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Differentiating Mild Papilledema and Buried Optic Nerve Head Drusen Using Spectral Domain Optical Coherence Tomography

Kaushal M. Kulkarni, M.D.^{1,2}, Joshua Pasol, M.D.², Potyra R. Rosa, M.D.², and Byron L. Lam, M.D.²

¹Sharp Rees-Stealy Medical Group, Department of Ophthalmology, San Diego, CA

²Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, FL

Abstract

Purpose—To evaluate the clinical utility of spectral domain optical coherence tomography (SD-OCT) in differentiating mild papilledema from buried optic nerve head drusen (ONHD).

Design—Comparative case series.

Participants—16 eyes of 9 patients with ultrasound-proven buried ONHD, 12 eyes of 6 patients with less than or equal to Frisén grade 2 papilledema due to idiopathic intracranial hypertension. 2 normal fellow eyes of patients with buried ONHD were included.

Methods—A raster scan on the optic nerve and retinal nerve fiber layer (RNFL) thickness analysis was performed on each eye using SD-OCT. Eight eyes underwent enhanced depth imaging SD-OCT. Images were assessed qualitatively and quantitatively to identify differentiating features between buried ONHD and papilledema. Five clinicians trained with a tutorial and masked to the underlying diagnosis reviewed the SD-OCT images of each eye independently to determine the diagnosis.

Main outcome measures—Differences in RNFL thickness in each quadrant between the two groups, and diagnostic accuracy of five independent clinicians based on the SD-OCT images alone.

Results—We found no statistically significant difference in RNFL thickness between buried ONHD and papilledema in any of the four quadrants. Diagnostic accuracy among the readers was low and ranged from 50–64%. The kappa coefficient of agreement among the readers was 0.35 (95% Confidence interval: 0.19, 0.54).

Conclusions—SD-OCT is not clinically reliable in differentiating buried ONHD and mild papilledema.

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Corresponding Author: Kaushal M. Kulkarni, M.D., Sharp Rees-Stealy Medical Group, 10243 Genetic Center Drive, San Diego, CA, 92110; Phone (858) 526-6072, Fax: (858) 526-6073, kaushal.kulkarni@gmail.com.

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Introduction

Optic nerve head drusen (ONHD) are acellular, calcific deposits which typically occur in small, crowded optic discs with abnormal vasculature.¹ When ONHD are on the optic disc surface, they usually can be easily visualized as refractile, beige, rounded deposits on ophthalmoscopy. However, when the drusen are buried within the optic nerve head, the optic discs may appear elevated bilaterally, mimicking optic disc edema due to papilledema or another process causing bilateral disc elevation.

The ability to correctly diagnose buried ONHD and distinguish it from true papilledema is often difficult, yet critical. This is because buried ONHD usually follow a benign natural course, whereas papilledema requires an emergent neurologic workup for potentially life-threatening conditions. Buried ONHD can be identified using various diagnostic modalities, including fundus autofluorescence, fluorescein angiography, and computed tomographic scanning. Currently, B-scan ultrasonography appears to be the most reliable method.²

Unfortunately, B-scan ultrasonography may not be readily and widely available in all clinical settings, and the diagnosis of buried ONHD requires a skilled ultrasonographer and interpreter, particularly in subtle cases. Optical coherence tomography (OCT), on the other hand, is widely available, and has been proposed as a potential diagnostic tool in the diagnosis of ONHD. Several studies have attempted to describe qualitatively the OCT findings in cases of ONHD, including changes in the retinal nerve fiber layer (RNFL) thickness,^{3–8} and a recent study⁹ compared enhanced depth imaging OCT (EDI-OCT) to B-scan ultrasonography in the detection of ONHD.

More importantly, several authors have attempted to assess the utility of OCT in differentiating cases of optic disc edema from ONHD.^{9–13} These studies have included eyes with disc swelling of varying etiologies other than elevated intracranial pressure (ICP), such as ischemic optic neuropathy, uveitis, optic neuritis, diabetic papillopathy, and central retinal vein occlusion. However, in our clinical experience, disc swelling due to these other conditions is rarely confused with ONHD. These studies also have included eyes with clinically visible ONHD, which usually can be accurately identified by careful fundoscopic examination and do not require further workup.

In the majority of patients, the main diagnostic challenge lies in differentiating buried ONHD from mild papilledema. The purpose of this study was to determine if spectral domain OCT (SD-OCT) can be used to realistically differentiate these two conditions in clinical practice.

Methods

The study was approved by the Institutional Review Board of the University of Miami Miller School of Medicine and performed in compliance with the tenets of the Declaration of Helsinki and Health Insurance Portability and Accountability Act. Informed consent was obtained from all patients.

