# Epiretinal Membrane Peeling in an Eye with Old Branch Retinal Vein Occlusion non responsive to multiple Anti VEGF injections: Case report

Dr Rubina Akther<sup>1</sup>, Dr Md Ripon Ali<sup>2</sup>, Dr Tasruba Shahnaz<sup>3</sup>, Dr Moutushi Islam<sup>4</sup>, Prof. Dr. S. M. Monowarul Islam<sup>5</sup>,

Prof. Dr Md Saleh Ahmed<sup>6</sup>

#### **Abstract**

Introduction: To evaluate the anatomical and functional outcomes of pars plana vitrectomy (PPV) and epiretinal membrane (ERM) peeling in 77 yr old male patient with old branch retinal vein occlusion (BRVO) The prevalence of ERMs in patients with RVO ranges between 14 and 16%, but it is likely underestimated. ERM may exacerbate macular edema in patients with RVO, may reduce drug penetration of intravitreal antiangiogenic agents, and may eventually progress to a pseudohole, or more rarely, a macular hole. Therefore, patients with RVO may potentially benefit from surgical removal of ERM.

In our case 77 yrs old male went to doctor with the complaint of sudden painless dimness of vision of Lt eye 1st time in 2017.Pt was hypertensive ,well controlled with medication. After proper examination & investigations he was advised for intra vitreal anti VEGF for BRVO with macular oedema, ERM (showed in OCT print done in 2017 1st). Then he had multiple anti VEGF injections, sectoral laser. In his earlier treatment period, macular oedema responded to treatment (anti VEGF inj , sectoral laser ).BCVA also improved, macular thickness decreased on OCT .But after few months, recurrent BCVA decreased ( both distance & near ) in Lt eye . On OCT macular thickness increased again. This time macular oedema was nonresponding to medical treatment, anti VEGF injection. Then came COVID period in our life. Pt did not have any kind of treatment for recurrent decrease vision in his Lt eye. Then he came to our hospital in November 2021. After clinical examination, investigations found that the cause of decreased vision in his Lt eye was recurrent macular oedema with prominent ERM on OCT due to Old BRVO. After discussion of the therapauetic options (like observation vs surgical intervention) to pts himself & his family member pt agreed for surgical intervention (PPV & ERM removal & AFX) in his Lt eye. Best-corrected visual acuity (BCVA) values and spectral-domain OCT (SD-OCT) scans were recorded at each visit after surgery. After surgery BCVA improved (Distant & Near) in Lt eye, Macular thickness reduces (found on OCT) done in each visit.

**Conclusions:** PPV and ERM removal provided encouraging functional and morphological results in eye with Old BRVO. Integrity of the outer retina and preservation of inner retinal segmentation were associated with better visual and anatomical outcomes after ERM removal, respectively.

**Keywords:** Anti-vascular endothelial growth factor (Anti VEGF), Cystoid macular edema, Epiretinal membrane, Branch Retinal vein occlusion (BRVO)

#### Introduction

Epiretinal membrane (ERM) refers to a sheet-like broglial cellular tissue proliferation over the internal limiting membrane (ILM) in the macular area [1]. ERM is the most commonly idiopathic, developing after posterior vitreous detachment (PVD) and migration of retinal glial and retinal pigment epithelial cells into the anterior retinal surface. Secondary ERM has been described in retinal vasculopathies, intraocular in ammation,

- 1. Senior consultant Bashundhara Eye Hospital & Research Institute
- 2. Senior Register Bashundhara Eye Hospital & Research Institute
- 3. Consultant Bashundhara Eye Hospital & Research Institute
- 4. Associates Professor & Joint director Bashundhara Eye Hospital & Research Institute
- 5. Professor Bashundhara Eye Hospital & Research Institute
- 6. Founder Director & Vitreo-Retina Professor Bashundhara Eye Hospital & Research Institute

Address of Correspondence: Dr Rubina Akther, Senior consultant - Bashundhara Eye Hospital & Research Institute

retinal detachment, retinal surgeries, and ocular trauma [2]. Secondary ERM may be an additive cause of visual loss in eyes with underlying ocular diseases. The prevalence of ERMs in patients with RVO ranges between 14 and 16%, but it is likely underestimated [4–6]. ERM may exacerbate macular edema in patients with RVO, may reduce drug penetration of intravitreal antiangiogenic agents, and may eventually progress to a pseudohole, or more rarely, a macular hole Therefore, patients with RVO may potentially bene t from surgical removal of ERM. Previous studies have examined the outcomes of secondary ERM surgical removal in eyes with tractional diabetic macular edema, reporting good anatomical and variable functional results [7,8]. In addition, pars plana vitrectomy (PPV) has been proven effective in ERM due to uveitis or trauma [9,10]. Limited data exist on eyes with RVO and coexistent ERM undergoing PPV and ERM peeling. Based on these observations, the purpose of this case presentation was to evaluate the anatomical and functional outcomes of PPV and ERM peeling in patient with treated old BRVO and secondary ERM.

