MEDICAL MANAGEMENT OF FULL-THICKNESS MACULAR HOLES



Topical therapy may be a good option for a subset of patients.

BY MRINALI GUPTA, MD; CASE EXAMPLE BY HEERAL R. SHAH, MD, FASRS; AND KEATON TABER, BS

An idiopathic full-thickness macular hole (FTMH), first described by Robert N. Johnson, MD, and J. Donald M. Gass, MD, in 1988, is a defect in the central fovea generally associated with marked vision impairment.[1] Early staging systems classified macular holes according to features identified on clinical examination and reflected the natural progression of the condition.[1] However, with increased anatomic resolution provided by OCT, the International Vitreomacular Traction Study (IVTS) Group developed a new classification system in 2013 for macular holes and the related conditions of vitreomacular adhesion (VMA) and vitreomacular traction (VMT).[2] The IVTS system is based strictly on anatomic OCT findings (Table).

The IVTS classification system reflects the current understanding of macular hole pathogenesis, which gives vitreofoveal traction a principal role. The standard surgical approach, therefore, centers on relief of traction through pars plana vitrectomy (PPV) with induction of a posterior vitreous detachment (PVD), epiretinal membrane (ERM) peel when relevant, and internal limiting membrane (ILM) peel, followed by gas tamponade and prone positioning. PPV and membrane removal not only alleviate traction, but also may induce retinal gliosis to bridge and close the hole. The closure rate of FTMH is 75% without ILM peeling and 90% to 95% with ILM peeling.[3,4]

Despite the high success rates for FTMH closure, surgery still comes with certain risks, including retinal detachment; infection; bleeding; phototoxicity and toxicity related to stains; and microtrauma to the retina during peeling maneuvers. In consideration of these risks, several groups have evaluated the potential for medical management of FTMHs.[5-10]

TABLE. CLASSIFICATION OF MACULAR HOLES AND RELATED CONDITIONS

Condition	Identifying Characteristics
Vitreomacular adhesion	- Perifoveal vitreous separation (generally due to normal senile vitreous degeneration) with persistent vitreofoveal attachment, but no distortion of foveal morphology.
Vitreomacular traction (VMT) without macular hole	- Anomalous posterior vitreous detachment, in which the vitreous remains attached at the fovea, creating anteroposterior traction that distorts foveal architecture. - The diameter of the vitreofoveal attachment may be classified further as focal (< 1,500 µm) or broad (> 1,500 µm).
Full-thickness macular hole (FTMH)	- An interruption in all retinal layers from the internal limiting membrane to the photoreceptors. - FTMHs are further classified as either with or without VMT; by size (small = < 250 µm, medium = 250 to 400 µm, large = > 400 µm); and primary versus secondary.

COMBINED TRACTIONAL-HYDRATION THEORY

There are multiple theories regarding the pathogenesis of FTMH. The *traction theory* for macular hole pathogenesis assigns a critical role to anteroposterior traction from the posterior vitreous cortex and (to a lesser extent) tangential traction from the vitreous cortex and ILM.[11,12] Alternatively, the *hydration theory* suggests that a defect in the inner retina allows vitreous fluid to accumulate into the middle and outer retinal tissues, ultimately leading to an FTMH.[13]

Medical management of FTMHs is based on the *combined tractional-hydration theory*.[11] According to this theory, macular hole pathogenesis begins with an initial tractional event: anteroposterior traction on the foveola creates an inner retinal defect, through which vitreous fluid enters the retina. Progressive accumulation of fluid in the form of cystic spaces in the outer and middle retina results in elevation and retraction of the inner retina, leading to subretinal fluid and the development of an FTHM. Dehydration of the cystic fluid through use of a retinal pigment epithelium (RPE) pump results in closure of the macular hole, followed by reabsorption of the subretinal fluid. In theory, the gas tamponade and prone positioning after surgery may facilitate hole closure via RPE-mediated dehydration by "plugging" the retinal defect

CASE EXAMPLE: MACULAR HOLE CLOSED BY TOPICAL THERAPY

By Heeral R. Shah, MD, FASRS, and Keaton Taber, BS

A 62-year-old woman presented with a chief complaint of cloudy vision and floaters in her right eye. She had an ocular history of bilateral cataract surgery, Nd:YAG laser capsulotomy in the right eye, and a macular hole in the left eye, which had been repaired by PPV 4 years earlier. Her VA was 20/80 OD and 20/40 OS. IOP was 9 mm Hg OD and 11 mm Hg OS. Dilated examination revealed a healthy nerve with a cup-to-disc ratio of 0.3, a PVD, normal vasculature and periphery, and an ERM with a small FTMH with a cuff of intraretinal fluid in the right eye. The left eye revealed no vitreous, a healthy nerve, an irregular foveal contour with no macular hole, and normal vessels and periphery. OCT imaging of the right macula confirmed the presence of a small FTMH (Figure 1). The patient was initiated on topical drops of 1% prednisolone acetate QID OD, 0.5% ketorolac QID OD, and 2% dorzolamide BID OD.

