

# Loss of aquaporin-4 and GFAP in lesions of neuromyelitis optica: Immunohistochemical study

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**Background:** Neuromyelitis optica (NMO) is an inflammatory disease mainly affecting optic and spinal cords, and was originally described by Devic in 1894. There has been a long controversy as to whether NMO is a variant of multiple sclerosis (MS) or a distinct disease. In Japan and Asian countries, relapsing NMO has been called as optic-spinal form of MS, but we reported in 2002 that optic-spinal MS was heterogeneous disease and comprised both typical NMO and MS with optic spinal presentation.<sup>1</sup> Recently, a highly specific serum autoantibody marker, NMO-IgG, was found in the sera of Caucasian NMO and Japanese optic-spinal MS cases<sup>2</sup>, and the target antigen was identified as the water channel protein aquaporin-4 (AQP4).<sup>3</sup> NMO-IgG has a 58% sensitivity and 100% specificity in optic-spinal MS, and a 73% sensitivity and 91% specificity in NMO.<sup>2</sup> So in NMO and optic-spinal MS, similar autoimmune backgrounds were revealed. Pathologically, humoral immunity such as the perivascular deposition of immunoglobulin and complement together with dilated or hyalinized vessels were the dominant immuno-pathological features in the lesions of NMO.<sup>4</sup> And we at the first time showed the loss of AQP4 in acute inflammatory lesions of NMO.<sup>5,6</sup>

Therefore, in this **presentation**, we focus on immunohistochemical analyses of AQP4 and GFAP in NMO cases to clarify whether the loss of AQP4 immunostaining in lesions commonly occurs in NMO lesions and is a distinctive pathological feature of NMO from MS.

**Methods:** We studied the expression of AQP4 in 26 postmortem cases, 12 of whom had NMO, 6 had MS and the other 8 were normal controls. Four to 7 tissue sections were taken from each patient from the medulla to the thoracic cord. The sections were stained with HE, KB and Bodian stains. Immunohistochemical stains were performed for AQP4, glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), PLP, CD45LCA, IgG, IgM and C9neo.

**Results and discussion:** We found that AQP4 was lost in 60 out of 67 acute or chronic lesions in NMO, but not in MS plaques. Especially in acute perivascular lesions, extensive loss of AQP4 accompanied by decreased GFAP staining was evident, but the myelin basic protein was relatively preserved. These results suggested that impairment of the astrocytic function due to AQP4 antibody may be involved in the pathogenesis of NMO, which is distinct from the primarily demyelinating condition of MS. Other **evidences supporting AQP4** as the target molecule in the pathogenesis of NMO are as follow: (1). NMO lesions commonly occurred in AQP4-rich areas of the central nervous system such as area postrema, hypothalamus or central portion of spinal cord<sup>7,8</sup>; (2). Loss of AQP4 is seen especially in the perivascular region, where the NMO-IgG binds to<sup>5,6,9</sup>; (3). The titre of anti-AQP4 antibody was correlated with disease severity<sup>10</sup>; and (4). The lesions where there was a lack of GFAP were infiltrated by Schwann cells suggesting the disruption of glia limitans.<sup>7,11</sup>

**Conclusion:** We conclude that astrocytic impairment associated with humoral immunity against AQP4 may be primarily involved in the lesion formation in NMO, and this is probably different from that of MS where demyelination is the primary pathology.

## References

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