## Case presentation

In our case 77 yrs old male went to doctor with the complaint of sudden painless dimness of

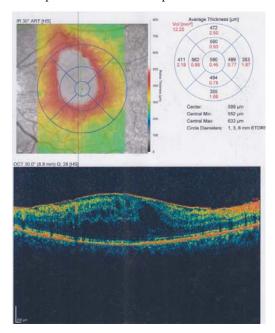


Figure 1 LT eye BCVA 6/60 NI, Near vision NI

vision of Lt eye 1<sup>st</sup> time in 2017. Pt was hypertensive, well controlled with medication . After proper examination & investigation he was advised for intra vitreal anti VEGF for BRVO with macular oedema, ERM (showed in OCT print done in 2017 1<sup>st</sup>). Then his BCVA in Lt eye was 6/60 & near vision not improved with refraction & Rt eye 6/6 & N5 with spectacles. Central macular thickness was 590 micro metre measured with OCT.

Then he had multiple anti VEGF injections, sectoral laser also. In his earlier treatment period, macular oedema responded to treatment ( anti VEGF inj , sectoral laser ).BCVA also improved 6/12 & N 10 with spectacles in Lt eye , macular thickness decreased on OCT .

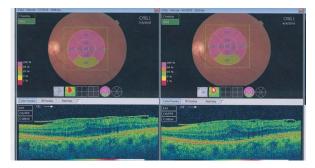


Figure 2 Lt eye : 6/12 & N10 with spectacles after multiple anti VEGF Injections , ERM more prominent on OCT

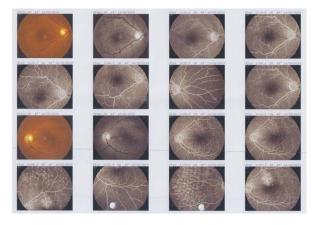


Figure 3: FFA Both eye, showing laser spot in Lt eye

But after few months, recurrent BCVA decreased (both distance & near) in Lt eye. BCVA 6/18 P & N18 with spectacles. On OCT macular thickness increased again. This time macular oedema was

nonresponding to medical treatment, anti VEGF injection. Then came COVID period in our life. Pt did not have any kind of treatment for recurrent decrease vision in his Lt eye. Then he came to our hospital in November 2021. After clinical examination, investigations found that the cause of decreased vision in his Lt eye was recurrent macular oedema with prominent ERM on OCT due to Old BRVO. BCVA in Lt eye was 6/18P & N18 with spectacles & CMT was 583 micro meters.

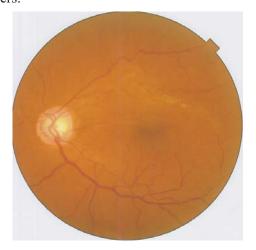


Fig 4: Showing ERM involving macula Lt eye

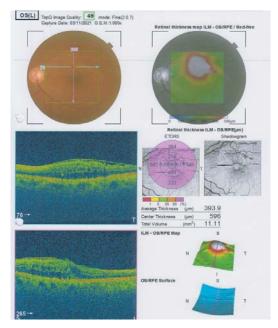


Fig 5: OCT showing prominent ERM, BCVA Lt eye: 6/18P & N18

After discussion of the therapauetic options (like observation vs surgical intervention) to pts himself & his family member pt agreed for surgical intervention (PPV & ERM removal & AFX) in his Lt eye. Best-corrected visual acuity (BCVA) values and spectral-domain OCT (SD-OCT) scans were recorded at each visit after surgery. After surgery BCVA improved (Distant & Near) in Lt eye, Macular thickness reduces (found on OCT) done in each visit. BCVA after 7 months post operative was 6/12 & N8P with spectacles. CMT also decreased to 392 micrometers.

