Characterization of Punctate Inner Choroidopathy Using Enhanced Depth Imaging Optical Coherence Tomography

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Purpose: To perform qualitative and quantitative analyses of retinal and choroidal morphology in patients with punctate inner choroidopathy (PIC) using enhanced depth imaging optical coherence tomography (EDI-OCT).

Design: Cross-sectional, consecutive series.

Participants: A total of 2242 patients attending 2 tertiary referral uveitis clinics at Moorfields Eye Hospital were screened; 46 patients with PIC diagnosis were identified, and 35 eyes (35 patients) had clinically inactive PIC had EDI-OCT images that met the inclusion criteria.

Methods: Punctate inner choroidopathy lesions were qualitatively assessed for retinal features, such as (1) focal elevation of the retinal pigment epithelium (RPE), (2) focal atrophy of the outer retina/RPE, and (3) presence of sub-RPE hyperreflective deposits and choroidal features: (a) presence of focal hyperreflective dots in the inner choroid and (b) focal thinning of the choroid adjacent to PIC lesions. Quantitative analyses of the retina, choroid, and choroidal sublayers were performed, and associations with clinical and demographic data were examined.

Main Outcome Measures: Prevalence of each lesion pattern and thickness of retinal and choroidal layers.

Results: A total of 90 discrete PIC lesions were captured; 46.6% of PIC lesions consisted of focal atrophy of the outer retina and RPE; 34.4% consisted of sub-RPE hyperreflective deposits; and 18.8% consisted of localized RPE elevation with underlying hyporeflective space. Focal hyperreflective dots were seen in the inner choroid of 68.5% of patients, with 17.1% of eyes presenting focal choroidal thinning underlying PIC lesions. By excluding high myopes, patients with "atypical" PIC had reduced retinal thickness compared with patients with "typical" PIC (246.65±30.2 vs. 270.05±24.6 μm; $P = 0.04$), and greater disease duration was associated with decreases in retinal thickness ($r = -0.53$; $P = 0.01$). A significant correlation was observed between best-corrected visual acuity and foveal retinal thickness ($r = -0.40$; $P = 0.03$).

Conclusions: In a large series of patients with clinically inactive PIC, one fifth of the lesions analyzed revealed RPE elevation with underlying hyporeflective space, described before as a sign of activity and suggesting sub-clinical inflammation. Retinal thickness seems to be associated with disease type and duration of disease in non—highly myopic eyes. Improved visualization of the inner choroid using EDI-OCT may allow noninvasive assessment of inflammatory status. *Ophthalmology 2014;■:1—8 © 2014 by the American Academy of Ophthalmology.*

Supplemental material is available at www.aaojournal.org.

Punctate inner choroidopathy (PIC), a disease that typically affects young myopic women, is characterized by the development of multiple, small, yellow-white spots in the posterior pole of each eye.[1—3] These "PIC lesions" are thought to occur at the level of the inner choroid and retinal pigment epithelium (RPE) and develop in the absence of clinically apparent intraocular inflammation. After a few weeks, these acute PIC lesions resolve, leaving atrophic spots with variable pigmentation. In many patients, such resolution leads to improvement or resolution of visual symptoms. However, in approximately 40% of patients, more severe visual loss subsequently occurs, primarily due to development of choroidal neovascularization (CNV).[1—4]

In recent years, the advent of intravitreal anti-angiogenic therapies has greatly improved the treatment options for patients with PIC who develop CNV.[4—9] Despite this, the underlying pathophysiology of the disorder remains poorly understood. For example, during the acute phase, patients often have photopsia and visual field defects out of proportion to lesion size and extent,[1,10] thus suggesting the presence of more widespread disease than is clinically evident (in fact, widespread focal areas of choroidal hypofluorescence may be seen on indocyanine green angiography).[11] Furthermore, in the continued absence of clinicopathologic correlative studies, the nature of the acute PIC lesions—and their role in CNV development—remains unclear (on fluorescein

angiography, these lesions show early hyperfluorescence with late staining).[3] However, recent advances in optical coherence tomography (OCT) imaging offer some exciting opportunities to address these issues.

In patients with uveitic disease, OCT is most commonly used for the evaluation of cystoid macular edema,[12,13] although its use for diagnosis and phenotyping has increased in recent years.[14] A recent case report described the evolution of an acute multifocal choroiditis without inflammation that was PIC-like.[15] Despite this, the OCT features of PIC have not been extensively evaluated. For the most part, the use of OCT in PIC studies has been restricted to assessment of treatment response in patients with CNV.[5,7,16] More recently, a small number of studies have attempted to evaluate PIC lesion characteristics in the absence of CNV.[17–19] Although these studies have used the latest generation of spectral domain OCT technology, the rarity of the disease means that their patient numbers are small (i.e., case reports or small case series). Furthermore, as a result of limitations with conventional OCT scanning, these studies have been unable to comprehensively evaluate disease features of the choroid. Given that PIC has long been regarded as a disease of the inner choroid—thus the name—this represents a significant shortcoming. In 2008, however, Spaide et al,[20] described a method by which OCT scanning protocols could be modified to permit direct visualization of the choroid, so-called enhanced depth imaging (EDI) OCT.[20] Since this seminal work, EDI-OCT has been used to evaluate the choroid in a variety of conditions, with examples including high myopia and Vogt-Koyanagi-Harada (VKH) disease.[21,22]

