Introduction

- Neuromyelitis optica (NMO) is an inflammatory disorder of the CNS, the cardinal manifestations of which are optic neuritis (ON) and longitudinally extensive transverse myelitis (LETM). Autoantibodies (NMO-IgG) targeting aquaporin-4 (AQP4) are found in the sera of the majority of patients with NMO.  
- NMO-associated ON is characterized by poor visual outcomes, often resulting in blindness.  
- Studies utilizing optical coherence tomography (OCT) have identified profound retinal axonal and neuronal loss in eyes with a history of NMO-ON, primarily thought to represent sequelae of optic nerve injury.  
- Abnormalities of the retinal vasculature have also been identified in NMO-ON eyes, suggesting that direct retinal injury may also be operant in NMO. Interestingly, AQP4 is highly expressed in the retina by Müller glial cells (the cell bodies of which are located in the inner nuclear layer [INL]), especially in end-feet membranes facing blood vessels.  
- Utilizing high-resolution spectral-domain OCT, we identified retinal morphologic abnormalities in the eyes of NMO patients, namely microcystic macular edema (MME) of the INL, an entity recently reported in a subset of patients with multiple sclerosis.  

Objectives

- To determine the prevalence of MME in NMO and to examine associations with quantitative OCT measures, visual dysfunction and ambulatory disability.

Methods

- 39 patients with NMO-spectrum disorders (30 definite NMO, 1 NMO-IgG (+) ON, 8 NMO-IgG (+) LETM) and 39 age and sex-matched healthy controls (HCs) underwent retinal imaging with spectral-domain Cirrus HD-OCT.
- All macular cube scans were assessed for MME and/or other morphologic abnormalities of the retina and vitreos-retinal interface.
- Muscular cone scans were automatically segmented9 yielding thicknesses of the following retinal layers: 1) macular – retinal nerve fiber layer (RNFL) 2) ganglion cell+inner plexiform layers (GCIP) 3) INL+outer plexiform layer (INL-OPL) 4) outer nuclear layer (ONL).
- Subjects with diabetes, history of ocular surgery/truma, glaucoma or other known ophthalmologic disorders were excluded from the study.
- Eyes within 3 months of acute ON were excluded from quantitative analyses, to minimize the effect of ON-related edema on OCT measurements.
- OCT measures and letter-acuity scores were compared between groups utilizing multivariate mixed-effects linear regression models including age and sex, and accounting for within-subject inter-eye correlations, unless otherwise specified. Other comparisons were performed utilizing chi2, Student’s t-test or Wilcoxon rank-sum test when appropriate.

Results

- MME was identified in 10 of 39 NMO patients (14 of 75 eyes) and none of the healthy controls.
- All patients with MME had a diagnosis of definite NMO.
- MME was exclusively found in eyes with ON history and the prevalence was greater than amongst non-MME eyes of definite NMO or NMO-IgG(+) ON patients (100% vs. 73%; p=0.03)

Discussion

- MME is common in NMO and is associated with severe axonal-neuronal loss and visual disability.
- MME may directly account for poor visual outcomes following NMO-ON or represent a marker of ON severity.
- Pathomechanisms underlying the observed pathology may include a primary retinal process occurring in conjunction with ON (possibly antibody-mediated, targeting AQP4 in the retina), or a retrograde process (trans-synaptic degeneration or retinal glial cell activation secondary to ganglion cell death).

References