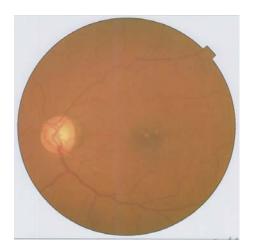


Fig 6

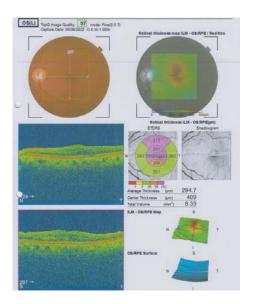


Fig 7: CMT decreased, BCVA 6/12, N8P with spectacles

#### Discussion

PPV + epi retinal membrane removal + Air fluid exchange in Lt eye with ERM secondary to old treated BRVO led to significant improvement in visual acuity and decrease macular thickening on OCT. Though older patients and those with BRVO had a higher risk of persistent macular thickening after surgery.

Both primary and secondary ERMs have two main components: an extracellular matrix (consisting of collagen, laminin, and fibronectin) and cells of retinal and extraretinal origin, such as glial cells, neurites, retinal pigment epithelium, immune cells, and fibrocytes [2, 17, 18]. The relative abundance of these components within each ERM case reflects the underlying etiology and the severity of the disease or its duration. In retinal ischemia or inflammation, such as in diabetic retinopathy or RVO, activation of Müller cells induces the upregulation of glial fibrillary acidic protein and vimentin, with reactive gliosis and ERM formation [19, 20]. As platelet-derived growth factor A (PDGF A) and VEGF receptors are expressed within ERM cells, intravitreal proangiogenic cytokines may accelerate ERM progression [21]. Contractile fibrils eventually exert traction on the underlying retina and distort the retinal tissue and the retinal vasculature, causing visual loss [22]. Removal of ERM may revert these processes, provided that inner and outer retinal integrity is preserved.

In our case pt had multiple intra vitreal Anti VEGF injections in his Lt eye. Intravitreal injections have been hypothesized to contribute to ERM formation. A higher number of intravitreal injections of anti-VEGF and the use of DEX implants have been associated with higher odds of ERM in patients with diabetic macular edema [23]. Possible effects of intravitreal VEGF inhibition include an increase of retinal ischemia, an imbalance towards the effect of pigment epithelium-derived factor, or an indirect increase in the expression of connective tissue growth factor, which stimulates tissue fibrosis and ERM formation [24]. We cannot exclude the possibility that intravitreal therapies contributed to the

pathogenesis of ERM in our BRVO patient.

The improvement in visual acuity after PPV and ERM peeling was rapid and sustained over time. It might be argued that spontaneous visual recovery is likely to occur in the natural history of RVO [26]. In the SCORE study, up to 26% of eyes in the sham group experienced a visual gain ranging from 5 to 15 letters, although no data were provided specifically about eyes with ERM [27].

Moreover, the removal of ERM may increase the drug penetration into the retina after intravitreal injections [7, 8]. A beneficial effect of ILM peeling during vitrectomy for RVO has also been correlated with decompression of the edematous retina [30]. BRVO eyes might have a tighter ERM due to the presence of epiretinal neovascularization, much more prevalent in BRVO. However, eyes with BRVO had persistent macular edema after surgery.

### **Conclusions**

PPV and ERM removal provided encouraging functional and morphological results in Lt eye with old treated BRVO in 77 yrs old male pt . Integrity of the outer retina and preservation of inner retinal segmentation were associated with better visual and anatomical outcomes after ERM removal, respectively.

# Acknowledgements

Authors do thank pt for his involvement in this case presentation.

# **Funding**

No funding or sponsorship was received for this case presentation or publication of this article.

#### References

- 1. Bu SC, Kuijer R, Li XR, et al. Idiopathic epiretinal membrane. Retina. 2014;34(12):2317–35. https://doi.org/10.1097/IAE.0000000000000349.
- 2. Sandali O, El Sanharawi M, Basli E, et al. Epiretinal membrane recurrence: incidence, characteristics, evolution, and preventive and risk factors. Retina. 2013;33(10):2032-8. https://

