Anatomical and functional outcomes of pars plana vitrectomy for inflammatory epiretinal membrane surgery in healed toxoplasmosis infection

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Epiretinal membrane over macula secondary to toxoplasmosis compromises vision. We describe the outcome of pars plana vitrectomy and epiretinal membrane removal after adequate treatment of acute infection. The average age of all four male patients was 36 years (range 20–60 years). Following surgery there was an average three or more lines visual acuity improvement, restoration of foveal contour with reduction in central macular thickness. One patient developed choroidal neovascular membrane postsurgery and was effectively treated with intravitreal bevacizumab. Surgery for ERM secondary to healed toxoplasmosis infection has good anatomical outcome and reasonable visual improvement, when the surgery is done in a quiet eye.

Key words: Epiretinal membrane, pars plana vitrectomy, toxoplasmosis

Acquired ocular toxoplasmosis is a common cause of posterior uveitis as a result of an infection caused by the protozoan *Toxoplasma gondii*. The clinical manifestations varies from a typical unilateral, unifocal, large retinochoroidal lesion (greater than 1 disc diameter [DD]) associated with vitritis located in the posterior pole in two thirds of cases to rare presentation like multifocal retinitis associated with vasculitis and neuroretinitis in the remaining.

Vision loss results from vitritis or from direct involvement of the macula or the optic nerve in the active stage of the disease. Vision loss occurs secondary to formation of permanent macular scar, epiretinal membrane (ERM), or optic atrophy in late or chronic stage of the disease. Severe visual field loss could occur when the scarring is close to the optic disc. In the active stage of the disease oral antitoxoplasmosis drugs with or without oral corticosteroids remains the mainstay of treatment, this helps in limiting the duration of active infection and prevents long-term complications. The late stage sequel
of ocular toxoplasmosis include cataract, glaucoma, vitreous opacification, vitreous hemorrhage, macular scarring, macular cystoid edema, choroidal neovascular membrane (CNVM), retinal detachment, vascular occlusion, optic disc edema, and optic atrophy.\[^{31}\]

ERM formation is one of the important causes of vision loss secondary to healed toxoplasmosis. Pars plana vitrectomy and ERM removal is an option though there is limited visual acuity improvement.\[^{9}\] The challenges and limiting factors are also related to the presence of concomitant pathology. In this paper, we report the results of pars plana vitrectomy with ERM removal in four consecutive cases of ERM secondary to healed toxoplasmosis infection.

### Methods

The search period was from November 2015 to March 2017. The common strategy was treatment of active infection before the ERM removal. The treatment of active infection included oral trimethoprim and sulfamethaxole (Bactrim-DS, 160 mg/800 mg, Abbott, India) thrice a day (in one case intravitreal cotrimoxazole, 1.28 mg in 0.08 mL) along with oral corticosteroid (prednisolone 1 mg/kg) and topical corticosteroids. The ERM removal surgery was performed with the following steps: 23-gauge pars plana vitrectomy, induction of posterior vitreous detachment (PVD) with triamcinolone acetonide (40 mg/ml, Aurocort, Aurolab, Madurai) staining of the posterior hyaloid, staining of the ERM with Brilliant Blue G (0.05%, Ocublue, Aurolab, Madurai), and peeling of the ERM with intravitreal forceps. Brief descriptions of these patients are as follows [Table 1]. Written informed consent was obtained from all patients before treatment.

#### Case 1

A 61-year-old man presented with complaints of pain, redness, and reduced vision in the right eye for 3 days. He had history of vision loss in the left eye 3 years ago. At presentation his best-corrected visual acuity (BCVA) was hand movements (HM) in both the eyes. The right eye had 2+ anterior chamber cells, 3+ vitreous cells, and an active focal retinchoroiditis lesion involving the macula. The left eye had faint fundus glow with vitreous membranes. Fundus fluorescein angiography (FFA) confirmed active retinitis with hyperfluorescence with late dye leakage. Optical coherence tomography (OCT) revealed incomplete PVD with hyperreflective lesion involving macula causing vitreomacular traction (VMT). The left eye B-scan revealed a tractional retinal detachment involving the posterior pole. His serum IgM titers for toxoplasma were positive indicating a current infection.

He was treated with oral Bactrim-DS thrice a day for initial 1 week along with oral corticosteroid 1 mg/kg and topical corticosteroids six times a day. The oral Bactrim-DS was reduced to twice a day a week later and stopped after 2 months. Oral corticosteroid was taper till 10 mg/day for next 6 weeks. Over the course of 5 months, vision improved to 20/125. The retinochoroiditis lesion healed to formation of thick ERM along with VMT. The central macular thickness (CMT) measured was 464 microns. The patient underwent vitrectomy and ERM removal; 14% C3F8 gas was used for tamponade.

