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Enhanced Depth Imaging Optical Coherence Tomography of Optic Nerve Head Drusen

A Comparison of Cases with and without Visual Field Loss

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Purpose: Enhanced depth imaging (EDI) spectral-domain optical coherence tomography (SD OCT) has been recognized as the most sensitive tool to diagnose optic nerve head drusen (ONHD). The relationship between OCT characteristics and visual loss has not been well documented. This study compares EDI SD OCT–determined morphologic characteristics of drusen in eyes with or without visual field (VF) defects.

Design: Descriptive study of patients attending the neuro-ophthalmology service of Moorfields Eye Hospital between January 2013 and October 2014.

Subjects: Patients with diagnosed ONHD and EDI SD OCT imaging of the optic nerve head.

Methods: Eyes with and without VF defects were compared with regard to retinal nerve fiber layer (RNFL) thickness, drusen morphology, size, extent, visibility on funduscopy, ultrasound, and fundus autofluorescence.

Main Outcome Measures: Difference in OCT characteristics of ONHD between patients with or without VF defects.

Results: Of 38 patients, 69 eyes with ONHD were included. Thirty-three eyes had a normal VF with average mean deviation (MD) −0.96 (±1.2) dB and pattern standard deviation (PSD) 1.6 (±0.3) dB (group I), and 36 eyes had VF defects with MD −13.7 (±10.4) dB and PSD 7.2 (±3.6) dB (group II). Mean global RNFL thickness was 62 (±20.9) μm in the latter group and 99.0 (±12.9) μm in group I. In group I, the predominant drusen type was peripapillary drusen, of variable size. In group II, most eyes had confluent ($P < 0.02$) and large (>500 μm; $P < 0.003$) drusen, and drusen were more commonly visible on funduscopy ($P = 0.001$), ultrasound ($P = 0.013$), and autofluorescence ($P = 0.002$). Differences between the 2 groups reached statistical significance in a clustered analysis. RNFL thinning and autofluorescence showed relative sparing of the temporal sector. Sixty-four percent of patients with a VF defect in 1 eye also had a VF defect in their fellow eye.

Conclusions: Drusen size and drusen type as classified by OCT morphologic characteristics are significantly different in patients with or without VF defects. Confluent, large, and autofluorescent drusen were more commonly found in patients with VF defects. These findings may assist in clarifying how drusen give rise to visual loss, which is currently not known. *Ophthalmology 2016;■:1–8 © 2016 by the American Academy of Ophthalmology*

Drusen of the optic disc were first described by Liebrich in 1868.[1,2] Although the clinical picture and associated complications of optic nerve head drusen (ONHD) have been well described since the last century,[3–5] the pathogenesis of ONHD and the mechanism of resultant visual field (VF) loss remain poorly understood. Based on findings on electron microscopy, Tso[6] concluded that drusen are related to axonal degeneration in the optic nerve head. He suggested that intracellular mitochondrial calcification with rupture of axons and subsequent progessive deposition of calcium on the surface of these nidi form calcified microbodies in the extracellular space.

ONHD are known to consist of calcium phospate ($Ca_3[PO_4]_2$), mucoproteins, acid mucopolysaccharides, amino and nucleic acids, and occasionally iron.[2,7] Tso[6] found drusen size to vary between 5 and 1000 μm.

Until recently, imaging of ONHD was limited to fundus autofluorescence (AF), computed tomographic scanning, and ultrasound, with ultrasound being most sensitive.[8] Today, spectral-domain optical coherence tomography (SD OCT), particularly with the application of enhanced depth imaging (EDI) algorithms, allows visualization of ONHD of hitherto unknown resolution.[9]

Generally, EDI SD OCT is known to improve image quality of deeper structures of the posterior pole.[9–11] In particular, it allows imaging of the posterior margin of buried ONHD. EDI SD OCT is now the most sensitive method of detecting ONHD.[9] A number of different morphologic types of ONHD have recently been described using OCT.

Johnson et al[12] identified a druse as a peripapillary "subretinal hyporeflective space" on Stratus OCT, an older

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"time-domain" OCT system. This possibly corresponds to the peripapillary "subretinal mass" with a reflectance similar to that of the inner and outer plexiform layers, as described by Lee et al.[13] Other published morphologic features of ONHD are small isolated or clustered hyperreflective bands[9] and hyporeflectant areas with fine hyperreflective borders within the optic nerve.[9,14]

Based on the published literature and on our own EDI SD OCT findings, we suggest that ONHD can be differentiated into 3 morphologic categories: (1) peripapillary subretinal hyperreflective drusen, (2) granular hyperreflective drusen, and (3) confluent hyporeflective drusen. These 3 morphologic categories will henceforth be referred to as peripapillary, granular, and confluent drusen for ease of reference.

Disc drusen are often associated with VF loss.[5,15,16] Nerve fiber bundle defects, a nasal step, enlargement of the blind spot, and concentric VF constriction have all been described. There is usually preservation of central vision. Retinal nerve fiber layer (RNFL) thinning of patients with ONHD is also well described in the more recent literature.[17–19] Peripapillary RNFL thickness changes are believed to be an indicator of anatomic location (superficial vs. buried) of ONHD and to be associated with VF defects. In a large retrospective cross-sectional study, Malmqvist et al[20] reported more RNFL loss as well as higher frequency and extent of VF defects in patients with superficial ONHD. However, to our knowledge, the relationship between OCT-determined morphologic characteristics of ONHD and visual field loss has not been investigated (see Silverman et al[21] for review).

