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Case Report

근위축성측삭경화증 환자에서의 myelin water fraction MRI 1예

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Myelin Water Fraction MRI in a Case of Clinically Probable Amyotrophic Lateral Sclerosis

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Amyotrophic lateral sclerosis (ALS) is a progressive motor neuron degenerative disease that clinically manifests both upper and lower motor neuron signs. However, it is unknown where and how the motor neuron degeneration begins, and conflicting hypotheses have been suggested. Recent advanced radiological techniques enable us to look into ALS neuropathology in vivo. Herein, we report a case with upper motor neuron-predominant ALS in whom the results of brain magnetic resonance imaging (MRI) and myelin water fraction MRI suggest axonal degeneration. (Korean J Clin Neurophysiol 2016;18:18-20)

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Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive neurodegenerative disease with heterogeneous clinical manifestations and both upper and lower motor neuron signs. Pathologically, ALS is characterized by motor neuron degeneration and death with gliosis replacing lost neurons.[1] It has not been established where ALS begins. Three hypotheses have been developed pertaining to the site of disease onset in ALS. The 'dying-forward' hypothesis proposes that ALS is mainly a disorder of corticomotoneurons, which connect monosynaptically with anterior horn cells, mediating anterograde degeneration of anterior horn cells. The 'dying-backward' hypothesis proposes that ALS begins in the muscle defect or neuromuscular junctional synaptic denervation and is retrograde transported up the presynaptic axon to the cell body. In contrast with two hypotheses mentioned above, some investigators have proposed that the upper and lower motor neuron degeneration occur independently.[1]

Herein, we report a case with upper motor neuron-predominant ALS supporting the dying-forward hypothesis of ALS pathology, through the corticospinal tract degeneration of brain magnetic resonance imaging (MRI) and myelin water imaging (MWI).

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Case Report

A 48-year-old woman complaining of dysarthria of seven months' standing was hospitalized in the neurology department. Examination revealed spastic dysarthria and minimal right side weakness; however, no fasciculation or muscle wasting was noted. She was hypertonic and hyperreflexic in the ipsilateral limbs. Hoffman's sign and Babinski sign were observed in all limbs. Based on the upper motor neuron-dominant unilateral symptom and signs, we speculated that her condition might arise from chronic stroke. Brain MRI was performed for detecting vascular etiopathogenesis. MRI showed bilateral hyperintensity along the corticospinal tract (CST), which was more prominent at the contralateral side to the symptomatic limb, on T2-weighted and FLAIR images (Fig. 1A, B). No additional lesion was seen that might be provoking her symptoms. From those findings, we suspected the possibility of motor neuron disease. To reveal the lower motor neuron involvement, we performed electromyography. There were signs of acute and chronic denervation with reinnervation in two of the four regions (cervical, lumbosacral), even in the asymptomatic contralateral limbs muscles. Laboratory results including complete blood count, chemistry, electrolytes, and thyroid function tests were all within normal ranges. According to the revised El Escorial criteria,[2] she was diagnosed with clinically probable ALS. On MWI, which is specific for myelin content, the mean myelin quantity was outnumbered in the abnormal CST area than the normal splenium of corpus callosum (Fig. 1C, D). The result of brain MRI and MWI indicated intact myelin with pure axonal degeneration in CST on both sides.