At 1-month follow-up vision remained stable at 20/125 with macular scarring. The affected right eye developed significant cataract by 3 months and; an active CNVM, was confirmed with FFA and OCT. We performed cataract surgery with intraocular lens insertion and 1.25 mg bevacizumab was injected intravitreally at the conclusion of the surgery. At last follow-up (15 months), the BCVA was 20/100, N18 with a scarred CNVM, and residual subretinal fluid but without recurrence of retinitis lesion. The CMT was 363 microns [Fig. 1].

#### Case 2

A 26-year-old male complained left eye reduced vision for 3 days. His BCVA was 20/20, N6 in the right eye and 20/80, N36 in the left eye. On examination right eye was normal. The left eye had a thick ERM with macular edema (643 microns) and traction involving the macula [Fig. 2]. There was a healed chorioretinal lesion at inferior mid-periphery suggestive of old toxoplasma infection. His serum IgG titers for toxoplasma were positive suggestive of past infection. There was incomplete PVD. Following vitrectomy and ERM removal vision improved to 20/30, N6. OCT at 6 months follow-up showed a few ILM folds and resolution of macular edema (228 microns).

#### Case 3

A 20-year-old man complained of reduction of vision in the left eye since 3 months. His BCVA was 20/20, N6 in the right eye and 20/320, N36 in the left eye. Left eye showed 2+ anterior chamber cells, 2+ vitreous cells, thickened preoculart vitreous tissue over the disc and ILM folds. His IgG titers for toxoplasma were positive suggestive of past infection. He was started on oral antitoxoplasma treatment (Bactrim-DS), posterior subtenon corticosteroid injection, and topical corticosteroids.

### Table 1: Pre- and post-operative clinical features

| Pt | Eye | Age/sex | Preop VA | Preop OCT (CMT) | Antitoxo treatment | Serum titers | Surgery | Postop VA | Postop OCT (CMT) | Follow up (months) |
|----|-----|---------|----------|-----------------|--------------------|--------------|---------|-----------|-----------------|------------------|
| 1  | OD  | 61/M    | HM+      | ERM with VMT (464 mic) | Yes (oral) | IgM+ | PPV + MP + IVTA + FGE | 20/100, N12 | Scarred CNVM (363 mic) | 7                |
| 2  | OS  | 26/M    | 20/80, N36 | ERM with traction (643) | No | IgG+ | PPV + MP + IVTA + FAE | 20/30, N6 | ILM folds (414 mic) | 6                |
| 3  | OS  | 20/M    | 20/320, N36 | ERM with VMT (649 mic) | Yes (oral) | IgG+ | PPV + MP + FGE | 20/100, N12 | ILM folds (427 mic) | 14               |
| 4  | OD  | 38/M    | 20/125, N24 | ERM with ILM folds (493 mic) | Yes (oral + intravitreal) | IgM+ | PPV + MP + IVTA + FGE | 20/20, N6 | Normal contour (360 mic) | 12               |

CNVM: Choroidal neovascular membrane, ERM: Epiretinal membrane, FGE: Fluid gas exchange, HM: Hand movement, IVBZ: Intravitreal bevacizumab, IVTA: Intravitreal triamcinolone, MP: Membrane peeling, PPV: Pars plana vitrectomy, VMT: Vitreomacular traction, ILM: Internal limiting membrane
At 3 months, vision improved to 20/125. There was thick ERM with VMT nasal to macula with central macular thickness of 649 microns. Following vitrectomy and ERM removal vision improved to 20/100, N12 and OCT showed normal foveal contour with minimal ILM folds and CMT of 222 microns, at the last follow-up (8 months) [Fig. 3].

Case 4
A 39-year-old man complained of reduction of vision associated with redness in the right eye for 1 month. His BCVA was 20/125, N24 in the right eye and 20/20, N6 in the left eye. On examination right eye showed 2+ anterior chamber cells, 3+ vitreous cells, and >4 DD size active yellowish retinochoroiditis lesion involving the inferotemporal arcade with peripheral vascular sheathing. His serum titers for toxoplasma revealed elevated IgM levels and normal IgG levels. He was treated with intravitreal cotrimoxazole (1.28 mg/0.08 mL) weekly for 6 weeks in addition to topical and oral corticosteroids (1 mg/kg). But due to minimal response to intravitreal cotrimoxazole we switched to oral trimethoprim and sulfamethaxole (Bactrim-DS), and in 2 months time there was beginning of resolution of inflammation. Over 3 months time of treatment with Bactrim-DS there was complete resolution and visual acuity improved to 20/40, N8. He developed an ERM at macula over 9 months period. He also had ILM folds and central macular edema noted was 493 microns. Following vitrectomy and ERM removal his BCVA improved to 20/20, N6 with OCT showing normal foveal contour and CMT of 360 microns [Fig. 4].

Discussion
ERM formation is the one of the important causes of reduced vision in patients with healed toxoplasmosis infection. The benefit of pars plana vitrectomy in ERM removal secondary to inflammatory pathologies like sarcoid uveitis, pars planitis is well documented. In this cohort, all four patients operated for posttoxoplasmosis ERM, benefited with stable or improved vision and reduced central macular thickness. But this surgery must be done only when the eye is quiet.

