Retinal Abnormalities in Neurodegenerative Diseases

OCT is increasingly utilized as an imaging tool in patients with neurodegenerative disorders, especially multiple sclerosis.

BY SZILÁRD KISS, MD

Parkinson disease, Alzheimer disease, and multiple sclerosis are progressive neurodegenerative disorders affecting distinctive collections of central nervous system neurons. Despite the progressive nature of these diseases, there are no objective, reliable, noninvasive diagnostic measures for their activity, progression, or response to treatment. In addition to motor and cognitive abnormalities, symptoms in Parkinson, Alzheimer and multiple sclerosis patients often include blurred vision, color vision abnormalities and decreased contrast sensitivity. These visual disturbances may be accompanied by distinctive structural changes within the eye and, in particular, within the retina. The retina, as a direct extension of the central nervous system (CNS), may offer a unique, quantifiable location to noninvasively investigate pathophysiology and to monitor disease activity in these disorders.

A recent literature search on PubMed identified a total of 63 published studies in multiple sclerosis, six in Alzheimer disease, and six in Parkinson disease involving the use of optical coherence tomography (OCT). As a comparison, in the last 10 months alone, there were 161 publications in age-related macular degeneration and 43 in diabetic macular edema dealing specifically with OCT. Most studies in neurodegenerative disorders are led by neurologists, with minimal input from ophthalmologists or retina specialists, with no standardized protocols or quality measures for retinal scanning, in relatively small numbers of patients, with limited control data and inadequate longitudinal follow-up.

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is an autoimmune disorder characterized by progressive axonal degeneration with resultant neurological deterioration. Most patients, at the time of their first clinically apparent symptoms, have occult MRI activity, signifying that sentinel clinical events do not necessarily represent the beginning of the disease process.[1] Optic neuritis (ON) may be a presenting sign of MS or may occur during an exacerbation of the disease. While most patients return to baseline visual acuity, contrast sensitivity and color vision abnormalities may persist, signifying more permanent retinal or optic nerve dysfunction. Anatomic correlates to this lasting dysfunction include optic-disc pallor and focal retinal nerve fiber layer (RNFL) defects as observed on dilated fundus examination.[2]

The first use of OCT in MS, published in 1999, reported a 46% reduction in average RNFL thickness in eyes affected by ON compared with controls and a 28% reduction in MS patients even without history of ON.[3] Since then, several groups have shown a reduction in both RNFL thickness and macular volume in patients with and, interestingly, even without a history of ON.[3] Based on these limited published reports, an expert panel concluded that OCT could be an appropriate adjunct to the diagnosis of MS and may serve as a measure of treatment effects of disease-modifying drugs compared with placebo in patients with MS. However, the same panel cautioned that more data are necessary to determine whether RNFL loss measured by OCT directly correlates with CNS axonal loss in patients with MS.[4]

PARKINSON DISEASE

Parkinson disease (PD) is a progressive neurodegenerative disorder with selective dopaminergic neuronal loss principally in the substantia nigra. The retina also contains dopaminergic neurons that modulate the receptive fields of ganglion cells and PD may have a degenerative effect on these retinal neurons as well.[5] Not surprisingly, in addition to motor dysfunction, PD patients often report decreased vision, dimin-

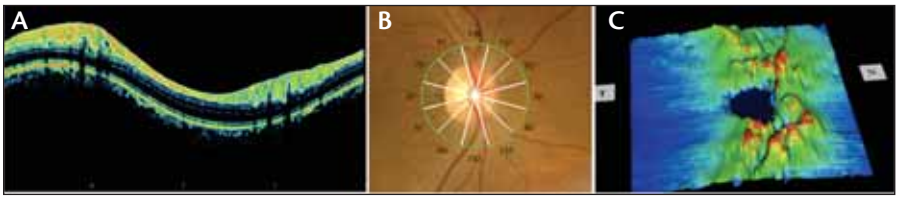

Figure 1. Right eye: Topcon 3D OCT shows the retinal nerve fiber layer (RNFL) thickness surrounding the optic nerve using a glaucoma protocol scan. The RNFL is borderline thinned compared with normal controls.

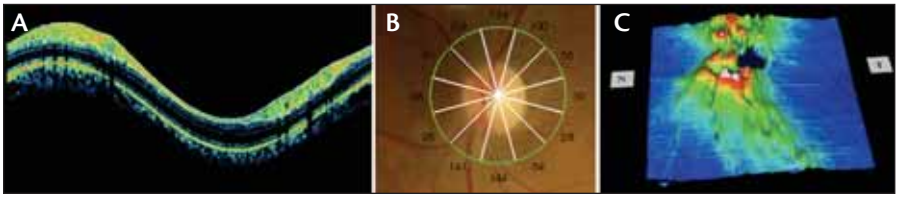

Figure 2. Left eye: Topcon 3D OCT shows the nerve fiber layer thickness surrounding the optic nerve. The RNFL is significantly thinned when compared with the right eye.

ished spatial contrast sensitivity, and dyschromatopsia.[6] There have been several reports of RNFL thinning and decreased macular volume in PD patients compared with controls using the Stratus OCT (Carl Zeiss Meditec, Dublin, CA).[7,8] Given the paucity of OCT data, the relationship between RNFL and macular thickness in patients with PD compared with control patients remains uncertain.

ALZHEIMER DISEASE

Alzheimer disease (AD) is the most common degenerative dementia, causing a progressive decline in cognitive function. Visual disturbances noted in AD patients include decreased or blurred vision and impairment of spatial contrast sensitivity, motion perception, and color discrimination.[9] Reports have attributed this visual dysfunction to damage in the primary visual cortex and to degeneration of the higher cortical area.[10] However, studies have also shown evidence of precortical involvement, with a reduction in the number of retinal ganglion cells and optic nerve axons.[11-15] As a substantiation of retinal dysfunction in AD patients, five published reports have indicated that there may be a reduction of peripapillary and macular RNFL thickness and macular volume.[15]

CASE PRESENTATION

A 38 year-old woman with a history of MS was referred by her neurologist for peripapillary RNFL evaluation. Her visual acuity was 20/20 in each eye. Although she reported some red color desaturation in her left eye, the patient had no afferent pupillary defect. Ocular history was significant for a distant history of ON in the left eye (at least 5 years previous, although the patient was unsure exactly how long ago). The patient underwent a circular scan OCT using the 3D OCT 2000 (Topcon, Paramus, NJ). The scan was centered on the optic nerve as is done in a glaucoma protocol. Despite the patient's lack of visual symptoms, the RNFL in the affected left eye was thinner compared with that in the right eye (Figures 1, 2). The RNFL in the right eye was also borderline thin compared with age-matched controls.

CONCLUSIONS

Although there is an indication of potential clinical utility of OCT in neurodegenerative disorders, especially in MS, at this time it is still premature to use OCT measurements as primary or secondary endpoints in clinical decision-making in these patients. Importantly, observations using the Spectralis OCT (Heidelberg Instruments, Vista, CA) must be confirmed with the newer generation high-resolution spectral-domain systems in larger cohorts, perhaps even in a prospective manner. ■

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