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Report

Choriocapillaris Compression Correlates with Choroidal Nevus–Associated Subretinal Fluid: OCT Analysis of 3431 Cases

Despite the clinical significance of choroidal nevus–associated subretinal fluid (SRF), its pathogenesis remains unclear. Current knowledge suggests that SRF development is multifactorial: (1) a fluid pressure gradient drives fluid extravascularly, (2) a site of permeability allows fluid extravasation, and (3) surrounding retinal pigment epithelium (RPE) is unable to remove fluid at a rate comparable to that of extravasation.[1] Choriocapillaris compression and distension of bordering vessels have recently been associated with choroidal nevus.[2,3] These findings implicate a local disruption of vascular competence as a potential cause of nevus-associated SRF.[2,3] We hypothesized that mechanical compression of the choriocapillaris would increase intravascular hydrostatic pressure near the choroidal nevus, resulting in fluid transudation that clinically manifests as SRF.

In this retrospective, observational study, we employed enhanced-depth imaging (EDI) OCT to further evaluate the association between choroidal vascular compression and presence of SRF. Our study included 3431 choroidal nevi of 3154 patients evaluated on the Wills Eye Hospital Ocular Oncology Service between 2007 and 2017. The study was performed in compliance with the Health Insurance Portability and Accountability Act and the Declaration of Helsinki. Institutional Review Board approval was obtained from Wills Eye Hospital. All participants provided informed consent.

All participants underwent dilated fundus examination, digital fundus photography, and EDI-OCT imaging (Heidelberg Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) using Spectralis Acquisition Module v6.5.2.0 and Spectralis Viewing Module v6.6.2.0. Images were independently evaluated for quality by a certified ophthalmic photographer (S.R.F.) and reviewed by trained ocular oncologists (L.A.D., D.A.L., C.L.S.).

All choroidal nevi were first classified by degree of associated choroidal vascular compression observed on EDI-OCT: (1) inner/outer compression, in which the choriocapillaris was markedly obliterated along with compression of the Haller and Sattler layers; (2) outer-only compression, in which only the Haller and Sattler layers were compressed, whereas the choriocapillaris was spared; and (3) none/no compression, in which all vascular layers were patent without compression. EDI-OCT was clinically correlated to morphologic characteristics of the nevus, overlying retina, and RPE, including presence, extent, and location of SRF, drusen, and RPE alterations.

When available, EDI-OCT images from follow-up examinations were evaluated for change in SRF status. If SRF was absent on initial examination, the appearance of SRF on subsequent visits was considered "new-onset SRF." If SRF was present on initial examination, SRF amount over time was categorized as increased, decreased, or unchanged.

Statistical analyses were performed for each listed feature by degree of vascular compression (inner/outer compression vs. outer only vs. none) using chi-square test, Fisher exact test, and analysis of variance.

Clinical and OCT features of choroidal nevus are listed in Table S1 (available at www.aaojournal.org). Comparison by vascular compression (inner/outer vs. outer only vs. none) revealed inner/outer compression with more frequent related SRF (22% vs. 3% vs. 1%, $P < 0.001$), imparting an 8.1-fold increased risk for nevus-associated SRF ($P < 0.001$). Inner/outer compression was correlated with more frequent bordering vessel distension (13% vs. 3% vs. 3%, $P < 0.001$). Inner/outer compression was associated with more frequent dome-shaped nevus configuration on OCT (87% vs. 31% vs. 35%, $P < 0.001$) and with greater prevalence of drusen (57% vs. 35% vs. 31%, $P < 0.001$) and RPE alterations (18% vs. 7% vs. 6%, $P < 0.001$) (Fig 1).

Increasing nevus thickness was associated with increased prevalence of inner/outer compression. Comparison by thickness (<1.50 mm vs. 1.50–2.50 mm vs. >2.50 mm) revealed increasing prevalence of inner/outer compression (23% vs. 60% vs. 74%, $P < 0.001$). After stratification by nevus thickness, the association between inner/outer compression and the presence of SRF remained significant ($P < 0.001$).

