RESEARCH LETTERS

Frequency of Unintended Vein and Peripheral Nerve Biopsy With Temporal Artery Biopsy

The frequency of unintended vein or peripheral nerve biopsy with temporal artery biopsy has not been addressed specifically in the literature. The results of an inadvertent biopsy of a temporal vein or branch of the facial or auriculotemporal nerve are not inconsequential. Depending on the precise location in the temporal region and the type of peripheral nerve (motor or sensory), inadvertent peripheral nerve biopsy can result in considerable morbidity. It also requires that the procedure be repeated to obtain the correct tissue and, in some institutions, triggers a tissue committee review and clarification from the surgeon for the discrepancy between the intended and submitted tissue.

Methods. We examined the frequency of unintended biopsy of a vein or peripheral nerve among consecutive patients undergoing temporal artery biopsy at 2 institutions (James A. Haley Veterans’ Hospital from January 1, 1993, through December 31, 2007, and Emory University Hospitals and Clinics from January 1, 1989, through December 31, 2006). Patients were identified through computerized medical records; slides from all biopsies were retrieved and reviewed by a board-certified pathologist (J.G.J. and H.E.G.). An unintended biopsy of a vein or peripheral nerve (motor or sensory), inadvertent peripheral nerve biopsy can result as the presence of a vein or peripheral nerve in the absence of a muscular artery. The institutional review board at the University of South Florida approved the study.

Results. A total of 567 consecutive biopsies were performed at the 2 institutions during the time of the survey. There were 14 cases (2.5% [95% confidence interval, 0.6%-4.6%]) in which either a vein or peripheral nerve was identified in the absence of an artery. The 14 inadvertent biopsies were divided equally between vein and nerve (7 each). The proportions of inadvertent biopsies between the 2 institutions (James A. Haley Veterans’ Hospital, 2 of 160 biopsies; Emory University Hospitals and Clinics, 12 of 407 biopsies) were not statistically different (Fisher exact test, P = .39). More than 85 surgeons submitted biopsies in this series; 10 accounted for the 14 unintended biopsies.

Comment. We were able to calculate the frequency of inadvertent vein or peripheral nerve biopsy from 1 other report. In that study, 4 of 250 consecutive biopsies (1.6%) were of either a nerve or vein rather than an artery, a result that fell within our 95% confidence interval. These estimates provide physicians with some guidelines on how to inform patients of the risk of repeat biopsy. Given the inconvenience, potential morbidity, cost of repeat temporal artery biopsy, and delay in obtaining a final diagnosis, efforts should be made to reduce the frequency of inadvertent biopsy as much as possible. The principle reason for inadvertent biopsy is unclear but may include lack of surgical experience or inadequate visualization of the tissue at the time of removal. Reducing inadvertent biopsies can be achieved first by raising awareness of the phenomenon and then by including a standardized procedure to confirm the correct tissue at the time of harvest. One method could use a magnifying lens (≈5×) to inspect the cut ends of the putative artery immediately after excision. These inexpensive lenses, which can be sterilized and packaged for use during surgery, have magnification sufficient to aid in the distinction of an artery of this caliber from a vein or nerve.

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Financial Disclosure: None reported.

In this article, we show by high-definition optical coherence tomography (OCT) in vivo the disruption of the photoreceptor (PR) layer and hyperreflective lesions located in the inner part of the RPE in a patient with fundus albipunctatus associated with cone dystrophy.

**Report of a Case.** A 47-year-old woman was referred to our department for gradual progression of visual impairment, including constriction of the visual field, night blindness, and photophobia. The patient, who had initially noticed poor night vision during childhood, was clinically diagnosed with fundus albipunctatus a few years earlier by a local ophthalmologist; this diagnosis was then confirmed by direct genomic sequencing, showing a homozygous Gly35Ser mutation of the *RDH5* gene. The patient signed a comprehensive consent form according to good clinical practice guidelines before proceeding with any examinations. Best-corrected visual acuity was 20/80 OU. Fundus examination revealed numerous yellow-white flecks throughout the midperipheral retina, and the maculae each showed a bull’s-eye lesion (Figure 1). Fundus autofluorescence showed an abnormal circular hypoautofluorescence within the macular area surrounded by a hyperautofluorescent halo in both eyes (Figure 1). The standard flash electroretinogram disclosed severely decreased a- and b-waves in both eyes after 30 minutes of dark adaptation. After 2 hours of dark adaptation, standard flash electroretinogram a- and b-waves showed recovery.

![Figure 1](https://archopht.jamanetwork.com/)
although not to the normal level. The photopic electroretinogram and multifocal electroretinogram responses were significantly reduced. High-definition spectral-domain OCT (OCT 4000 Cirrus; Humphrey-Zeiss, San Leandro, California) showed reduction of central macular thickness in both eyes and allowed for visualization of transverse PR loss in the foveal region as well as disruption and focal loss of the inner segment (IS)–outer segment (OS) junction. In correspondence with retinal flecks, high-definition spectral-domain optical coherence tomographic scans in the right (C) and left (D) eyes show hyperreflective lesions (arrowheads in enlarged view) seen as dome-shaped deposits located in the inner part of the retinal pigment epithelium (RPE) layer and at the level of the OS of the photoreceptor continuous with the RPE layer.

