Debate: aquaporin 4 antibody negative nmosd is a new disease

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In 2007, the term neuromyelitis optica spectrum disorders (NMOsd) was defined to include NMO and limited forms of the disease in the presence of anti-AQP4 antibodies, as these antibodies predict a relapsing course, AQP4 loss and astrocytic injury in CNS lesions.In 2015, new NMOsd criteria required at least one core clinical characteristic (optic neuritis, myelitis, area postrema syndrome, brain stem syndrome, diencephalic clinical syndrome with typical diencephalic lesions and symptomatic cerebral syndrome with typical brain lesions) and AQP4-antibodies, or two core clinical characteristics (one of which should be optic neuri-tis, transverse myelitis or an area postrema clinical syndrome) with specific MRI findings, without AQP4-antibodies.Seronegative and seropositive NMOsd groups have similar phenotypes, and there is not yet neuropathological proof or therapeutic basis distinguishing them. Moreover, some “seronegative” patients may have undetectable AQP4-antibodies as the sensitivity of antibody assays is never 100%. These findings support that AQP4-seronegative NMOsd is a subset of NMOsd. However, clinical differences between seropositive and seronegative NMOsd have been observed, including M/F ratio and likelihood of simultaneous optic neuritis and transverse myelitis. Moreover, other autoantibodies have been identified in some anti-AQP4 seronegative patients, such as anti-MOG and anti-AQP1. Indeed, in an AQP4-seronegative NMOsd patient with MOG-antibodies, increased levels of MBP (marker of myelin injury) but not of GFAP (marker of astrocytic injury, increased in AQP4-seropositive NMOsd) were detected in CSF. These findings support AQP4-seronegative NMOsd as a new disease. Such questions, whether anti-AQP4 seronegative NMOSD is a new disease or not, will be raised and discussed.