Nevus-related outcomes are listed in Table S2 (available at www.aaojournal.org). Follow-up was achieved in 1808 (53%) nevi with mean duration of 38.2 months (median 29.9, range 0.3–129.8). Inner/outer compression was associated with increased prevalence of new-onset SRF (10% vs. 3% vs. 0%, $P < 0.001$) and interval worsening of pre-existing SRF (50% vs. 4% vs. 0%, $P < 0.001$), with a relative risk of 16.2 (95% confidence interval: 11.1–23.6, $P < 0.001$) (Fig S2, available at www.aaojournal.org).

Our findings suggest a link between choriocapillaris compression and the development of nevus-associated SRF. We suspect that choriocapillaris compression results from nevus mass effect, which explains why larger nevi are associated with higher rates of choriocapillaris compression. This compression in turn creates resistance to blood flow, increasing vascular hydrostatic pressure proximal to the obstruction, and subsequently leading to fluid extravasation and accumulation in the potential space between the retina and RPE.[2,3] Our presumption that choriocapillaris compression contributes to increased hydrostatic pressure is corroborated by our concurrent observation of distended choroidal vessels at nevus margins, which has been reported in OCT and indocyanine green angiography studies.[3,4] This distension likely reflects vascular congestion arising from shunted choriocapillaris flow.[2,3]

RPE transport mechanisms must also be compromised for fluid to persist in the subretinal space.[1] In our study, we observed RPE alterations likely resulting from choriocapillaris compression. Histopathologic examination of age-related macular degeneration has revealed that loss of choriocapillaris density can precede RPE alterations.[5] Other studies have similarly implicated

