Original Research

Pathognomonic macular ripples are revealed by polarized infrared retinal imaging

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Impact statement

Fovea plana is a condition characterized by the partial or complete absence of the foveal pit. Presently, the diagnosis is made upon inspection of the foveal architecture on optical coherence tomography imaging. However, because fovea plana is commonly associated with nystagmus, not all patients can achieve the fixation necessary to generate a high-quality scan. In this study, we demonstrate that the use of polarized scanning laser ophthalmoscopy reveals a pathognomonic macular ripple sign in patients with fovea plana. This imaging strategy can be used to promptly screen for the condition.

Abstract

A pathognomonic macular ripple sign has been reported with scanning laser ophthalmoscopy images in patients with foveal hypoplasia, though the optical basis of this sign is presently unknown. Here we present a case series of seven individuals with foveal hypoplasia (based on spectral domain optical coherence tomography). Each patient underwent infrared scanning laser ophthalmoscopy retinal imaging in both eyes, acquired with and without a polarization filter and assessment for a ripple-like effect in the fovea. On imaging, macular ripples were present in all eyes with foveal hypoplasia when using a polarization filter, but not when imaged without the filter. We conclude that the macular ripple sign is an imaging artifact attributable to the unique pattern of phase retardation of the Henle fiber layer in the setting of foveal hypoplasia. By utilizing a polarization filter with retinal photography, this feature can be exploited to promptly identify foveal hypoplasia in settings where OCT is not possible due to nystagmus.

Keywords: Polarization, scanning laser ophthalmoscopy, foveal hypoplasia, fovea plana

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Introduction

The complete or partial absence of the foveal pit is anatomically termed foveal hypoplasia, a finding commonly observed in conditions such as albinism, aniridia, and retinopathy of prematurity. Foveal hypoplasia is usually diagnosed by assessing pit morphology using optical coherence tomography (OCT), although this may be complicated in some patients by nystagmus or poor cooperation.[1]

It has previously been shown that the use of scanning laser ophthalmoscopy with infrared reflectance reveals a concentric ring pattern in the macula of patients with foveal hypoplasia.[2] This sign is a valuable clinical tool because it is non-invasive, simple to identify, and appears to be pathognomonic; however, the basis of this sign is presently unknown.

Concentric macular rings are evident in retinal images collected with the Heidelberg HRA2 (Heidelberg Engineering Inc., Heidelberg, Germany) and not the Spectralis HRA. How the HRA2 elicits this finding is unknown. A clue was suggested to us by differences in the optical layout of the HRA2 compared to the Spectralis HRA. In particular, the HRA2 includes a polarization filter within the emitted path of light; this filter is absent in the

Spectralis HRA. Curiously, the bowtie macular reflex is similarly elicited in normal retinas via polarization.[3] Hence, we hypothesized that the macular ripple sign is a polarization-specific finding in foveal hypoplasia. We tested this hypothesis by imaging patients with foveal hypoplasia in the presence and absence of a polarization filter. Herein, we demonstrate that the macular ripple sign can be generated in patients with foveal hypoplasia by applying a polarization filter to infrared scanning laser ophthalmoscopy.

Materials and methods

Design and execution of this investigation were in adherence with the tenets of the Declaration of Helsinki. This study was approved by the Institutional Review Board at the University of Illinois at Chicago and written informed consent was obtained from each patient or their appropriate adult guardian.

We retrospectively identified patients with foveal hypoplasia based on clinical diagnosis and the absence of a foveal depression on spectral domain OCT (SD-OCT). Severe nystagmus precluding SD-OCT acquisition was an exclusion criterion. Patients deemed eligible for the study via initial medical record screening were then prospectively recruited for examination and imaging. One normally sighted individual without known foveal hypoplasia was also recruited and imaged for comparison.

All subjects underwent visual acuity testing, ocular motility assessment for the presence of nystagmus, and dilated retinal examination. Thereafter, each study participant underwent imaging by infrared scanning laser ophthalmoscopy, infrared scanning laser ophthalmoscopy with a polarization filter, and SD-OCT. Infrared images were taken with the Spectralis HRA+OCT with OCT2 (Heidelberg Engineering Inc., Heidelberg, Germany), a confocal laser scanning system that uses a diode laser at 830 nm wavelength for infrared imaging. A 55° objective lens was used for all infrared scanning laser ophthalmoscopy images collected in this study. A linear polarization filter in the incoming path of light was added or removed by changing the filter lever position on the side of the instrument (Figure 1). The tracking feature was disabled. SD-OCT images were acquired using the HRA+OCT with the 30° objective lens. Degree of foveal hypoplasia was graded according to the modified Thomas scale.[4]

Figure 1. The Heidelberg Spectralis HRA+OCT filter lever wheel includes a polarization filter when in the "P" position. (A color version of this figure is available in the online journal.)

