Often, surgery in a patient with uveitis is deferred as long as possible to avoid inflammatory complications. The difficulty typically lies not in the technical aspects of the procedure, but often in the perioperative management to avoid recurrences of and complications from uveitis.

However, modern vitreoretinal surgery has evolved to employ minimally invasive approaches that incur only minimal postoperative inflammation in routine cases. Because of these advances, the risk-benefit ratio has changed over time for these complex cases.

The literature on vitrectomy for macular pathology in uveitic eyes is sparse and disjointed, owing to its relatively uncommon nature, but it is succinctly distilled by Shree K. Kurup, MD, and Tanu Thomas, MD, in this installment of Practical Retina. They provide useful insights for evaluating and treating these uncommon cases.

It is not very often that the retinal specialist has to deal with nondiagnostic surgical approaches to patients with severe uveitis, especially for posterior or panuveitis. Typically, the strategy has been to take a conservative approach, and macular holes (MHs) or epiretinal membranes (ERMs) have been often observed almost forever. The focus has been on reducing or eliminating the macular edema and maintaining structural integrity in the better-seeing eye.

Here we argue macular pathologies, including MHs, ERMs, and macular edema, are causes of irreversible vision loss in the setting of uveitis. Current indications for pars plana vitrectomy (PPV) in a patient with uveitis include diagnostic biopsies, recalcitrant macular edema, and other conditions that would usually call for PPV, such as rhegmatogenous and tractional retinal detachments, vitreous hemorrhage, and ERMs generating traction.1 No prospective, controlled trials have been performed to provide evidence-based treatment guidelines due to constraints in this population. Small case series, retrospective reviews, and individual case reports in the literature suggest inconsistent visual outcomes.

The largest review of literature to date analyzed 44 interventional case studies between 1981 and 2005 and determined evidence for PPV for improving visual outcomes in uveitic eyes was fair or poor. This conclusion was based on the lack of methodology in the studies, the heterogeneity of uveitic etiologies analyzed together, and inconsistent follow-up. This study did not specifically examine the outcomes of surgery on macular pathology.1-4 The authors herein performed a literature review from 2006 to 2016 for studies involving PPV in the context of uveitis for ERM and MH.3

Whether to Ignore the Macular Hole in a Uveitic Patient: A Discussion of the Pros and Cons of Elective Macular Surgery in a Challenging Population

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However, in this article, we advocate for judicious intervention.

**UVEITIC MACULAR HOLES: EPIDEMIOLOGY AND PATHOGENESIS**

MHs are a rare complication of uveitis, as described by Nussenblatt et al. A large review of 413 uveitic eyes reported macular abnormalities confirmed on spectral-domain optical coherence tomography (SD-OCT) in 58.6% of eyes and estimated the prevalence of MH to be 2.5%. Uveitic MHs affect a younger demographic (third and fourth decade of life) compared with idiopathic MHs, which occur in the sixth and seventh decade of life.
It is known that MHs associated with uveitis are more difficult to close via conventional surgical methods (vitrectomy, internal limiting membrane [ILM] peel, and gas tamponade) compared to nonuveitic MHs. Chronic inflammation in combination with recurrent cystoid macular edema (CME) and choroidal ischemia in the macula creates atrophied retinal epithelium that is less amenable to closure compared with idiopathic MH.\(^1\) The visual outcomes after vitreoretinal surgery can often be unpredictable. Reports indicate improved visual acuity (VA) of two lines or better in 73% of patients following PPV for idiopathic MH, which is improved compared to that of uveitic MH.\(^3\) The natural history of idiopathic MH appears to be progressive enlargement and worsening vision with few reports of spontaneous resolution. In contrast, uveitic MHs may improve with immunomodulatory therapy, and there have been case reports of spontaneous closure.\(^6\)

The mechanism for MH formation in uveitis was thought to be similar to that seen in nonuveitic eyes. The mechanism involves inflammatory degeneration of the inner retinal layers, recurrent CME, and ERM formation leading to vitreomacular traction (VMT) through both anteroposterior and centrifugal forces generated by ERMs.\(^1\)\(^4\) Evidence of VMT leading to macular edema formation with progression to MH has been observed in several uveitis cases.\(^3\) More commonly, we believe vitritis may also cause cortical vitreous contraction and generate tangential forces on the macula.\(^1\)\(^3\)

In a review of literature of MHs in the context of intraocular inflammation, Bonnin et al. reported a predominance of MHs associated with Behcet’s disease in the literature.\(^6\) Other authors have demonstrated success with PPV in closing uveitic MH. Postoperatively, surgeons have observed resolution of intraretinal CME and subsequent closure of the MH. Mizuno et al. described a case of acute inflammation in a VKH patient causing posterior vitreous detachment formation and severe VMT leading to a MH.\(^4\) The authors postulated that inflammatory MH can occur when chronic inflammation causes RPE migration along the retina, eventually contracting and thus creating traction on the macula. PPV with ILM peeling effectively thwarts this mechanism by releasing the traction force, and removes the traction medium, which should prevent future MH when combined with corticosteroid treatment.\(^3\)

Vitrectomy has a pro-inflammatory effect, and it is considered preferable to operate on an eye with no evidence of active inflammation ideally for at least 3 months prior to surgery. Overall, there is inconsistent reporting of perioperative ocular inflammation.
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surrounding PPV in uveitis, and we are unaware of studies correlating the degree of inflammation at the time of surgery with visual outcomes.

