＜シンポジウム 05―4＞中枢神経の免疫疾患とグリア

Pathogenesis of Neuromyelitis Optica: aquaporin 4 autoimmunity and astrocytopathy

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Recently, a disease-specific antibody was found in the serum from neuromyelitis optica (NMO) patients, and its target antigen was identified as aquaporin-4 (AQP4), mainly expressed in astroglial foot processes. Recent growing evidences have suggested a pathogenic role of AQP4 antibody in NMO.

In our pathological study, the loss of AQP4 was evident in about 90% of NMO lesions, and glial fibrillary acidic protein (GFAP), an astrocyte-specific protein, was also lost in those lesions. In contrast in those lesions, myelin basic protein (MBP)-stained myelinated fibers were relatively preserved. Furthermore, NMO-like lesions develop in transfer EAE following application of purified IgG from NMO patients, which strongly suggests the pathogenic role of AQP4 autoimmunity in NMO. NMO pathology did not occur in young animals with leaky blood brain barrier, but needed T cell-mediated brain inflammation for the development. Absorption of NMO IgG with AQP4-transfected cells was associated with a reduction of NMO pathology. Several in vitro evidences also supported the cytotoxic effect of AQP4 antibody to cultured astrocytes in the presence of compliments.

In our recent clinical cerebrospinal fluid (CSF) biomarker study, the CSF-GFAP levels during relapse in NMO (2,476.6 ± 8,815.0 ng/m*l*) were significantly higher than those in multiple sclerosis (MS) (0.8 ± 0.4 ng/m*l*) and controls (0.7 ± 0.5 ng/m*l*). In contrast, CSF-MBP was not significantly different between NMO and MS. CSF-GFAP in acute phase of NMO strongly correlated with the disability and spinal lesion lengths, and rapidly normalized after treatment. Therefore, astrocytic damage associated with AQP4 autoimmunity is clinically-relevant, primary pathological process in NMO, and is distinct from MS.

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