At the 1-month follow-up, the patient was still experiencing cloudy vision, but noticed mild improvement in the right eye. Her VA remained at 20/80 OD and 20/40 OS. IOP was 15 mm Hg OU. Dilated examination of the right eye showed that the macular hole had closed with residual subretinal fluid. OCT imaging confirmed the findings (Figure 2). At this time, the prednisolone acetate was decreased to BID OD, and the ketorolac and dorzolamide were continued at BID OD.

The patient returned 6 weeks later and reported improved central vision and was still using the topical drops as instructed. Her VA improved to 20/40 OD and 20/20 OS. IOP was 14 mm Hg OD and 13 mm Hg OS. The macular hole remained closed, and the subretinal fluid had improved (Figure 3). The patient was instructed to discontinue the prednisolone acetate, continue the ketorolac BID OD and dorzolamide BID OD and return to clinic in 4 to 6 weeks. If her condition continues to improve, the patient will continue to taper off topical drops.

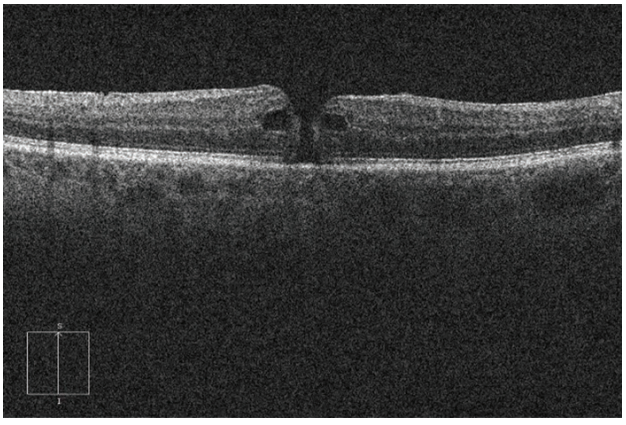

Figure 1. OCT of the right macula revealed a macular hole with intraretinal fluid.

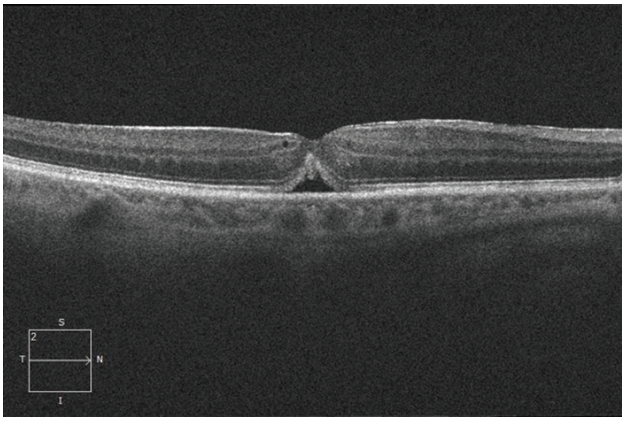

Figure 2. OCT of the right macula at the 1-month follow-up showed a closed macular hole and residual subretinal fluid.

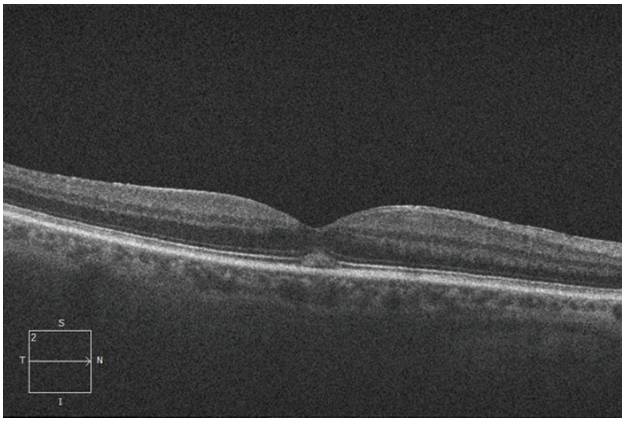

Figure 3. OCT of the right macula on the next follow-up 6 weeks later showed the closed macular hole with disruption of the retinal pigment epithelium. At this point, prednisolone acetate was discontinued, and the patient was instructed to continue ketorolac OD and dorzolamide OD, both BID, until next follow-up in 4 to 6 weeks.