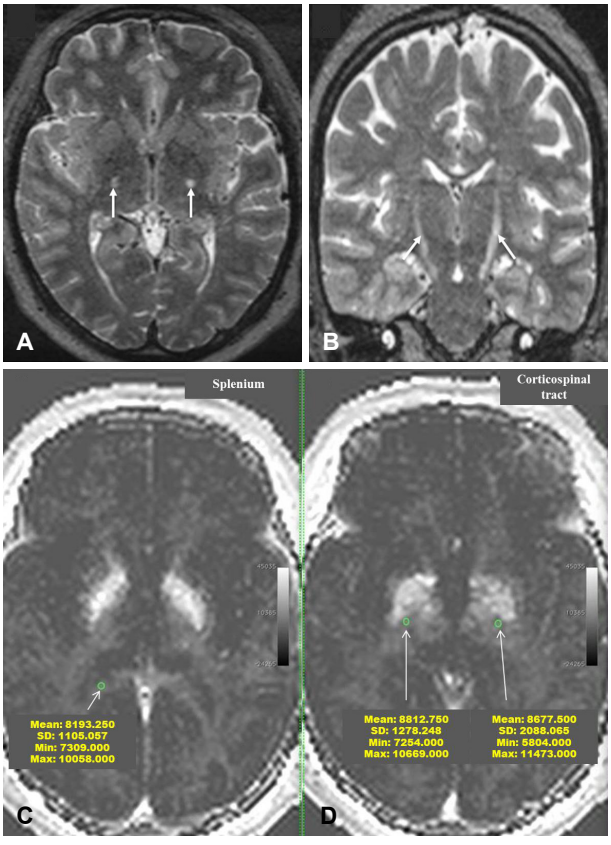

Figure 1. (A, B) Axial (A) and coronal (B) T2-weighted MRI of the brain display bilateral high signal intensity along the corticospinal tract (CST) (white arrows). (C, D) The mean myelin quantity was larger in the CST area than in the adjacent splenium of corpus callosum (right CST = 8,812, left CST = 8,677, splenium = 8,193) (green circles). MRI; magnetic resonance image.

Discussion

ALS involves in both upper and lower motor neurons. Therefore, patients of ALS present spasticity, pathologic reflexes with muscle atrophy, fasciculation, and paralysis at the same myotome.

The pathophysiology of ALS, where it begins from, is not established: whether the motor neuron degeneration begins in the neuronal cell body and proceeds anterograde, or from the muscle and neuromuscular junction and proceeds retrograde.[1] Recent advances in neuroimaging such as diffusion tensor image (DTI), magnetic resonance spectroscopy (MRS) and functional MRI are utilized to reveal upper motor neuron-pathology in ALS.[3] Furthermore, these tools could provide the supportive evidences for dying-forward hypothesis.

A small percentage of ALS patients displayed bilateral CST hyperintensity in the brain MRI.[4] It was thought that cortical motor cells disappear, leading to anterograde axonal loss and gliosis in the CST, and this gliosis results in the bilateral white matter changes sometimes seen in the brain MRI. Some dispute over the clinical meaning of CST hyperintensity exists, because it has been described in healthy subjects,[5] and in patients with other conditions, such as liver cirrhosis.[6] However, several studies suggested that CST hyperintensity was seen more frequent in ALS patients and it reflected the upper motor neuron dysfunction due to pyramidal tract degeneration.[7] Non-conventional studies supporting the 'dying-forward axonal de-

generation' hypothesis include: 1) transmagnetic stimulation studies documenting cortical hyperexcitability in patients with early sporadic ALS,[8] 2) DTI studies identifying abnormal diffusion properties involving CST at the multiple level,[4] 3) 11C-flumazenil PET which indicate reduced inhibitory GABAergic cortical effects, and 4) MRS showed a reduced primary motor cortex N-acetylaspartate to creatine ratio, implicating upper motor neuron dysfunction in the patients of ALS.[4]

MWI shows specificity for myelin content and integrity in both abnormal and normal appearing regions of white matter tissue. It has been used to evaluate myelin content in patients with multiple sclerosis, phenylketonuria, schizophrenia and chronic stroke.[9] However, it has been rarely studied in ALS as a tool exploring white matter alteration. Only one study found that MWI can be used to distinguish primary lateral sclerosis from ALS, and may have value as a marker of extra-motor involvement.[10] Our patient showed a preserved myelin signal in the corresponding CST hyperintensity. Although it is single case, we thought these images resulted from the anterograde primary axonal degeneration, not secondarily due to demyelination, suggesting the possible ALS mechanism of the dying-forward hypothesis. Because of prominent upper motor neuron signs, absence of muscle atrophy and fasciculation and minimal muscle weakness, we did not consider the dying-backward hypothesis. We thought MWI can be complementary to DTI for the evaluation of brain microstructure, although the relationship between white matter status and upper motor neuron dysfunction needs to be further examined.

In conclusion, this case implies the pathophysiology of ALS as a primary 'dying-forward' axonal degeneration by combination of two MRI results, CST degeneration with preserved myelin water content. We suppose to conduct further study with larger ALS subjects to evaluate a role of MWI in ALS research in the future.

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