Results

A total of 14 eyes from 7 patients with foveal hypoplasia were included in the study (Table 1). The median age of the patients was 15 years (range 6–48 years), and 3 (43%) were male. A clinical diagnosis of oculocutaneous albinism was present in all individuals. Mild or moderate nystagmus was present in five patients (71%). The most common foveal hypoplasia grade by modified Thomas scale[4] was 1 (6 of 7; 86%), followed by 2 (1 of 7; 14%). In the absence of the polarization filter, infrared images of each eye were unremarkable (Figure 2(c) and (d)). With the addition of the polarization filter, infrared images of each eye in the

Table 1. Demographic information of the study participants.

Age, years	Sex	Diagnosis	Foveal hypoplasia grade	Visual acuity[a] OS	Visual acuity[a] OD	Nystagmus
7	M	OCA	1	20/60	20/60	Absent
6	M	OCA	2	20/35	20/35	Present
9	F	OCA	1	20/30	20/30	Absent
36	F	OCA	1	20/30	20/25	Present
29	F	OCA	1	20/20	20/30	Present
48	F	OCA	1	20/25	20/30	Present
15	M	OCA	1	20/25	20/25	Present

M: male; F: female; OCA: oculocutaneous albinism.
[a]Visual acuity reported in Snellen equivalents.

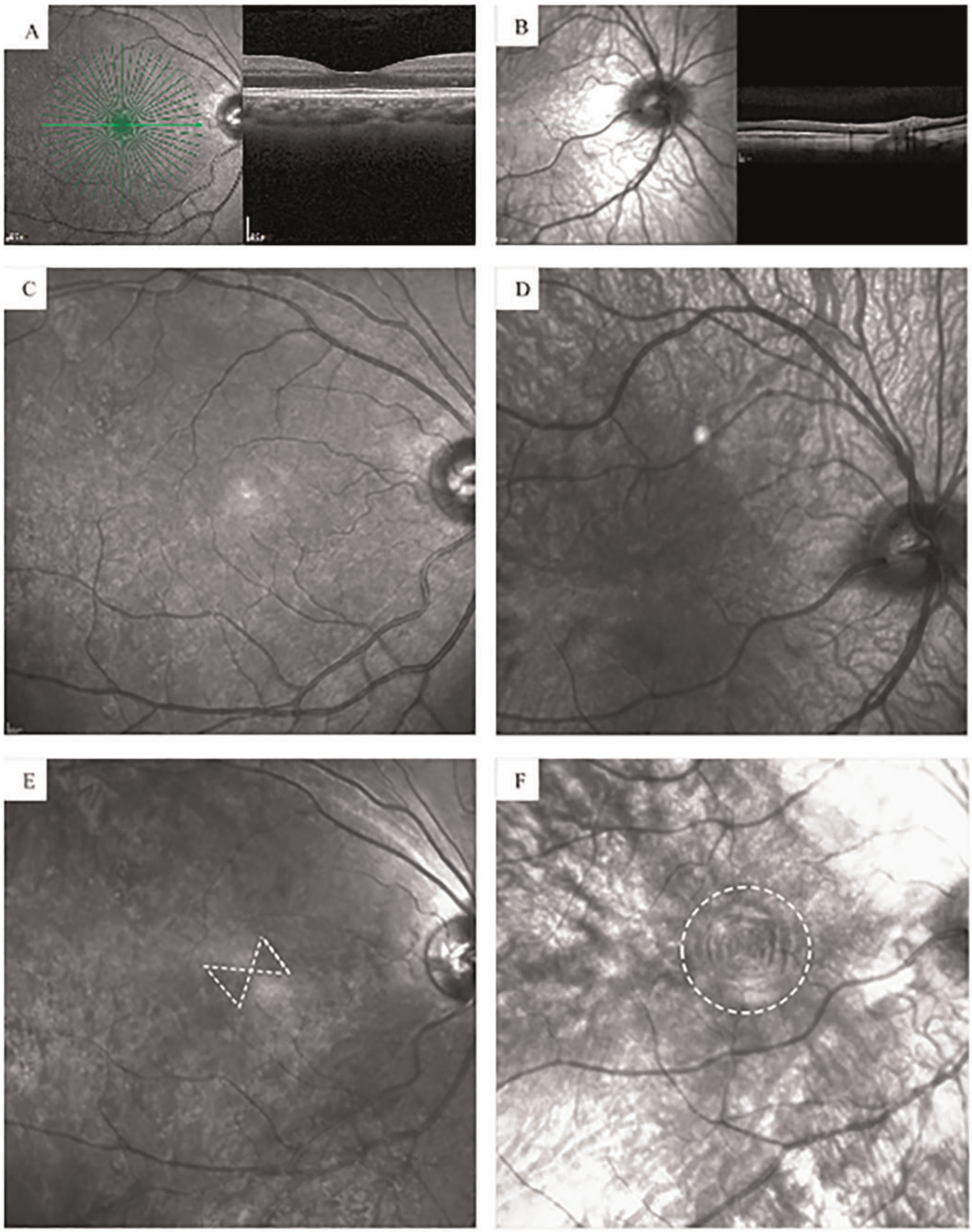

Figure 2. (a) SD-OCT of a normal eye displays a foveal pit. (b) Characteristic lack of a foveal pit is observed in a representative patient with foveal hypoplasia. (c) Infrared image of the control eye without polarization filter displays no sign. (d) Infrared image in foveal hypoplasia displays no sign in the absence of the polarization filter. (e) Bowtie reflex (dashed lines) observed in the normal eye with a polarization filter. (f) Infrared with polarization filter elicits a macular ripple pattern (dashed circle) in foveal hypoplasia. (A color version of this figure is available in the online journal.)

presence of the polarization filter revealed a bowtie reflex in the normal eyes and macular ripples in all 14 eyes with foveal hypoplasia (Figure 2(e) and (f)). In 14 of 14 eyes, presence of the macular ripples sign was completely reversible with the removal of the polarization filter, consistent with the test-retest phenomenon.

