TEMPORAL CHANGES IN LOWER-LUMBER SPINAL CORD IN EAE MOUSE

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INTRODUCTION

Multiple sclerosis (MS), an inflammatory and demyelinating condition of the central nervous system (CNS), is generally considered as an autoimmune disease in nature. Previous study demonstrated that autoreactive T cells access the CNS via the blood-brain barrier at the dorsal blood vessels of the 5th lumbar spinal cord and induce experimental autoimmune encephalomyelitis (EAE) [1]. Non-invasive monitoring of the spinal cord before/after neuro-inflammation may lead to an understanding of the injury and repair of CNS. MRI of the lower-level spinal cord of mice is challenging because its structure is too thin to visualize *in vivo*, therefore, we need higher sensitivity. This study explored the temporal and spatial profiles monitored by T_2- and diffusion-weighted MRI at the lumber code of EAE mice.

METHODS

EAE induction was performed as described previously [1], in brief, C57BL6/J mice were injected with a MOG peptide in complete Freund's adjuvant followed by intravenous injection of the pertussis toxin. Pathogenic $CD4^+$ T cells from the resulting mice were sorted, and EAE was induced in wild-type C57BL6/J mice via intravenous injection of pathogenic $CD4^+$ T cells. Our model of adoptive transfer closely mimics MS [2] and allows us to detect the signs of delicate changes in the CNS. Mice were weighed and assessed for neurological symptoms using defined clinical scoring methods everyday [3]. MR imaging was performed 5, 7, 9, 12, and 14 days after T cell transfers using a Bruker 11.7 T scanner and a home-made 12-mm diameter transmit/receive surface RF coil. Each measurement of MRI corresponds to phases of precritical (day 5), onset (day 7), peak (day 9), and remission (days 12 and 14) of clinical score. Axial T_2 RARE sequence (T_2WI; TR/TE = 5000/38 ms, number of averages (NA) = 16, matrix = 256 × 256, FOV = 1.5 cm × 1.5 cm, slice thickness = 0.3 mm) and diffusion-weighted imaging (DWI) sequence with transverse MPG (b value = 1600, TR/TE = 7500/20 ms, NA = 2, matrix = 256 × 256, FOV = 1.5 cm × 1.5 cm, slice thickness = 0.3 mm) were acquired at the level of the third to sixth lumbar vertebra. The mice were anaesthetized during imaging with respiratory rate and body temperature monitored in real time. At each measurement, size and signal changes of spinal cord were calculated in multiple MR images.

RESULTS AND DISCUSSION

The lumber spinal cord, especially in 5th lumber code, swelled gradually up to 2-3 times larger than in a precritical period. This alteration in size was correlated with clinical score and inversely correlated with animal weight loss (Fig. 1). In addition, DWI with transverse MPG shows signal reduction in dorsal white matter of the lower level of lumber code in the early phase of EAE (Fig. 2). This increasing of diffusion reverted to be almost normal to the remission phase. Previous research reported that the accumulation of pathogenic T cells was much greater in the dorsal blood vessels of the 5th spinal cord than in the ventral ones. These *in-vivo* MRI results support the hypothesis that autoreactive T cells access the CNS via the blood-brain barrier at the dorsal blood vessels of the lower-lumbar spinal cord in EAE mice [1].

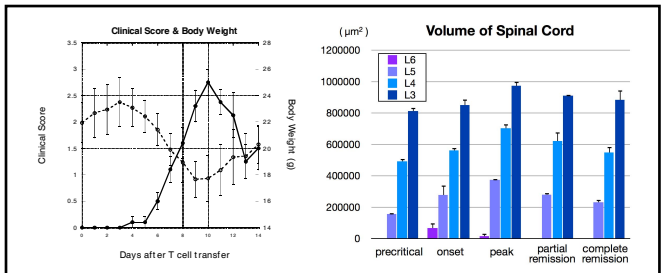

Fig. 1: Clinical score (left; solid line) and animal weight (left; dotted line), and the volume of spinal cord at each lumber level before and after disease progression manifestation (right).

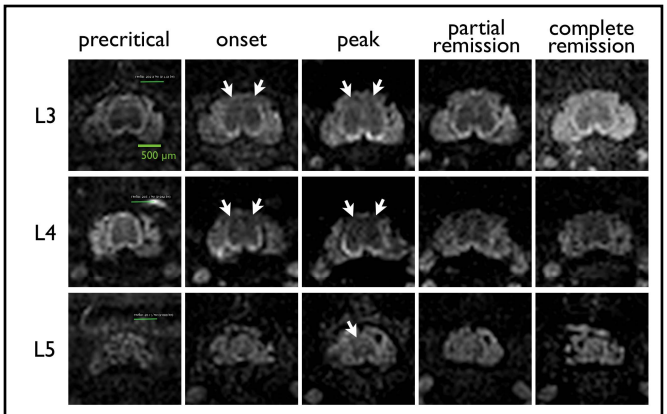

Fig. 2: Representative DWI with transverse MPG. Signal reduction in dorsal white matter was visualized (arrows). These alterations were correlated with neurological symptoms.

CONCLUSION

This study suggests that T_2WI and DWI are sensitive measures of tissue injury and recovery of EAE mouse. High spatial resolution imaging reveals that the swelling occurs around 5th lumber spinal cord in early phase of EAE, and the increasing diffusion occurs locally in dorsal white matter. The swelling and the alteration of diffusion relate to the severity of MS. Our MRI data coincided with an entry site at the dorsal blood vessels of the 5th lumbar cord for T cells into the CNS, so that the changes in MRI attributed to infiltration of T cells and inflammation.

REFERENCES

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