The Macular Hole

Histopathologic Studies

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Objective: To delineate the light and electron microscopic features of tissue removed at the time of macular hole surgery.

Methods: The ocular fluid specimens were concentrated using Millipore filters and stained with a modified Papanicolaou and the periodic acid–Schiff stains in 697 cases. In 92 cases, surgically isolated tissue was processed and examined by electron microscopy.

Results: The findings in the specimens studied by the Millipore filter technique included vitreous strands; cellular fragments in 108 cases (13.3%); fibrocellular fragments in 75 (9.2%); and fragments of internal limiting lamina (ILL) of the retina in 104 (12.8%). Findings in the 92 specimens with tissue studied by electron microscopy included native vitreous collagen in 48 cases (52.2%); new collagen in 6 (6.5%); native and new collagen in 1 (1.2%); ILL of the retina in 54 (58.7%); and a variety of cells in 22.5% of cases, including fibrocytes, myofibrocytes, fibrous astrocytes with and without myoblastic features, Mueller cells, retinal pigment epithelium with and without myoblastic features, and inflammatory cells. The organization of the tissue elements included a cellular layer along one surface of a layer of cortical vitreous in 18 cases, cortical vitreous along the inner surface of the ILL of the retina in 10, and cortical vitreous sandwiched between the ILL of the retina and a layer of cells in 9.

Conclusions: Tangential traction induced by fluid movements affecting the cortical vitreous is a major factor in the pathogenesis of idiopathic macular holes. Cellular proliferation is a secondary change seen in 22.2% of cases.


Until recently there was little enthusiasm for the treatments of macular holes. The emergence of a classification that incorporated new ideas on pathogenesis and the recognition that vitreous surgery may be beneficial for some patients have generated a renewed interest in idiopathic macular holes and their precursor features. Kelly and Wendel1 found that the surrounding area of macular detachment could be eliminated by vitrectomy, gas tamponade, and meticulous face-down positioning. Since then, vitrectomy has become the standard treatment for macular holes. The histopathologic study of ocular fluid specimens obtained at vitrectomy for macular holes is the subject of this report.

METHODS

Eight hundred fifteen ocular fluid specimens were obtained at macular hole surgery over a 30-year period in the Wilmer Eye Pathology Laboratory, Baltimore, Md. This is an extension of a previous study of 200 consecutive cases.2 The specimens were concentrated using a Millipore filter (Millipore Filter Corp, Billerica, Mass) and were stained with a modified Papanicolaou and the periodic acid–Schiff techniques.

In 118 cases, tissue clinically considered to be opercula or “epiretinal membranes” were isolated by the surgeon and placed in a buffered solution of 2% glutaraldehyde and 4% formaldehyde for transmission electron microscopy. Identification of cell types and native collagen was based on previously reported criteria.3

RESULTS

MILLIPORE FILTER

Of the 815 cases, almost all had vitreous strands. Cellular fragments (Figure 1) and fibrocellular fragments were observed in 108 cases (13.3%) and 75 cases (9.2%), respectively. Fragments of internal limiting lamina of the retina were present in 104 cases (12.8%). Possible retinal fragments were present in 55 cases (6.7%) and chronic inflammatory cells, in 39 (4.8%). Blood vessels were present in 4 cases (0.5%) and posterior lens capsule fragments, in 110 (13.5%). Forty-three cases (5.3%) were reoperations, 9 (1.1%) had an associated retinal detachment, and 4 (0.5%) followed ocular trauma.

ELECTRON MICROSCOPY

Of the 118 cases, no tissue was identified in 26 (22.0%). The 92 specimens with tis-
sue contained native vitreous collagen in 48 cases (52.2%), new collagen in 6 (6.5%), and native and new collagen in 1 (1.2%). Fragments of internal limiting lamina of the retina were present in 54 cases (58.7%). A variety of cell types present included fibrocytes, 20 cases (21.9%); myofibrocytes, 12 (13.0%); fibrous astrocytes, 39 (42.4%); fibrous astrocytes with myoblastic features, 4 (4.3%); Mueller cells, 14 (15.2%); retinal pigment epithelium, 14 (15.2%) and retinal pigment epithelium with myoblastic features, 9 (9.8%); lymphocytes, 3 (3.2%); macrophages, 13 (14.1%); degenerated cells, 4 (4.3%); and an unidentified type of cell in 15 cases (16.3%). Retinal neurons were present in 3 cases (3.3%) and retinal nerve fibers, in 12 (13.0%). Fibrin and blood vessels were present in 2 cases (2.2%) each.