This study compares EDI SD OCT characteristics of ONHD in patients with or without VF defects.

Methods

This retrospective descriptive study was approved by the institutional review board of Moorfields Eye Hospital and adhered to the tenets of the Declaration of Helsinki. Thirty-eight patients attending the neuro-ophthalmology clinics of Moorfields Eye Hospital between January 2013 and October 2014 were included. Patients with diagnosed optic disc drusen, with available EDI SD OCT imaging of the optic nerve head, were included. Diagnosis of ONHD was based on OCT, because this has been shown to be the most sensitive diagnostic tool.[9] However, ultrasound, AF imaging, or both were obtained in some patients as well. All patients had full ophthalmologic examinations including slit-lamp biomicroscopy, applanation tonometry, dilated fundus examination, color disc photography, and automated perimetry (Humphrey Field Analyzer, Carl Zeiss Meditec, Inc., Dublin, CA; strategy SITA-standard, 24-2 threshold). Eyes with other ophthalmic pathologies known to affect the optic nerve head structure or VF were excluded, as well as fellow eyes without evidence of ONHD. Eyes with and without VF defects were compared with regard to best-corrected visual acuity (Snellen chart), color vision (Ishihara plates), RNFL thickness, ONHD type, ONHD layer, ONHD size, ONHD extent, and visibility on funduscopy, on ultrasound, and on AF.

The definition of VF defects was based on the criteria published by the Idiopathic Intracranial Hypertension Treatment Trial group.[22] An abnormal VF test was defined as having a Glaucoma Hemifield Test (GHT) outside normal limits and/or a pattern standard deviation (PSD) $P < 5\%$.

Table 1. Clinical and Enhanced Depth Imaging Spectral-Domain Optical Coherence Tomography Features of Eyes without (Group I) or with (Group II) Visual Field Defects

	Group I	Group II	*P* Values
Eyes (n)	33	36	
Age	34±11.7	39±14.1	
MD (dB)	−0.96±1.2	−13.7±10.4	<0.001
PSD (dB)	1.64±0.3	7.2±3.6	<0.001
BCVA (Snellen)	1.1±0.2	0.9±0.3	0.003
Ishihara	13/13 plates	11.5/13 plates	0.053
RNFL (μm)	99.0±12.9	62.1±20.9	<0.001
Abnormal RNFL	0/33	25/36	0.004
Predominant ONHD type			0.02
Peripapillary	17/33	5/36	
Granular	6/33	10/36	
Confluent	10/33	21/36	
ONHD types (presence or absence)			
Peripapillary	29/33	29/36	
Granular	19/33	33/36	
Confluent	12/33	28/36	
ONHD layer			0.92
Retinal	26/33	17/36	
Choroidal	1/33	1/36	
Scleral	6/33	18/36	
ONHD size			0.003
Small (<300 μm)	11/33	2/36	
Medium	11/33	6/36	
Large (>500 μm)	11/33	28/36	
ONHD extent			0.001
Minimal	4/33	1/36	
Small	17/33	5/36	
Moderate	4/33	5/36	
Large	6/33	10/36	
Extensive	2/33	15/36	
+ Funduscopy	11/33	30/36	0.001
+ Ultrasound	15/31	30/36	0.013
+ Autofluorescence	11/31	29/34	0.002

+ Autofluorescence = ratio of eyes with autofluorescent ONHD; + Funduscopy = ratio of eyes with visible ONHD (remaining patients had buried ONHD); + Ultrasound = ratio of eyes with gross ONHD on ultrasound; BCVA = best-corrected visual acuity; dB = decibels; Ishihara = color vision; MD = mean deviation; ONHD = optic nerve head drusen; PSD = pattern standard deviation; RNFL = global retinal nerve fiber layer thickness.
In group I, both ultrasound and autofluorescence were not available for 2 eyes each. In group II, autofluorescence was not available for 2 eyes.

Patients included in this study had serial horizontal or vertical volume scans of the optic nerve head with EDI using the Spectralis SD OCT system (Heidelberg Engineering GmbH, Heidelberg, Germany; Eye Explorer Version 1.9.3.0, Acquisition Software Version 5.7.5.0, Viewing Module Version 6.0.7.0). Mean B-scan distance was 87.9 μm (±61 μm standard deviation), mean scan quality 23.6 dB (±5.7), and mean ART (automatic real-time function) 42.7 (±10.4).

The average peripapillary RNFL thickness was automatically obtained using a 12-degree-diameter (3.5 mm) circle centered on the optic disc. All scans were reviewed. Absence of motion artifacts and good centering on the optic disc was checked. Scans also were evaluated in terms of the adequacy of the algorithm for detecting the RNFL. Scans with gross algorithm failure in detecting the retinal layers were excluded, whereas scans with minor algorithm failures over an angle of less than 2 clock hours were manually corrected and included in the present study. Mean RNFL scan quality was 27.4 dB