- doi.org/10.1097/IAE.0b013e31828d2fd6.
- 3. McIntosh RL, Rogers SL, Lim L, et al. Natural history of central retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2010;117(6):1113-1123.e1115. https://doi.org/10.1016/j.ophtha.2010.01.060.
- 4. Fraser-Bell S, Ying-Lai M, Klein R, et al. Prevalence and associations of epiretinal membranes in latinos: the Los Angeles Latino Eye Study. Invest Ophthalmol Vis Sci. 2004;45(6):1732–6. https://doi.org/10.1167/joys.03-1295.
- 5. Duan XR, Liang YB, Friedman DS, et al. Prevalence and associations of epiretinal membranes in a rural Chinese adult population: the Handan Eye Study. Invest Ophthalmol Vis Sci. 2009;50(5):2018–23. https://doi.org/10.1167/iovs.08-2624.
- 6. Mitchell P, Smith W, Chey T, et al. Prevalence and associations of epiretinal membranes. The Blue Mountains Eye Study, Australia. Ophthalmology. 1997;104(6):1033–40. https://doi.org/10.1016/s0161-6420(97)30190-0.
- Hwang S, Kang SW, Kim KT, et al. Three-year outcomes of vitrectomy combined with intraoperative dexamethasone implantation for non-tractional refractory diabetic macular edema. Sci Rep. 2021;11(1):1292. https://doi.org/10.1038/s41598-020-80350-w.
- 8. Ghassemi F, Bazvand F, Roohipoor R, et al. Outcomes of vitrectomy, membranectomy and internal limiting membrane peeling in patients with refractory diabetic macular edema and non-tractional epiretinal membrane. J Curr Ophthalmol. 2016;28(4):199–205. https://doi.org/10.1016/j.joco.2016.08.006.
- 9. Coassin M, Mori T, Mastrofilippo V, et al. Surgical management of post-uveitic epiretinal membranes. Eur J Ophthalmol. 2021. https://doi.org/10.1177/11206721211017750.
- 10. Assi A, Chacra CB, Cherfan G. Combined lensectomy, vitrectomy, and primary intraocular lens implantation in patients with traumatic eye injury. Int Ophthalmol. 2008;28(6):387–94. https://doi.org/10.1007/s10792-007-9151-9.
- 11. DeCroos FC, Shuler RK Jr, Stinnett S, Fekrat S. Pars plana vitrectomy, internal limiting membrane peeling, and panretinal endophotocoagulation for macular edema secondary to central retinal vein occlusion. Am J Ophthalmol. 2009;147(4):627-633.e621. https://doi.org/10.1016/j.ajo.2008.10.024.

- Kang HM, Koh HJ, Lee SC. Visual outcome and prognostic factors after surgery for a secondary epiretinal membrane associated with branch retinal vein occlusion. Graefes Arch Clin Exp Ophthalmol. 2015;253(4):543–50. https://doi.org/10.1007/s00417-014-2731-2.
- 13. Zur D, Iglicki M, Feldinger L, et al. Disorganization of retinal inner layers as a biomarker for idiopathic epiretinal membrane after macular surgery—the DREAM study. Am J Ophthalmol. 2018;196:129–35. https://doi.org/10.1016/j.ajo.2018.08.037.
- 14. Chan EW, Eldeeb M, Sun V, et al. Disorganization of retinal inner layers and ellipsoid zone disruption predict visual outcomes in central retinal vein occlusion. Ophthalmol Retina. 2019;3(1):83–92. https://doi.org/10.1016/j.oret.2018.07.008.
- 15. Mimouni M, Segev O, Dori D, et al. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with macular edema secondary to vein occlusion. Am J Ophthalmol. 2017;182:160–7. https://doi.org/10.1016/j.ajo.2017.08.005.
- 16. Lange C, Feltgen N, Junker B, et al. Resolving the clinical acuity categories "hand motion" and "counting fingers" using the Freiburg Visual Acuity Test (FrACT). Graefes Arch Clin Exp Ophthalmol. 2009;247(1):137–42. https://doi.org/10.1007/s00417-008-0926-0.
- 17. Lesnik Oberstein SY, Lewis GP, Dutra T, Fisher SK. Evidence that neurites in human epiretinal membranes express melanopsin, calretinin, rod opsin and neurofilament protein. Br J Ophthalmol. 2011;95(2):266–72. https://doi.org/10.1136/bjo.2010.180679.
- 18. Mackenzie SE, Gandorfer A, Rohleder M, et al. Ultrastructure and retinal imaging of epiretinal membrane: a clinicopathologic correlation of trypan blue staining in epiretinal membrane surgery. Retina. 2010;30(4):648–54. https://doi.org/10.1097/IAE.0b013e3181bceda9.
- 19. Lee SY, Surbeck JW, Drake M, et al. Increased glial fibrillary acid protein and vimentin in vitreous fluid as a biomarker for proliferative vitreoretinopathy. Invest Ophthalmol Vis Sci. 2020;61(5):22. https://doi.org/10.1167/iovs.61.5.22.
- Romano MR, Ilardi G, Ferrara M, et al. Intraretinal changes in idiopathic versus diabetic epiretinal membranes after macular peeling. PLoS ONE. 2018;13(5): e0197065. https://doi.org/10.1371/