Figure 1: (a and b) Preop fundus photo shows active retinochoroiditis lesion involving macula; OCT shows increased reflectivity in inner retinal layers with epiretinal membrane (ERM) and vitreomacular traction. (c and d) Postop fundus photo shows scarred CNVM; OCT shows hyperreflective lesion in subretinal space suggestive of scarred CNVM with residual SRF

Figure 2: (a and b) Preop fundus photo shows thickened ERM with traction involving the macula; OCT shows thick ERM over the macula with distortion of inner retinal layers and increased macular thickness. (c and d) Postop fundus photo shows absence of ERM with few ILM striae; OCT shows distorted foveal contour with ILM folds and minimal macular edema

Figure 3: (a and b) Preop fundus shows thickened precortical condensed vitreous with ERM and VMT; OCT shows distorted foveal contour with thick ERM with VMT. (c and d) Postop fundus shows absence of ERM with few ILM striae; OCT shows distorted foveal contour with ILM folds

Figure 4: (a and b) Preop fundus photo shows ERM involving macula and healed pigmented toxoplasmosis lesion in inferior quadrant. (c) OCT shows thin ERM with increased central macular thickness. (d and e) Postop fundus shows normal macula without ERM; OCT shows normal foveal contour with no macular edema
and free of inflammation for minimum period of 3 months. An active toxoplasmosis infection needs treatment with trimethoprim-sulfamethoxazole (first line of treatment) or intravitreous clindamycin and dexamethasone (alternative treatment for patients intolerant, unresponsive or with a contraindication such as pregnancy).[12] In this series three of four patients (patients 1, 3, and 4) had active toxoplasmosis infection at presentation, two with macular lesion and other with lesion at inferotemporal arcade.

Choudhury et al.[13] have reported use of intravitreal trimethoprim/sulfamethoxazole and dexamethasone combination as an alternative treatment strategy in patients with active toxoplasmosis. Because of a large inflammatory lesion of >4 DD and dense vitritis we treated patient 4 more aggressively with six intravitreal cotrimoxazole injections followed by oral Bactrim-DS for 3 months. Incidentally, Soheilian et al. have shown that lesion size reduction occurs differentially in IgM titer-elevated and IgM titer-normal cases—the former responded better to classic therapy and the latter responded better to intravitreal therapy.[14]

CNVM formation is a well-documented sight-threatening complication of posterior segment intraocular inflammation.[15] It occurs in different locations at different stages of the disease process—anywhere in the active toxoplasma retinitis lesion in the active stage and at the edge of the toxoplasma scar in the healed stage of the disease.[16] In our cohort, one patient (case 1) developed CNVM at 3 months postvitrectomy and ERM removal. It could be secondary to inflammatory response to disease per se or could be secondary to surgery (break in Bruch’s membrane, formation of vascular proliferation and retinochoroidal anastomosis leading to formation of CNVM). Management of CNVM in cases of healed toxoplasmosis with anti-VEGFs has been fraught with fear of reactivation of the retinochoroiditis lesion; hence a concomitant use of oral antitoxoplasma therapy as a treatment prophylaxis has been suggested.[17] In our cohort, this patient responded well to intravitreal bevacizumab because the toxoplasmosis lesion had already healed well.

Three of four patients in this series had evident ERM with VMT. All of them benefitted from surgery similar to a larger series by Miranada et al.[9] Two of our patients had active infection and we waited for 5 months (first case) to 14 months (second case) for resolution of infection with oral antitoxoplasma treatment. One patient (case 1) had a small amount of residual subretinal fluid with scarred CNVM nasal to macula. There was no recurrence of ERM or macular edema at last follow-up (15 months). It is necessary to wait for complete resolution of both infection and inflammation before planning for any vitreomacular surgery. It appears that once the inflammation is subsided, the presenting vision determines the final visual outcome after a successful ERM surgery. In this series two patients, patients 1 and 3 had poor preoperative vision (HM and 20/320, respectively), and they regained 20/125 and 20/100, respectively. On the contrary, patients 2 and 4 had a better presenting vision (20/80 and 20/125, respectively) and they regained 20/30 and 20/20, respectively. In all of them the CMT was between 464 and 649 microns.

There is no consensus regarding the use of prophylactic oral cotrimoxazole after either pars plana vitrectomy or cataract surgery.[18] There is controversy on the possibility of reactivation of infection following any intraocular surgery.[19,20] In our series, one of four patients received prophylactic treatment as the lesion was close to macula, but others did not receive as the toxoplasma scar was away from macula. None of them had any reactivation of infection at last visit. There are two weaknesses in this study. One, the entire data are retrospective and it is a small case series.

Conclusion
ERMsurgery in an eye with well-healed toxoplasmosis benefits patients of Indian origin. We hope this will encourage others as surgery is well tolerated and to a limited extent rewarding.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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