Distinct distribution of microglia/macrophage and dendritic cells in the spinal white matter of amyotrophic lateral sclerosis

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Results-1

Both markers indicated that the number of activated microglia/macrophage in the ALFoc was comparable to that in the corticospinal tract (CST).

Results-2 (novel findings)

The presence of CD11c-positive cells has been rarely documented in ALS spinal white matter (Henkel JS, et al. Neurology, 2004). Treatments of granulocyte-macrophage colony-stimulating factor (GM-CSF) induced mature dendritic cell-like phenotype, CD11c, on the surface of microglia (Acevedo G, et al. J Neurochemistry, 2013). However, it was reported that in the CSF of ALS patients, GM-CSF concentration was not elevated. (Tateishi T et al. J Neuroimmunol, 2010, upper panel). Accordingly, other factors should be taken into account for the presence of CD11c-positive cells in ALS spinal white matter. Another candidate for the presence of CD11c-positive cells is macrophage/monocyte chemoattractant protein-1 (MCP-1/CCL2). MCP-1 is a potent chemoattractant and activating peptide expressed mostly in astrocytes. It attracts CCR2-expressing myeloid dendritic cells, microglia, monocytes, and activated T cells. Thus, MCP-1 is significant for recruitments of immune/inflammatory cells into the central nervous system, and more specifically the recruitment of dendritic cells and monocytes. This mechanism is likely, since MCP-1 concentrations were repeatedly observed to be elevated in ALS patients CSF (Lower panels).

Discussion

1) In ALS spinal white matter, CD68- and Iba-1-positive cells predominated in the corticospinal tracts (CST), while those of CD11c, in the anterolateral funiculus outside the CST (ALFoc).
2) Henkel JS et al. documented the existence of MCP-1 and CD11c-, CD68-, and Iba-positive cells encompassed in the entire ALF of ALS spinal white matter. These data were obtained from 30 slices of 5 ALS patients. Y axes indicate the numbers of CD11c-, CD68, and Iba-1-positive cells (from upper to lower rows, respectively). All X axes indicate the numbers of MCP1-immunopositive cells.

Conclusions

1) The aim of this study is to further expand the significance of infiltrating immune cells in the ALFoc of ALS spinal cord.
2) Henkel JS et al. documented the existence of MCP-1 and CD11c-, CD68-, and Iba-positive cells encompassed in the entire ALF of ALS spinal white matter. These data were obtained from 30 slices of 5 ALS patients. Y axes indicate the numbers of CD11c-, CD68, and Iba-1-positive cells (from upper to lower rows, respectively). All X axes indicate the numbers of MCP1-immunopositive cells.
3) The pathomechanism for varying degree of infiltrating these cells between CST and ALFoc remains to be elucidated.