In this report, we describe the use of EDI-OCT to perform an enhanced characterization of morphologic abnormalities in a large cohort of patients with PIC. Furthermore, we apply customized image analysis software to perform quantitative analysis of retinal and choroidal thickness in this cohort of patients with PIC. To avoid bias in the assessment and interpretation of retinal and choroidal parameters in EDI-OCT scans, only patients with clinically inactive PIC were included in the study.

Methods

Inclusion Criteria and Clinical Demographic Data

Clinical and imaging data were collected retrospectively from patients attending 2 tertiary referral uveitis clinics (M.C.W., C.E.P.) over a 5-month period. Patients with a clinical diagnosis of PIC who had undergone EDI-OCT according to a set protocol were included. The criteria used for the diagnosis of PIC at Moorfields Eye Hospital have been described in detail elsewhere.[2] Briefly, eyes with "typical" PIC had predominantly small lesions confined to the vascular arcades, whereas those eyes with "atypical" PIC demonstrated larger lesions with a peripapillary distribution.

Clinical and demographic data were obtained from patient records and included age, sex, refraction (high myopia was defined as ≥−6 diopters [D]), best-corrected visual acuity (BCVA), type of disease, disease duration, disease activity, current systemic treatment, previous intravitreal treatments with anti−vascular endothelial growth factor drugs, and history of CNV. This study was approved by the local ethics committee for Moorfields Eye Hospital and was conducted in adherence to the tenets set forth in the Declaration of Helsinki.

Enhanced Depth Imaging-Optical Coherence Tomography Image Acquisition Protocol

All OCT image sets were acquired using the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) with custom EDI scanning protocols. This device allows for near infrared (NIR) fundus photographs, with a 55° field of view, to be obtained simultaneously with registered OCT images. Each EDI-OCT image set consisted of 7 OCT B-scans obtained in a 20°×5° horizontal raster pattern centered in the fovea; each individual B-scan was generated from 50 averaged scans (Fig 1, available at www.aaojournal.org). For inclusion in the study, all OCT image sets had to be of sufficient quality to allow visualization of the retinal and choroidal layers for qualitative and quantitative analyses. In the case of the accompanying NIR fundal images, inclusion required the optic disc and vasculature to be in optimal confocal plane with well-defined edges.

Image Analysis

Qualitative Analysis. The number of visible PIC lesions was then counted using macula-centered NIR fundal images (55° field of view). Only those lesions that were included in the 7 raster OCT scans covering the 20°×5° scanned area were selected for analysis. The OCT lesions that could be interpreted as previously active CNV were classified as "definitely CNV" or "questionably CNV"; were correlated with previous clinical records, color fundus photographs, and fluorescein angiography images; and were excluded from qualitative analysis. Location of definite CNV lesions was addressed with these clinical data as subfoveal, juxtafoveal, and extrafoveal for subgroup analysis purposes. Each PIC lesion included in OCT image sets was then evaluated for the following changes in retinal morphology: (1) focal elevation of the RPE (with underlying hyporeflective space between the RPE and Bruch's membrane and increased penetration of light through the inner choroid), (2) focal atrophy of the outer retina/RPE, and (3) presence of sub-RPE deposits (with hyperreflective signal within the lesion). These retinal features have been described in OCT studies of PIC.[17–19] Choroidal morphology was then assessed, including (1) presence of focal hyperreflective dots in the inner choroid and (2) focal thinning of the choroid adjacent to PIC lesions. No choroidal features have been consistently reported in OCT in patients with PIC. Examples of each retinal and choroidal morphologic feature are illustrated in Figure 2.

Quantitative Analysis. Quantitative analysis of EDI-OCT images was performed using custom software (OCTOR; Doheny Image Reading Center, Los Angeles, CA). This software first allows manual delineation of any morphologic compartment of interest and then provides detailed quantitative analysis of this compartment. Its use has been described and validated in previous reports.[23–26] For the purposes of this study, boundaries for the neurosensory retina, RPE plus subretinal deposits, and choroid were manually segmented in the 7-line raster EDI-OCT scans covering a 20°×5° area centered in the foveal region (Fig 3B). The choroidal layer was further subdivided into Haller's large vessel and Sattler's medium vessel layers (on OCT, the walls of blood vessels appear hyperreflective, and their lumens appear hyporeflective) (Fig 3C). Haller's large vessel layer was defined as a space consisting of large hyporeflective areas (where the luminal-to-vessel wall ratio is >50%). The outer boundary of this space is the choroidal-scleral junction, and the