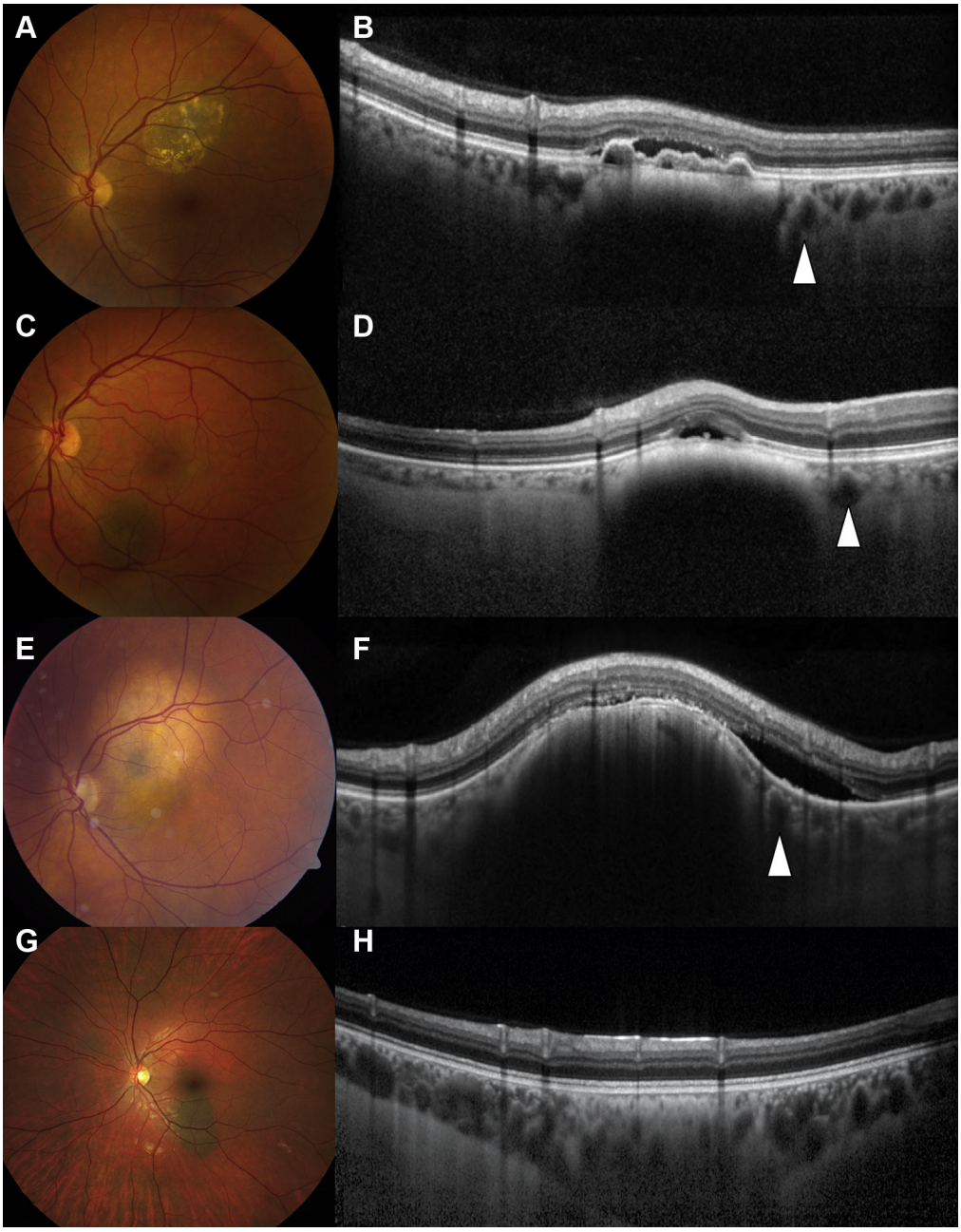

Figure 1. Choriocapillaris compression is associated with subretinal fluid (SRF) based on choroidal nevus elevation. **A,B,** A flat choroidal nevus (**A**) causing choriocapillaris compression on OCT (**B**) was associated with distension of bordering vasculature (white arrowhead), subclinical SRF, and confluent drusenoid pigment epithelial detachments. **C,D,** A mildly elevated choroidal nevus (**C**) with dome configuration on OCT (**D**) caused choriocapillaris compression, vascular distension (white arrowhead), and a cleft of apical SRF. **E,F,** A markedly elevated choroidal nevus (**E**) with dome configuration on OCT (**F**) caused choriocapillaris compression with vascular distension (white arrowhead), and associated SRF. Lack of choriocapillaris compression is associated with no SRF. **G,H,** A bland, pigmented choroidal nevus (**G**) with patent choriocapillaris on OCT (**H**) was associated with no SRF or overlying retinal pigment epithelium alterations.

choriocapillaris fall-out in RPE degeneration, proposing that decreased choriocapillaris density and related impaired blood perfusion impact nutrient transport at the level of the RPE.

Our study noted that nevus thickness correlates with choriocapillaris compression, which independently elevates SRF risk. These findings could plausibly explain the clinical association between SRF and choroidal melanoma. Histopathology and OCT angiography studies have demonstrated significantly decreased choriocapillaris flow overlying large choroidal melanoma.[6,7] We presume this occurs at least in part owing to mass effect, similar to that induced by a large dome-shaped nevus, leading to increased hydrostatic pressure, fluid transudation, and clinical SRF. If so, perhaps SRF is not a risk factor for malignant transformation so much as a downstream effect of a nascent malignant process.

Our findings suggest that choriocapillaris compression can drive the development of choroidal nevus–associated SRF and seems to reliably predict the formation of SRF on follow-up. This association might have future implications for not only the management of choroidal nevus–associated SRF, but also improved understanding of the relationship between SRF and nevus versus melanoma.

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Carol L. Shields, MD, has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

HUMAN SUBJECTS: Human subjects were included in this study. The study was performed in compliance with the Health Insurance Portability and Accountability Act and the Declaration of Helsinki. Institutional Review Board approval was obtained from Wills Eye Hospital. All participants provided informed consent.

No animal subjects were included in this study.

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