- journal.pone.0197065.
- 21. Chen YS, Hackett SF, Schoenfeld CL, et al. Localisation of vascular endothelial growth factor and its receptors to cells of vascular and avascular epiretinal membranes. Br J Ophthalmol. 1997;81(10):919–26. https://doi.org/10.1136/bjo.81.10.919.
- 22. Romano MR, Cennamo G, Schiemer S, et al. Deep and superficial OCT angiography changes after macular peeling: idiopathic vs diabetic epiretinal membranes. Graefes Arch Clin Exp Ophthalmol. 2017;255(4):681–9. https://doi.org/10.1007/s00417-016-3534-4.
- 23. Kang YK, Park HS, Park DH, Shin JP. Incidence and treatment outcomes of secondary epiretinal membrane following intravitreal injection for diabetic macular edema. Sci Rep. 2020;10(1):528. https://doi.org/10.1038/s41598-020-57509-6.
- 24. Marticorena J, Romano MR, Heimann H, et al. Intravitreal bevacizumab for retinal vein occlusion and early growth of epiretinal membrane: a possible secondary effect? Br J Ophthalmol. 2011;95(3):391–5. https://doi.org/10.1136/bjo. 2009.177287.
- 25. Panjaphongse R, Stewart JM. Vitreomacular traction after dexamethasone intravitreal implant (ozurdex) injection: the effect of anomalous posterior vitreous detachment. Retin Cases Brief Rep. 2016;10(1):55–7. https://doi.org/10.1097/ICB.00000000000000172.
- 26. Hayreh SS, Podhajsky PA, Zimmerman MB. Natural history of visual outcome in central retinal vein occlusion. Ophthalmology. 2011;118(1):119-133.e111-112. https://doi.org/10.1016/j.ophtha. 2010.04.019.
- 27. Ip MS, Scott IU, VanVeldhuisen PC, et al. A randomized trial comparing the efficacy and safety of intravitreal triamcinolone with observation to treat vision loss associated with macular edema secondary to central retinal vein occlusion: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) study report 5. Arch Ophthalmol. 2009;127(9):1101–14. https://doi.org/10.1001/archophthalmol.2009.234.
- 28. Spooner K, Fraser-Bell S, Hong T, Chang AA. Five-year outcomes of retinal vein occlusion treated with vascular endothelial growth factor inhibitors. BMJ Open Ophthalmol. 2019;4(1): e000249. https://doi.org/10.1136/bmjophth-2018-000249.

- 29. Diabetic Retinopathy Clinical Research Network Writing C, Haller JA, Qin H, et al. Vitrectomy outcomes in eyes with diabetic macular edema and vitreomacular traction. Ophthalmology. 2010;117(6):1087-1093.e1083. https://doi.org/10.1016/j.ophtha.2009.10.040.
- 30. Mandelcorn MS, Nrusimhadevara RK. Internal limiting membrane peeling for decompression of macular edema in retinal vein occlusion: a report of 14 cases. Retina. 2004;24(3):348–55. https://doi.org/10.1097/00006982-200406000-00002.
- 31. Chatziralli I, Theodossiadis G, Chatzirallis A, et al. Ranibizumab for retinal vein occlusion: predictive factors and long-term outcomes in real-life data. Retina. 2018;38(3):559–68. https://doi.org/10.1097/IAE.0000000000001579.
- 32. Battaglia Parodi M, Iacono P, Scaramuzzi M, Bandello F. Outer retinal layer changes after dexamethasone implant for central retinal vein occlusion. Retina. 2017;37(10):1888–95. https://doi.org/10.1097/IAE.0000000000001429.
- 33. Chatziralli I, Dimitriou E, Xirou T, et al. Optical coherence tomography biomarkers as predictive factors for postoperative visual acuity in patients with epiretinal membrane treated with vitrectomy. Oman J Ophthalmol. 2020;13(3):136–40. https://doi.org/10.4103/ojo.OJO 79 2020.
- 34. Garnavou-Xirou C, Xirou T, Gkizis I, et al. The role of disorganization of retinal inner layers as predictive factor of postoperative outcome in patients with epiretinal membrane. Ophthalmic Res. 2020;63(1):13–7. https://doi.org/10.1159/000499370.
- 35. Koss MJ, Pfister M, Rothweiler F, et al. Comparison of cytokine levels from undiluted vitreous of untreated patients with retinal vein occlusion. Acta Ophthalmol. 2012;90(2):e98–103. https://doi.org/10.1111/j.1755-3768.2011.02292.x.
- 36. Hayreh SS, Rojas P, Podhajsky P, et al. Ocular neovascularization with retinal vascular occlusion-III. Incidence of ocular neovascularization with retinal vein occlusion. Ophthalmology. 1983;90(5):488–506. https://doi.org/10.1016/s0161-6420(83)34542-5.