All pathology in NMO is AQP4-IGG and complement dependent: pro position

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The pathology of lesions in neuromyelitis optica spectrum disorders (NMOSD) with aquaporin-4 IgG has been shown to be necrotic with prominent antibody and complement activation, evidenced by C9neo antigen detection indicating terminal complement activation. While other pathologies are now reported in NMOSD, including diffuse non-lesional astrocyte hypertrophy, and non-lytic lesions without demyelination despite loss of immunoreactive aquaporin-4 and inflammation, the significance of these pathologies remains unclear; they are not clearly associated with the cardinal manifestations of NMOSD, namely optic neuritis and myelitis. Whether or not there are cognitive, emotional or other behavioral phenomena in patients with NMOSD as a result of these pathologies is uncertain and the subject of ongoing study. Experimental models of passively induced NMO by transfer of pathogenic immunoglobulin into rodents clearly establish that in the absence of any one of AQP4 expression (AQP4 knockout mice), AQP4-IgG (use of control IgG) and complement (failure to administer concomitant human complement), pathological changes cannot be produced. Selective complement depletion is highly effective in prevention of NMOSD attacks. It would be more accurate to argue that “all acute attacks of optic neuritis and myelitis in NMOSD are likely AQP4-IgG and complement dependent”, but if these manifestations could be controlled by effective treatment, most patients and physicians would be pleased with the results and would consider that at least 90% of NMOSD has been vanquished.