearby objects within the visual field. This type of AHS is typically caused by lesions located in the anterior CC and the adjacent frontal lobe. Callosal AHS, resulting from a callosal lesion, is characterized primarily by intermanual conflict affecting the nondominant hand. Considering the clinical manifestation and results of the MRI scan, we think that this patient showed correspondence with frontal AHS. Previous studies of patients with CC lesions^{3-6,24-34} have reported a high variability of CDS symptoms, which were dependent on the location and extent of damage to the CC in each individual. However, even if the location and extent of CC lesions were similar, the manifestation of symptoms could still vary. In general, lesions located in the anterior CC (from the genu to the anterior portion of the CC body) are believed to be responsible for development of frontal AHS,^{24,25} and those located in the posterior CC (from the posterior portion of the CC body to the splenium) were associated with tactile anomia, agraphia, somatosensory deficit, alexia, neglect, visual anomia, and impairment of visual recognition.^{26-28,30,31,33,34} The occurrence of apraxia, callosal AHS, and motor deficit usually follows damage to the CC body.^{3,5,6,24,29,30,32} The symptoms of CDS can be caused by involvement of the anterior CC (frontal AHS), the posterior CC (left agraphia, left neglect, and impaired visual recognition), and the CC body (right hemiparesis). In this patient, because of the presence of lesions in most of the CC, excluding the anterior genu and posterior splenium, all symptoms were observed. Findings on DTT revealed the disruption of most interhemispheric CC fibers in this patient, except for those in the anterior genu and posterior splenium. Also,

our results reveal that FA value and tract number of CC fibers in the patient were lower than those in the normal subjects. FA values represent the degree of directionality of microstructures, such as axons, myelin, and microtubules, and the tract number was determined by counting the number of voxels contained within a neural tract.³⁵⁻³⁷ The deterioration of neuronal microstructure in a neural tract can reduce FAs and tract numbers. Considering these phenomena, we are able to confirm the damage of CC fibers after an infarct of the CC. These DTT findings appear to explain the various CDS symptoms observed in this patient.

Several studies have described CC lesions observed on conventional MRI or CT in patients with CDS and CC lesions after infarct of the CC.^{3-6,25-27,30-34} None of the previously reported studies used DTT for visualization of CC fiber connections. Therefore, this is the first DTT study to show CC disconnection after an infarct of the CC. To the best of our knowledge, only 3 previous studies have reported on DTT findings in patients with CDS. In 2002, Molko et al¹³ described a patient with left hemialexia resulting from a posterior CC lesion after surgery for removal of a hemorrhagic left mesial parietal arteriovenous malformation. Using DTT and functional MRI, they found a CC disconnection between the left fusiform gyrus and the right occipital cortex. In 2005, Le et al¹² reported the disruption of white matter at the posteroinferior margin of the splenium of the CC in a patient with left hemialexia after diffuse axonal injury. In 2012, Jang et al¹¹ reported a patient with hemorrhage of the right pericallosal artery who had various symptoms of CDS, including callosal AHS, left ideomotor apraxia, left ideational apraxia, left tactile anomia, left somatosensory deficit, and right neglect. Disruption of most CC fibers, except for those passing through the splenium toward the occipital cortices, was observed on the patient's DTT scan.

In conclusion, we describe a case involving a patient with CDS after an infarct of the CC. The neurologic manifestations of CDS and DTT findings appear to be well correlated. We believe that DTT is useful for detection of CC lesions in patients with CDS. The current study is limited in that it is a case report. Moreover, because DTT data were acquired in the early stage after an infarct of CC, the DTT finding for CC fibers in our patient could be affected by various factors, such as perilesional edema, volume effect of stroke lesion, or the penumbral condition around the lesion.^{38,39} Therefore, additional studies involving larger numbers of patients with CC infarct after the early stage are warranted.

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