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to prevent further fluid entry. Reconstitution of the external limiting membrane is often the last step of this process.[11]

MEDICAL THERAPY FOR MACULAR HOLES

Based on the combined tractional-hydration theory of FTMH pathogenesis, several groups have reported individual cases or small case series of FTMH closure with topical therapies.[5-8] More recently, two larger studies reported on treatment of FTMH through topical therapy aimed at cystoid dehydration.[9,10]

Sokol et al reported a multicenter, retrospective observational case series of 14 patients who were treated with topical steroids (1% prednisolone every 6 to 8 hours or 0.05% difluprednate every 8 to 12 hours); topical nonsteroidal antiinflammatory drugs (NSAIDs; 0.5% ketorolac every 6 to 8 hours or 0.07% bromfenac every 6 to 24 hours); and carbonic anhydrase inhibitors (CAIs; 1% brinzolamide or 2% dorzolamide every 8 to 12 hours).[9] The FTMHs in this study tended to be small with mean diameter of 166 µm, and all FTMHs were associated with cystoid macular edema (CME) on OCT. Half of all eyes had undergone prior PPV for retinal detachment or FTMH. Patients were treated until initial hole closure, after which drops were tapered. All FTMHs in the study closed, and BCVA improved from 20/70 to 20/40 on average. Two eyes experienced FTMH reopening 6 months after closure. Based on these findings, the authors concluded that small FTMHs (200 µm or less) with significant cystoid hydration and without VMT may be good candidates for topical therapy.[9]

Niffeneger et al conducted a retrospective case series of nine patients with secondary FTMHs treated with topical therapy at a single center. Three patients had undergone prior PPV, while the remaining six had undergone previous pneumatic retinopexy, laser, and/or scleral buckles. All patients were treated with topical steroids (0.05% difluprednate), and seven received one or more additional topical agents (CAI, NSAID, or a combination of both). Average FTMH diameter was 79 µm (range 44 to 132 µm), and all patients had CME. Of note, all FTMHs in this series also had an ERM. The authors found that 89% of eyes achieved hole closure at an average of 6 weeks (range 2 to 19 weeks), with average improvement in BCVA from 20/100 to 20/50. At the conclusion of the study, six eyes were still being treated with topical medications. Of the three eyes that stopped topical therapy, one experienced macular hole reopening and then closure with resumption of drops.[10]

Limitations of these studies include their retrospective nature, lack of a control group (eg, surgery with or without a period of observation beforehand), and small sample size. Without a control group, it is difficult to ascertain if some of the FTMHs treated with topical drops may have closed with observation alone, given that some macular holes close spontaneously (especially small ones such as those included in these studies). However, topical agents likely played an important role in at least some cases, given that several patients achieved resolution of FTMH with topical therapy and experienced reopening when the topical drops were tapered. Half of the patients in the Sokol et al series, and a third of patients in the Niffeneger et al series had prior PPV, so the lack of the cortical vitreous in vitrectomized eyes may have facilitated closure. Therefore, the reported outcomes may not be generalizable to patients without prior PPV. A significant portion of the Niffeneger et al participants were still on topical therapy at last follow-up.

TAKEAWAYS

The combined tractional-hydration theory of macular hole pathogenesis suggests that cystoid hydration of the retina plays a central role in FTMH development; in turn, dehydration of the retina is critical for FTMH closure.[11] Several observational studies suggest that treatment of FTMH with topical steroids, CAIs, and/or NSAIDs may facilitate cystoid dehydration.[9-10]

The studies also suggest that the best candidates for the nonsurgical approach include those with small FTMHs with cystoid degeneration and no significant tractional component. Important questions include whether some of these small holes may have also closed spontaneously without treatment, and how visual outcomes compare to those after surgery. Although these drops are safe, risks of long-term topical therapy—such as IOP elevation with steroids and corneal epitheliopathy or melt with NSAIDs—should be considered.

While further studies are necessary, topical therapy may be particularly worthwhile for treatment of small FTMHs with CME and no significant tractional component in patients who are unable or reluctant to undergo surgery, or in patients for whom surgery may be delayed due to the COVID-19 pandemic or other reasons. A trial of topical therapy may also be considered for 4 to 6 weeks while awaiting scheduled surgery. ■

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