Patients with ultrasound-proven buried ONHD and patients with mild (grade 2 or less using the Frisén staging scheme¹²) disc swelling due to papilledema were recruited from the neuro-ophthalmology service. All patients in the papilledema group met the modified Dandy criteria¹³ for idiopathic intracranial hypertension (IIH), including unremarkable magnetic resonance imaging and magnetic resonance venography of the brain, and cerebrospinal fluid (CSF) pressure of at least 23 cm H₂O in the lateral decubitus position. In addition, all patients in the papilledema underwent B-scan ultrasound with no identifiable ONHD.

Patients with any visible ONHD were excluded from the study. Two patients with both buried ONHD and co-existing papilledema were excluded. Patients were excluded if they had any co-existing retinal or other optic nerve pathology. Patients were also excluded if they had significant systemic disease including hypertension, diabetes, and autoimmune disease.

All patients underwent a complete neuro-ophthalmic examination, automated visual field testing (Humphrey SITA), color fundus photographs, autofluorescence of the optic discs, and B-scan ultrasonography by a certified, professional ultrasonographer.

OCT Protocol

The optic nerve heads of all subjects were assessed with the Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) and the Cirrus High Density SD-OCT (Carl Zeiss Meditec, Dublin, CA) on each eye. For the Spectralis SD-OCT, the device was set to image a 10×15 degree rectangle to obtain a vertical raster scan centered on the optic disc in automatic retinal tracking (ART) mode. This rectangle was scanned with 48 sections, and each section had 25 frames averaged. For the Cirrus SD-OCT, a cube scan consisting of 512 A-scans $\times$ 128 B-Scans centered on the optic disc, a 5-line raster scan centered on the optic disc, and RNFL thickness analysis were performed on each eye.

In addition, four eyes with buried ONHD and four eyes with papilledema underwent Spectralis enhanced depth imaging SD-OCT (EDI-OCT). The device was set to image a 10×15 degree rectangle to obtain a vertical raster scan centered on the optic disc in enhanced depth imaging mode. This rectangle was scanned with 97 sections, and each section had 20 frames averaged.

All of the patients in the buried ONHD group were evaluated with OCT on the same day of diagnosis. In the papilledema group, all patients were evaluated with OCT after confirmation of elevated opening CSF pressure on diagnostic lumbar puncture. All patients in the papilledema group were under treatment with acetazolamide at the time of OCT evaluation. Some patients in the group had demonstrated improvement of their initial level of optic disc edema at the time of OCT evaluation. However, no patient in the group had Frisén grade 3 disc swelling or higher at baseline or at any time during their initial diagnosis or follow-up at our institution.

OCT Assessment and Statistical Analysis

OCT images were assessed qualitatively to identify distinguishing features between eyes with papilledema and buried ONHD. Mean RNFL thickness in all four quadrants was compared between the two groups using the Cirrus OCT data in the right eye.

In addition, OCT images were evaluated by five independent, experienced clinicians (one corneal specialist, one retina specialist, one glaucoma specialist, and two neuro-ophthalmologists). The clinicians (readers) were initially given a tutorial with representative OCT images of both buried ONHD and papilledema based on the qualitative analysis that was done to identify morphologic characteristics of the two groups. The readers then were given the complete set of OCT images through the optic nerve of each eye in the study and were masked to the underlying diagnosis as well as patient identifiers. To make the assessment clinically relevant, they then were asked to choose one of the following management options based on the OCT images through each eye:

1. Clearly identifiable buried ONHD. I would not perform any further diagnostic workup;

2. Optic disc edema (papilledema) without evidence of buried ONDH. I would proceed with further diagnostic workup;
3. Normal-appearing optic nerve on OCT. I would not perform any further diagnostic workup.

The accuracy of each reader was calculated, and the inter-reader agreement was evaluated using a kappa coefficient of agreement, including a 95% confidence interval (CI).

Results

Patient demographics are shown in Table 1.

Qualitative Analysis

In several patients with buried ONHD, a hyper-reflective mass causing focal, irregular elevation of the optic nerve head and adjacent retina was identified on SD-OCT (Figure 1). In several patients with papilledema, optic disc elevation with a smooth contour was identified on SD-OCT, without any underlying hyper-reflective bodies (Figure 2). However, these findings were variable. A specific, focal, hyper-reflective mass was absent in many of the drusen cases. Several papilledema eyes showed hyper-reflective areas underneath the optic disc that mimicked ONHD (Figure 3).

Quantitative Analysis

We found no statistically significant difference in RNFL thickness between the two groups in any of the four quadrants (Table 2). Using the SD-OCT images alone for diagnosis, the accuracy of the 5 readers ranged from 50–64%. The kappa coefficient of agreement among the readers was 0.35 (95% CI: 0.19, 0.54). Overall, 41–75% of eyes with papilledema were mistaken as buried ONHD or normal, whereas 13–56% of eyes with buried ONHD were mistaken as papilledema or normal.

