Using Optical Coherence Tomography to Diagnose Multiple Sclerosis

New findings suggest a novel in-office imaging technique can help identify MS patients who are likely to have increased disease severity. An investigator explains.

A Q&A with Shiv Saidha, MBBCh, MRCPI

Utilizing a novel retinal segmentation protocol, a new study found that MS patients with predominant macular thinning had significant thinning of both the inner and outer nuclear layers, when compared with other patients with multiple sclerosis (P< =0.001 for both), with relative sparing of the retinal nerve fiber and ganglion cell layers. For the study published in Brain (2011 Feb;134(Pt 2):518-33.), the authors identified 50 patients with MS with predominantly macular thinning (normal retinal nerve fibre-layer thickness with average macular thickness <5th percentile), a previously undescribed optical coherence tomography defined phenotype in MS, and compared them with 48 patients with MS with normal optical coherence tomography findings, 48 patients with MS with abnormal optical coherence tomography findings (typical for multiple sclerosis) and 86 healthy controls.

According to the investigators, “These findings support the possibility of primary retinal pathology in a subset of patients with multiple sclerosis. Multiple sclerosis severity scores were also significantly increased in patients with the macular thinning predominant phenotype, compared with those without this phenotype (n=96, P=0.006).”

Here, lead study author, Shiv Saidha, MBBCh, MRCPI, clinical neuroimmunologist at the Johns Hopkins University School of Medicine, explains how to interpret his team’s study and the novel optical coherence tomography technique they used.

What is OCT and how is it used to diagnose MS?
While MS is traditionally regarded as an inflammatory demyelinating disorder of the central nervous system (CNS), neurodegeneration characterized by axonal and subsequent neuronal loss represents important components of MS pathobiology. These neurodegenerative processes are primarily regarded as sequelae of the underlying demyelination which occurs in MS.

Optical coherence tomography (OCT) is an office-based imaging technique allowing high resolution imaging of the retina and assessment of the neurodegenerative changes that may occur in the eyes of MS patients. In general, these retinal changes in MS are thought to be the result of optic nerve demyelination. Conventional OCT allows quantification of the integrity of the axonal retinal nerve fiber layer, the axons of which coalesce to form the optic nerves behind the eyes. These and the cell bodies (ganglion cells) that give rise to them are thought to degenerate as a consequence of optic neuropathy, although until now in vivo assessment of their cell bodies has not been performed. This is because it requires the use of OCT segmentation techniques which were previously not available.

What did your study find?
In addition to using conventional OCT measures in this study, we also utilized OCT segmentation, enabling quantification of the integrity of discrete neuronal layers within the retina. In so doing we were also able to assess the integrity of the inner retinal neuronal layer (ganglion cell layer) which gives rise to the optic nerve axons, as well as deeper retinal neuronal layers, including those comprised of the rods and cones and also the neurons that relay signals from these toward the optic nerves. The use of this
technology made it possible to localize and quantitatively assess layer-specific retinal changes in the eyes of MS patients included in this study.

One of the main findings in this study is that the MS disease process, at least in a subset of MS patients, may target and afflict the retina directly, independent of optic nerve pathology; in other words, primary retinal pathology may occur as part of the MS disease process. OCT segmentation of the retinal layers in the maculae of a subset of MS patients in this study without a clinical history of acute optic neuritis revealed selective thinning of deeper retinal layers (the inner and outer nuclear layers), with relative sparing of the inner retinal layers (the retinal nerve fiber and ganglion cell layers) in which changes are typically expected and indeed observed following optic neuritis. MS patients with these OCT findings were described in this study as having a macular thinning predominant (MTP) phenotype.

**What are the clinical implications of these findings?**

This novel MS OCT phenotype conceptually challenges conventional thinking of MS as being an exclusively demyelinating disorder, since the retina is an essentially unmyelinated structure, which makes it unique within the central nervous system. Since there is no myelin in the retina, this could change how we think about visual loss in MS and ultimately how we treat the disease. Ongoing studies are addressing whether neuronal pathology in the eyes of MS patients is associated with neuronal pathology in the grey matter structures of MS brains.

From a clinical standpoint, MTP MS patients acquired disability faster than non-MTP MS patients, evidenced by their higher multiple sclerosis severity scale (MSSS) scores. This implies that this MS phenotype in which primary retinal neuronopathy may occur might be a harbinger of a more aggressive form of MS. In addition, MTP MS patients appear to have unique visual symptoms not typically seen following optic neuritis, including photophobia, excessive glare, photopsia, and nyctalopia.

This report suggests that practicing neurologists should consider the possibility that some types of MS may be associated with primary retinal pathology and consider referring these patients to retinal specialists for assessment. Possible causes for this retinal pathology include anti-retinal antibodies, uveitis, or a concomitant autoimmune retinopathy, which may not be specifically associated with only MS. Further work is required to determine the etiology and exact nature of the observed findings in this study.