Comment. High-definition OCT is a high-speed OCT system using spectral- or Fourier-domain detection with an axial image resolution of 5 µm. Hence, in vivo visualization of intraretinal structures and especially the RPE as well as the inner segment and outer segment of the PR layer is possible. In our patient, high-definition OCT allowed not only visualization of transverse PR loss in the foveal region but also, in correspondence with retinal flecks, hyperreflective lesions located in the inner part of the RPE, similar to type 1 lesions reported for Stargardt disease. Moreover, these high-definition OCT hyperreflective lesions due to a deficiency of 11-cis–retinol dehydrogenase look similar to the retinal deposits reported by Berson in squirrels that are deprived of vitamin A by dietary restriction.

To our knowledge, there is no histopathologic study of eyes with fundus albipunctatus and no previous description of the layer within the retina in which the flecks in this disease occur.

Figure 2. High-definition spectral-domain optical coherence tomographic scans in the right (A) and left (B) eyes allow for visualization of transverse photoreceptor loss in the foveal region as well as disruption and focal loss of the inner segment (IS)–outer segment (OS) junction. In correspondence with retinal flecks, high-definition spectral-domain optical coherence tomographic scans in the right (C) and left (D) eyes show hyperreflective lesions (arrowheads in enlarged view) seen as dome-shaped deposits located in the inner part of the retinal pigment epithelium (RPE) layer and at the level of the OS of the photoreceptor continuous with the RPE layer.
In conclusion, we show in vivo the disruption of the PR layer in fundus albipunctatus (a disease caused by a gene [RDH5] expressed in the RPE) associated with cone dystrophy as well as hyperreflective lesions similar to those reported for Stargardt disease (a disease caused by a gene [ABCA4] expressed in the PR). This may be the first solid evidence indicating the location of the flecks in fundus albipunctatus.

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Author Contributions: Dr G. Querques had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Financial Disclosure: None reported.


COMMENTS AND OPINIONS

Methodologic Aspects of Glaucoma Pharmacogenomic Studies

McCarty et al1 studied the association between intraocular pressure (IOP) response to topical β-blockers and genotype. Several factors are associated with IOP response such as concurrent use of IOP-lowering medication, baseline IOP,2,4 and cup-disc ratio.4 Patients’ races were not provided. Whether treatment was monocular might matter because of association with glaucoma type (eg, angle recession) and because binocular treatment provides 2 opportunities for a specified pressure drop. The criteria of McCarty et al might have included patients with ocular hypertension, primary open-angle glaucoma, or glaucoma due to chronic angle closure, pseudoxfoliation, angle recession, pigmentedary change, steroid response, uveitis, neovascularization, or other causes. Genotyping will be most helpful when it provides information not already known. Race, concurrent IOP-lowering medication regimen, baseline IOP, type of glaucoma, number of eyes treated, and cup-disc ratio should be controlled for in the multivariable prediction of IOP response (Table 4 of McCarty et al).3

The stated IOP response median of −23.3 mm Hg and range from −70.8 mm Hg to +25.0 mm Hg seem quite high. The conversion of binocular IOP data at several baseline and follow-up visits to a binary variable based on maximal IOP drop reduces the value of the information. The best routinely available IOP response measurement is mean IOP during treatment minus the mean IOP without treatment.2,3 Preservation of IOP response as a continuous (or rank) variable can increase the sensitivity to detect differences among genotypes. Multivariable linear regression can be used to predict the IOP response.2,3 Nonnormality can be approached by modifying outliers, data transformation, or using a nonparametric equivalent.

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Financial Disclosure: None reported.


We welcome the opportunity to address the questions raised by Dr Leffler and to provide further details about our methods, first in relation to the suggestion for additional variables to include in the multivariate analyses. The Personalized Medicine Research Project cohort is 98% white, with 78% reporting German ancestry.1 Only subjects with primary open-angle glaucoma or ocular hypertension were eligible for inclusion in this study, and only 1 eye per subject (the one with the greatest decrease in IOP) was included in the analyses. We acknowledge that baseline IOP was not used directly in multivariate analyses. Our reasoning was that this information was already contained in the relative decrease in IOP and that it was too highly correlated with the relative change to include in the multivariate analyses. This variable (relative change) was the primary outcome of the study. Cup-disc ratio was used as a criterion to confirm glaucoma diagnosis, but data were not available for all subjects at the time of β-blocker use to include in multivariate analyses.

We elected to use a binary outcome rather than a continuous outcome because the binary outcome represents a threshold used during the process of clinical decision-making. We did so hoping that the results would more readily translate into clinical practice. Had the results been of bor-