Discussion

Differentiating buried ONHD from papilledema is an important yet difficult diagnostic challenge. Several studies have attempted to describe the OCT findings in ONHD. These studies have reported a wide variability in the reflectivity, shape, size, and location of the drusen on OCT. Some authors^{5–7} have described elevation of the optic nerve head and adjacent retina with round, optically empty spaces and a discrete boundary corresponding to the areas of the drusen, with anterior and posterior lines of reflectance. The hyporeflective nature was thought to represent the homogeneous nature of the drusen. EDI-OCT revealed signal-poor regions surrounded by short, hyper-reflective bands, or isolated/clustered hyper-reflective bands without a signal-poor core.⁸ Other authors¹¹ have found that ONHD can be visualized as a focal hyper-reflective mass with clear margins posterior to the outer plexiform and outer nuclear layers. In our study, we found that buried ONHD, when identifiable on OCT, appeared as a focal, round, hyper-reflective mass causing optic nerve head elevation.

Most authors agree that optic nerve head elevation with a smooth internal contour is seen in eyes with optic disc edema. OCT analysis also has been used to characterize the morphology of the peripapillary RPE and Bruch's membrane in cases of papilledema. Kupersmith et al¹⁶ reported inward deflection of the RPE/BM layer on OCT in eyes with papilledema, presumably due to biomechanical forces in the retrolaminar subarachnoid space. However, in our cases of mild optic disc elevation from papilledema, we did not observe this phenomenon; instead, in several cases of mild papilledema, we observed non-specific hyper-

reflective areas underneath the optic nerve (Figure 3), that were easily confused with drusen; the etiology of these hyper-reflective areas is unclear.

Quantitatively, several studies^{12–15} have reported a difference in measures of the subretinal hyporeflective space and/or RNFL thickness in different quadrants between eyes with disc swelling of various etiologies and eyes with visible or buried ONHD. We found no statistically significant difference in RNFL thickness in any quadrant between eyes with mild papilledema and eyes with buried ONHD. Furthermore, in our study, the ability of five clinicians (including two neuro-ophthalmologists) to differentiate buried ONHD from mild papilledema using the OCT images alone was poor, as was the inter-reader agreement. In particular, several eyes with papilledema were mistaken for buried ONHD or normal, suggesting that a potentially life-threatening condition may be missed.

The difficulty of using OCT to differentiate between mild papilledema and congenitally crowded and anomalous optic nerves has been demonstrated by Karam et al.¹⁷ Similarly, we demonstrate the difficulty of using OCT to differentiate between mild papilledema and buried ONHD. Therefore, in cases where the differentiation between these two conditions is uncertain, B-scan ultrasonography should be performed if available, and if no calcified buried ONHD are identified, one should proceed with appropriate neurologic workup as clinically indicated.

The limitations of this study include the small sample size, lack of widely accepted and standardized morphologic criteria for identifying buried ONHD and papilledema on OCT, and difference in timing of the OCT evaluation between the study groups (ie., initial visit in the buried ONHD group vs. follow-up period while on treatment in the papilledema group).

At this time, whether or not ONHD appear as a hyper-reflective or hypo-reflective space on OCT is still unclear.¹⁸ The variable appearance of ONHD on OCT may be related to variable composition and anatomical location. It is likely that surface drusen will appear as a hypo-reflective space on OCT due to a shadowing effect, with anterior and posterior lines of reflectance, whereas buried drusen, as shown in the present study, will appear as a hyper-reflective mass.

To the best of our knowledge, this is the first study to investigate specifically the role of SD-OCT in differentiating mild papilledema and buried ONHD in a clinical setting. This remains an important but difficult diagnostic challenge. At the present time, OCT alone is unreliable in differentiating these two conditions.

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Figure 1. Buried optic nerve head drusen. (A) Right and (B) Left eyes demonstrating a focal, round, hyper-reflective mass causing nasal optic disc elevation with an irregular contour (arrows).

Figure 2. Papilledema. (A) Right and (B) left eyes demonstrating a smooth elevation of the optic disc without underlying hyper-reflective bodies causing elevation.

Figure 3. Papilledema. Irregular optic nerve contour with hyper-reflective areas mimicking buried optic nerve head drusen.

Table 1

Patient demographics.

	Buried ONHD	Papilledema	p-value
Number of patients	9	6	
Number of eyes	16	12	
# (SD) Female	5 (55.5%)	6 (100%)	0.1 *
Mean (SD) age	19.8 (12.8)	27.8 (21.4)	0.9 **

* Fisher exact test;

** t-test;

Optic Nerve Head Drusen (ONHD); Standard deviation (SD)

Table 2

Mean (SD) retinal nerve fiber layer thickness by quadrant.

Quadrant	Buried ONHD	Papilledema	p-value*
Superior	137.2 (48.2)	177.6 (81.4)	0.25
Nasal	77.2 (20.3)	132.8 (84.2)	0.17
Inferior	139.5 (28.0)	205.8 (113.5)	0.22
Temporal	77.1 (12.6)	83.1 (15.5)	0.42

*
t-test;

Optic Nerve Head Drusen (ONHD); Standard deviation (SD)