MH closure in uveitis is often not correlated with improved visual function in prior reviews. Woo et al. published a case series of seven patients with intermediate/posterior/pan uveitis of varying etiologies with MH that underwent PPV with ILM peeling and gas placement resulting in complete closure of MH in all cases but with minimal improvement in vision in four cases. Poor visual outcomes were attributed to retinochoroidal atrophy from chronic posterior uveitis.

Other reports demonstrate that visual recovery can occur with medical treatment alone. Ucar et al. described the resolution of full-thickness macular hole (FTMH) with improved VA after the administration of oral corticosteroids and immunosuppressants with the addition of subcutaneous interferon alfa2b in a patient with Behcet’s disease uveitis. Bonnin et al. described three cases of uveitis-associated MH that closed spontaneously with treatment of underlying etiologies with improved VA. In 2011, Shukla et al. reported closure of FTMH intractable to PPV with sub-Tenon triamcinolone acetonide injection.

Figure 3. (A) Patient with multifocal choroiditis with unilateral recalcitrant cystoid macular edema. The right eye is well-controlled on adalimumab, ciclosporin, and methotrexate. (B) After pars plana vitrectomy and silicon oil 5,000 cs.

**EPIRETINAL MEMBRANE: EPIDEMIOLOGY AND PATHOGENESIS IN UVEITIS**

ERM formation with or without CME occurs in up to 12% to 41% of uveitic eyes and is a well-known complication of chronic uveitis, which causes visual impairment. The presence of ERM has been associated with chronic uveitis, higher age at onset, and persistent duration of uveitic attacks with the end result of a poor VA outcome compared to without ERM.

Although clinically indistinguishable, histologic studies have differentiated ERMs secondary to uveitis from idiopathic ERMs based on the presence of inflammatory cells and the absence of retinal pigment epithelium (RPE) cells. ERMs occurring with ocular inflammation has been associated with the migration and proliferation of RPE cells on the ILM. The ERM is known to exert anterior-posterior vitreomacular traction, and in the setting of vitritis may cause tangential traction on the macula.

Data on surgical outcomes in ERM pathology are limited by the fact that some studies classify ERMs as only membranes, causing retinal distortion or wrinkling, whereas others classify any hyperreflective sig-
nal in the inner retinal surface as an ERM without separating the two categories. This may be problematic since studies have shown significantly worse response to medical therapy for macular edema and poor visual outcomes in uveitic eyes with ERM and retinal wrinkling compared to ERM without retinal wrinkling.3,9

Although PPV is commonly utilized in the setting of idiopathic ERM, the role of vitrectomy for ERM peeling in uveitic ERM is debated. Some small case series suggest improved vitritis and improved VA, as well as a reduced number of drugs postoperatively. One of the larger studies addressing this question was a retrospective, interventional case series of 16 eyes with uveitis and OCT-confirmed ERM undergoing PPV with ERM peeling and combined with ILM peeling in eight of the eyes. Improved VA was noted in only 31% of eyes at 6 months, was unchanged in 31%, and was worse in 37%. The major reason for worsened VA was pre-existing progressive macular pathology. Of the six eyes with preoperative VMT, the VA only improved in two cases.2 Other authors have suggested that surgical removal of ERM be performed based on SD-OCT showing focally attached ERMs involving the fovea area associated with photoreceptor disruption and vision loss.3,9 Most authors agree that surgery should only be pursued after intraocular inflammation is controlled and complicating pathologies such as cataracts are addressed.

Our experience has been more rewarding. Although anecdotal cases, we have shown large chronic MHS do seal and can result in visual improvement.13 This is because we believe the MH in diseases like Behcet’s is almost traumatic by origin and thus will lend itself to surgical success if inflammation is controlled (Figures 1A-1F). Another patient with lamellar hole with decreasing VA in the absence of inflammation is shown in Figures 2A and 2B. We also demonstrated the utility of ERM removal for persistent mechanical complications such as focal edema. The application of silicon oil to reduce recalcitrant CME in a background of adequate immune modulators is a heroic measure to buy time prior to exploring new systemic therapies (Figures 3A and 3B). The constraints of this article limit the number of cases that can be illustrated. The caveat is that our cases are small in number and highly selective, but outcomes have been positive.

CONCLUSION

Current literature provides conflicting outcomes for PPV for macular pathology in uveitis. As retinal imaging is becoming more efficient and less invasive, future studies should be performed to evaluate the progression of structural maculopathy associated with uveitis. Our data and potentially data from Bascom Palmer (personal communication with Thomas Albini, MD) show that there may be value in surgery in selected cases. It is difficult to advocate for aggressive surgical approaches to immune mediated disease, but as the literature unfolds, we may be in a better position to understand who will benefit from intervention. It would be valuable to evaluate elective macular surgery in uveitic eyes in a collaborative manner since controlled trials will be near impossible in this entity.

REFERENCES