Discussion

Use of confocal infrared scanning laser ophthalmoscopy in patients with albinism was first reported by Cornish *et al.*, who noted the appearance of concentric macular rings on images captured by the HRA2; thereafter, macular ripples were observed on ultra-widefield fundus imaging using the Optos (Optos PLC, Dunfermline, United Kingdom) in a large retrospective analysis of 32 patients with varying underlying etiologies of foveal hypoplasia.[4] Although the macular ripples sign was present in all patients in both of these studies, neither study demonstrated the presence of the sign on near-infrared reflectance imaging with the Spectralis. Based on the optical configurations of each of these respective instruments, we hypothesized that the elicitation of the sign is dependent upon the use of polarized light. To this end, we captured infrared retinal images in a series of seven patients with foveal hypoplasia and demonstrated that the addition of a polarizing filter reliably reproduces and is required for the macular ripple sign.

Our present finding that the elicitation of the ripples sign in foveal hypoplasia is dependent upon polarization is consistent with the hypothesis that the sign is dependent upon the phenomenon of form birefringence.[2] When a beam of polarized light enters the retina, the birefringence induces a phase shift known as retardation.[5] In healthy individuals, infrared fundus imaging reveals a characteristic bow-tie reflex that is believed to result from the birefringence of the cornea, Henle fiber layer, and retinal nerve fiber layer (Figure 2(e)).[6,7] The persistence of concentric macular ripples after compensation for corneal birefringence suggests that corneal birefringence does not play a role in causing macular ripples.[2]

Cense *et al.*[8] used polarization-sensitive OCT (PS-OCT) to measure the phase retardation induced by the Henle fiber layer. The phase retardation is oriented in an annular bow-tie shape that is consistent with this layer's radially oriented photoreceptor axons. In eyes with distortion of the normal Henle fiber layer architecture, either due to foveal hypoplasia or epiretinal membrane, studies using en face OCT have revealed concentric rings that were not present in any other layer,[9,10] suggesting that the macular ripple sign is attributable primarily to the Henle fiber layer. This was later corroborated by a series of en face OCT images in 28 eyes with foveal hypoplasia, which revealed concentric rings surrounding the incipient fovea that were exclusive to the depth of the Henle fiber layer, rather than at any other layer.[5] These birefringent properties of the Henle fiber layer have also been proposed as the mechanism by which Haidinger brushes are visualized.[11,12]

There are practical implications of the macular ripple sign. Despite the broad applicability and ubiquity of OCT in clinical practice, acquiring an OCT through the foveal center is difficult in patients with severe nystagmus due to the lack of fixation necessary to generate a high-resolution scan. The presence of the ripple sign is independent of nystagmus, visual acuity,[2] and foveal hypoplasia grade.[5] Importantly, the finding that the ripple sign is present in a wide range of foveal hypoplasia grades suggests that it is not unique to any specific severity; the majority of individuals in our cohort had grade 1, indicating mild foveal hypoplasia. The ripple sign has been described in patients with both congenital and acquired etiologies of foveal hypoplasia.[5] Our study indicates that in patients with suspected foveal hypoplasia for whom OCT acquisition may be difficult, screening for the condition can be accomplished more easily with polarized fundus imaging.

The original Heidelberg HRA2 features both a polarization filter and a quarter-wave plate (to convert linear to circular polarized light), similar to the Optos, which features a circular polarization filter.[3] Conversely, the original Heidelberg Spectralis HRA+OCT includes neither the polarization filter nor the quarter-wave plate, resulting in absent polarization when the filter is not set to the "P" position. Previously, the macular ripple sign was observed in images taken with the HRA2 or the Optos, but not the Spectralis HRA+OCT.[2,5,10] Our finding that the macular ripple sign is dependent on polarized light provides an explanation for this observation. Clinicians with access to instruments that feature polarized fundus photography can elicit the pathognomonic macular ripple sign as a diagnostic alternative to OCT in patients with suspected foveal hypoplasia.

AUTHORS' CONTRIBUTIONS

DA, XY, and MAG participated in the design of the study; DA, PPB, FTC, NZ, JC, NW, PLD, GAF, and MAG participated in the recruitment of study participants; NZ, JC, NW, and MAG participated in data collection; DA, FTC, XY, and MAG interpreted the study results and analyzed the data; DA, PPB and MAG drafted the initial manuscript; FTC, JC, and GAF critically revised the manuscript; MAG supervised the study. All authors approved the final manuscript.

DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICAL APPROVAL

This study was approved by the Institutional Review Board at the University of Illinois at Chicago.

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