The organization of the tissue elements supports the role of vitreous in the pathogenesis of macular holes. In 18 instances, a layer of native collagen was present with a cellular proliferation along one surface (presumably the inner surface) (Figure 2). A layer of native collagen was present along the inner surface of the internal limiting lamina of the retina in 10 cases (Figure 3). In 11 instances, a layer of native collagen was sandwiched between the internal limiting lamina of the retina and a layer of cells (Figures 4, 5, and 6). A layer of cells was present along the inner surface of the internal limiting lamina of the retina in 9 cases.

In recent years, several authors, using ultrasonography and optical coherence tomography, have reported posterior vitreous detachment in eyes with macular holes. Johnson and colleagues stated that perifoveal vitreous detachment is the primary pathogenesis event in idiopathic macular hole formation. I take exception with this and offer an alternative interpretation. I believe that these authors are likely imaging a cellular proliferation along the inner surface of the tapered cortical vitreous.

There are 2 main scenarios regarding age-related vitreous degeneration. One is extensive central vitreous liquefaction and posterior vitreous detachment, which
may lead to retinal tears and detachment. The other is extensive central liquefaction where a rim of cortical vitreous remains attached to the retina (Figure 7). Unfortunately, we cannot consistently see this layer even with a slitlamp, contact lens biomicroscopy, optical coherence tomography, or ultrasonography.

In a study of 22 eyes with idiopathic macular holes obtained post mortem, Guyer et al observed epiretinal cortical vitreous in 16 (73%) (Figure 8 and Figure 9). The findings of a cellular proliferation along the inner surface of a layer of cortical vitreous and cortical vitreous sandwiched between the internal limiting membrane of the retina and a layer of cells by electron mi-
The presence of cystoid macular edema, a surrounding area of retinal detachment, and tangential vitreous traction establishes rationale for the surgical treatment of macular holes and the associated secondary reparative cellular proliferation. Fluid movement and countercurrents of the central liquefied vitreous affecting the rim of the cortical vitreous is likely the pathogenesis of most idiopathic macular holes. With the removal of the tapered cortical vitreous, the edges of the hole come together, and healing with glial cell proliferation occurs in most instances.

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CONCLUSIONS

The presence of cystoid macular edema, a surrounding area of retinal detachment, and tangential vitreous traction establishes rationale for the surgical treatment of macular holes and the associated secondary reparative cellular proliferation. Fluid movement and countercurrents of the central liquefied vitreous affecting the rim of the cortical vitreous is likely the pathogenesis of most idiopathic macular holes. With the removal of the tapered cortical vitreous, the edges of the hole come together, and healing with glial cell proliferation occurs in most instances.

Figure 9. Postmortem eye. Nasal (A) and temporal (B) margins of an idiopathic macular hole with a cellular proliferation (arrows) along the inner surface of cortical vitreous (asterisks) (periodic acid–Schiff, original magnification ×100).

crosscopic studies of tissue removed at macular hole surgery support this concept.

Important developments in the history of macular holes were the observation of spontaneous resolution, the evolution of the tangential traction theory, and that vitreous surgery support this concept.

That macular holes can undergo spontaneous resolution suggested that whatever caused the hole was no longer in play. Sealing of macular holes with glial cell proliferation after vitrectomy supports the tangential traction theory.

Studies of eyes with macular holes obtained postmortem and tissues recovered at the time of vitrectomy for macular hole support the tangential vitreous traction theory. The posterior cortical vitreous tapers to a thin layer over the foveal area where it is somewhat more firmly attached. With movement of the eye, there are countermovements of the fluid vitreous. The countermovements create tension against the remaining cortical vitreous and the tension is transmitted where the cortical vitreous is thinnest—at the fovea. Deformation of the eye, as with rubbing, also contributes to tension on the cortical vitreous. These forces lead to chronic, low-grade traction with localized foveal detachment and hole formation. This low-grade traction also stimulates proliferation of cells (fibrous astrocytes, Mueller cells, and retinal pigment epithelium) to extend onto the inner surface of the cortical vitreous in some cases.

In some cases, the cellular proliferation may be pulled away from the macular area, giving rise to a pseudo-operculum, and, in some cases, contributing to persistence or recurrence of the macular hole.

REFERENCES


Archives Web Quiz Winner

Congratulations to the winner of our November quiz, Eman Hussein Hammouri, MD, King Hussein Medical Center, Jordan. The answer to our November challenge was West Nile virus meningoencephalitis. For a complete discussion of this case, see the Clinicopathologic Reports, Case Reports, and Small Case Series section in the December Archives (Myers JP, Leveque TK, Johnson MW. Extensive chorioretinitis and severe vision loss associated with West Nile virus meningoencephalitis. Arch Ophthalmol. 2005;123:1754-1756).

Be sure to visit the Archives of Ophthalmology Web site (http://www.archophthalmol.com) and try your hand at our Clinical Challenge Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also be able to choose one of the following books published by AMA Press: Clinical Eye Atlas, Clinical Retina, or Users’ Guides to the Medical Literature.