Anti-aquaporin-4 antibody research update from Kyushu University, Japan

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We sought to elucidate the significance of the anti-aquaporin-4 (AQP4) antibody across the whole spectrum of multiple sclerosis (MS) patients by immunofluorescence technique using a GFP-AQP4 transfected cell line. We attempted to clarify distinctions of neuroimaging and immunological features among anti-AQP4 antibody-positive MS, anti-AQP4 antibody-negative optic-spinal MS and the antibody-negative conventional MS in 113 consecutive patients with clinically definite MS based on Poser criteria[1], 4 idiopathic recurrent transverse myelitis patients, 52 patients with other neurological diseases, and 35 healthy controls. Our test was validated by immunohistochemical staining; we also sent 119 samples to the Mayo Clinic for the same assay and our test was found to 83.3% (15/18) sensitive and 100% specific (101/101).[2]

The anti-AQP4 antibody positivity rate was higher in optic-spinal MS patients (13/48, 27.1%) than in those with conventional MS (3/54, 5.6%), brainstem-spinal form of MS (0/11), other neurological diseases (0/52), and in healthy controls (0/35). The anti-AQP4 antibody was found almost exclusively in females. Multiple logistic analyses revealed that the emergence of the anti-AQP4 antibody was positively associated with higher numbers of exacerbations (1.1 ± 0.6 versus 0.7 ± 0.6 per-annum, OR=6.612, 95%CI = 1.299 to 33.664, p=0.0229), but not with optic-spinal MS or the presence or absence of longitudinal extensive spinal cord lesions (LESCLs). We also found no correlation between the titre of anti-AQP4 antibody with the patients' final EDSS score or with the length of spinal cord lesion.

LESCLs in anti-AQP4 anitbody-positive patients tended to demonstrate a central gray matter pattern involving the mid-thoracic cord; while those in anti-AQP4 antibody-negative optic-spinal MS patients appeared throughout the cervical-to-mid-thoracic cord presenting holocord involvement. LESCLs in anti-AQP4 antibody-negative conventional MS patients showed a more dominant involvement of the cervical cord with a peripheral white matter pattern. Anti-AQP4 antibody-positive MS patients fulfilling definite neuromyelitits optica (NMO) criteria showed a greater frequency of brain lesions and less frequent responses to interferon beta-1b as compared with anti-AQP4 antibody-negative optic-spinal MS patients with LESCLs.

Patients who are positive for either anti-SSA/SSB or antinuclear antibody had higher titre of anti-AQP4 antibody (p=0.0289 and p=0.0338). Comparing with anti-AQP4 antibody-positive MS (n=13) or anti-AQP4 antibody-negative conventional MS patients (n=43), anti-AQP4 antibody-negative optic-spinal MS patients (n=28) showed significantly higher percentages of α-interferon producing CD4+ T cells (p=0.015 and p=0.00002) and greater intracellular α-interferon / interleukin-4 ratio of CD4+ T cells after stimulation with PMA and ionomycin (p>0.05 and p=0.024).

These findings suggested that neuroimaging features such as LESCLs and brain lesions fulfilling McDonald criteria, peripheral blood Th1/Th2 balance, and responses to β-interferon are distinct among anti-AQP4 antibody-positive MS, anti-AQP4 antibody-negative optic-spinal MS, and anti-AQP4 antibody-negative conventional MS patients. However, the presence of intermediate cases among these subtypes suggests that these are a continuum in Japanese patients.

References

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