

Tissue Analysis From Two Patients With Premacular Hole Lesions

To the Editor.—In a recent clinicopathologic study Campochiaro et al¹ reported immunocytochemical analysis of tissue obtained at the time of vitrectomy from two patients with “premacular hole lesions.” I agree with their conclusion that this tissue is most likely posterior vitreous cortex removed from the premacular region. I furthermore agree with the contention that the cells in this tissue are likely responsible for the contractile forces that act on the macula, inducing striae, pucker, cysts, and in some cases, holes. The suggestion that these cells derive from retinal pigment epithelium and retinal glia is interesting but not conclusive. Although the authors invoke growth factor–stimulated cellular infiltration of the vitreous cortex as a possible mechanism, it is difficult to concur given that the retina is intact in the two cases that they studied. Furthermore, there is another equally plausible, if not more likely, explanation for these findings.

Studies²⁻⁴ have demonstrated that the vitreous cortex contains a single layer of well-spaced cells that, in the posterior cortex, are flat with long, thin processes and microvilli. This is precisely the description offered by Campochiaro et al¹ of their two specimens. Hyalocytes, as these cells are called, are 10 to 15 μm in diameter, contain a lobulated nucleus, and are embedded in the vitreous cortex approximately 20 to 50 μm anterior to the internal limiting lamina of the retina. That these cells could have the immunocytochemical properties reported by Campochiaro et al¹ was not ruled out in their study. Indeed, these authors may well have characterized the immunocytochemistry of human hyalocytes in their report.

Vitreomaculopathies often result from anomalous posterior vitreous detachment. In the cases described by Campochiaro et al¹ there was likely a split in the vitreous cortex (“vitreoschisis”) leaving the outer layer of vitreous cortex with hyalocytes attached to the internal limiting lamina of the retina.³ In their case 1 the authors identified a “membrane that spanned the posterior vitreous cavity inserting at about the equator,” which they initially believed to be the posterior vitreous cortex. However, this was likely the inner wall of the split vitreous cortex, as the authors found the outer wall of the split cortex still attached to the macula. In case 2 they described “a large syneresis cavity overlying the posterior pole.” Each of these descriptions is consistent with anomalous posterior vitreous detachment splitting the vitreous cortex, leaving the outer layer with hyalocytes still attached to the retina and forming a cavity in the posterior vitreous. In this abnormal milieu the hyalocytes, no longer modulated by the more anterior portions of the posterior vitreous cortex,³ can induce contraction of the cortex and tangential traction on the macula, resulting in the observed abnormality.

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1. Campochiaro PA, van Niel E, Vinore SA. Immunocytochemical labeling of cells in cortical vitreous from patients with premacular hole lesions. *Arch Ophthalmol.* 1992;110:371-377.

2. Hogan MJ, Alvarado JA, Weddel JE. *Histology of the Human Eye: An Atlas and Textbook.* Philadelphia, Pa: WB Saunders Co; 1971.

3. Grabner G, Baltz G, Forster O. Macrophage-like properties of human hyalocytes. *Invest Ophthalmol Vis Sci.* 1980;19:333-340.

4. Sebag J. Structure of the vitreous. In: *The Vitreous: Structure, Function and Pathobiology.* New York, NY: Springer-Verlag NY Inc; 1989:43-46.

In Reply.—We would like to thank Dr Sebag for his interesting comments. He agrees with our suggestion that

cells in a layer of attached cortical vitreous may contribute to the formation of macular cysts and holes and he offers the following two speculations: (1) The cells that we observed were hyalocytes rather than retinal pigmented epithelium or glia; and (2) the situation observed by us and others in which there is a layer of cortical vitreous on the surface of the retina with a fluid-filled space just anterior to the retina results from splitting of the cortical vitreous during posterior vitreous detachment, a process that he refers to as vitreoschisis.

We agree with Dr Sebag that hyalocytes may be present in the specimens removed from our patients and they could contribute to the development of macular cysts and holes. However, a recent study examining the immunohistochemical staining of hyalocytes *in situ* and *in vitro* demonstrated that hyalocytes do not stain for cytokeratins or for glial fibrillary acidic protein.¹ The cells in our specimens that stain for these markers most likely (but not with absolute certainty) represent retinal pigmented epithelium and glia, but there are other cells that are negative for both markers, and it is quite possible that they are hyalocytes. The possibility that hyalocytes play a role in various abnormalities at the vitreoretinal interface is intriguing and deserves further study, but it does not preclude participation by other cell types.

We are unaware of any firm evidence indicating that splitting of the cortical vitreous occurs, but it offers an interesting alternative hypothesis to explain the situation in which there is an apparent posterior vitreous detachment when in fact there is still residual vitreous tissue on the surface of the retina. We have noted that in some patients with macular cysts or holes, there is a thick membrane on the surface of the retina, while in others it is very thin. Perhaps in the former there was formation of a large syneresis cavity, while in the latter there was splitting of the cortical vitreous.

Thus, Dr Sebag's speculations provide a slightly different perspective on our observations, but are very much in line with our general concepts of possible pathogenic mechanisms in the formation of some macular holes and cysts.

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1. Lazarus HS, Russell SR, Zahn S, Hageman GS. Histochemical evidence for vitreous hyalocytes as components of pathologic vitreous membranes. *Invest Ophthalmol Vis Sci.* 1992;33(suppl):858.

Immune-Related Disease and Normal-Tension Glaucoma

To the Editor.—We read the article by Cartwright and coworkers,¹ published in the April 1992 issue of the ARCHIVES, with much interest. The investigators compared the prevalence of immune-related disease among patients with normal (low)-tension glaucoma (NTG) with that among controls with ocular hypertension (OHT) based on a retrospective analysis of medical records, concluding that there is an association between NTG and “immunoreactive tendencies.” We believe that there are design flaws in the study that may render such a conclusion premature.

The study's foundation, according to its authors, is based on the presumptive differences in susceptibility to intraocular pressure in the development of glaucomatous optic neuropathy between the NTG cases and OHT controls. This contention is not necessarily valid. Furthermore, its implicit inclusion in the study design only serves to complicate the analysis from an epidemiologic standpoint. If the hypothesis being tested is that immune-related disease is associated with NTG, then the control group would preferably be patients with *high-tension* glaucoma. This is important since a statis-