Recalcitrant cystoid macular oedema in an eye with ischaemic central retinal vein occlusion- what's next?

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SUMMARY
We report a case of a middle-aged gentleman with recalcitrant macular oedema (RMO) secondary to ischaemic central retinal vein occlusion (CRVO). He was given six injections of intravitreal ranibizumab (anti-VEGF) monthly. However, his visual acuity (VA) deteriorated and the macular oedema worsened. He then received an intravitreal dexamethasone implant eight months post-CRVO. His VA and macular oedema improved dramatically and significantly at first follow-up and remained stable at six months after implant.

This case can be a reference for those who treating recalcitrant macular oedema. It shows the effect of an intravitreal dexamethasone implant might have in a patient with RMO due to CRVO. The patient enjoyed improvement of vision, with clinical evidence of reduction in central macular thickness (CMT) and with no serious adverse events after a single injection up to six months post implant.

INTRODUCTION
Central retinal vein occlusion (CRVO) is a retinal vasculocclusive disorder. Complications of CRVO include rubeosis iridis and macular oedema. Macular oedema as the major cause of visual impairment is generally treated with anti-vascular endothelial growth factor (anti-VEGF). However, some patients may not respond to anti-VEGF and lead to persistent macular oedema or reoccurrence of macular oedema.

Recalcitrant macular oedema (RMO) is a clinical challenge with devastating impact on patient's vision and psychosocial function. Failure of treatment with anti-VEGF agents is a challenge for the ophthalmologist. There are no well established recommendations or guidelines in these cases.

CASE PRESENTATION
A 53 years old gentleman with a background history of dyslipidaemia who had defaulted treatment, presented to the eye casualty with sudden painless loss of left eye (LE) vision. There was no prior history of floaters, flashes, trauma or similar problems.

His visual acuity (VA) was 6/24 N- OS, 6/9 N- OD. Clinically the LE had a reactive pupil without a relative afferent pupillary defect (RAPD). The anterior segment of left eye on presentation was normal with an intraocular pressure of 12mmHg. Fundus examination of the left eye revealed generalised retinal haemorrhages (flame shaped/dots and blots). The optic disc was hyperaemiac with blurred margin while the macula was oedematus. There was no evidence of retinitis, choroiditis or vasculitis. There was bilateral mild nuclear sclerotic cataract. His right eye was otherwise normal with normal cup: disc ratio of 0.3.

On spectral optical coherence tomography (SD-OCT), his LE central macular thickness (CMT) was 526µm, compared to RE CMT of 292µm. Based on the history and ocular features, a diagnosis of left eye central retinal vein occlusion with cystoid macular oedema (CMO) was made. Screening for metabolic disease revealed persistent dyslipidaemia and no clinical evidence of diabetes mellitus or hypertension. The patient's coagulation profile and carotid Doppler ultrasound were normal.

In view of the dense retinal haemorrhages, initial laser treatment with pan retinal photocoagulation (PRP) was limited. He developed rubeosis iridis with an intraocular pressure (IOP) of 34mmHg three months after initial presentation. At the same time his LE VA deteriorated to 6/60, N36. He was then treated with extensive pan-retinal photocoagulation and 6 injections of intravitreal ranibizumab (Lucentis™, Genentech, USA) monthly. Medically he was commenced aspirin and anti-lipid agents. Fundus fluorescein angiography at eight months post CRVO showed a normal foveal avascular zone size with some capillary drop-out.

Following the initial treatment, there was resolution of rubeosis iridis, reduction of retinal haemorrhages and normalisation of IOP with a single anti-glaucoma medication. However, LE VA remained at 6/60, N36. His fundus findings and OCT (Figure 1) showed increasingly severe macular oedema with CMT of up to 699µm. In view of the poor response to ranibizumab, intravitreal dexamethasone implant (Ozurdex™, Allergan, Irvine CA, USA) was given following informed consent eight months after the CRVO.
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OUTCOME AND FOLLOW-UP
At first follow-up post-implantation, the LE VA improved to 6/24, N12. His LE CMT improved from 699µm to 365µm. The patient reported a subjective improvement in the vision in his left eye and appreciated the long injection-free period post implant. At last review seven months later, his VA remained at 6/24 N12 with CMT of 340µm (Figure 2). His LE IOP was 16mmHg on oral acetazolamide, which was added immediately post Ozurdex™ implantation for two weeks. IOP monitoring showed an increasing trend to 22mmHg three months after the implant. Gonioscopy revealed an open angle with no peripheral anterior synenchia or iris neovascularisation. Subsequently IOP was well controlled with three topical antiglaucoma agents. There was no worsening of cataract documented during seven months of follow-up or occurrence of retinal detachment.

DISCUSSION
Central retinal vein occlusion (CRVO) is a retinal vaso-occlusive disorder that commonly presents with unilateral sudden onset vision loss. Hyperlipidaemia is an established risk factor. CRVO is typically classified as ischaemic or non-ischaemic. Non-ischaemic CRVO can become ischaemic in up to 34% and occurs more rapidly in the first four months (15%). In this case the conversion probably occurred at three months. Complications of CRVO include rubeosis iridis and macular oedema as illustrated here. Rubeosis iridis is a complication of ischaemic CRVO and is treated with panretinal photocoagulation. It can also lead to rubeotic glaucoma which is difficult to control and a devastating complication of ischaemic CRVO.

Macular oedema is a major cause of vision impairment after CRVO as in this man. Laser treatment of macular oedema was noted to be unsatisfactory in the CRVOS with no role of macular grid laser in CRVO. Usage of ranibizumab for macular oedema in CRVO was proven in the ROC study. Usage of intravitreal steroids was proposed in the SCORE study which utilised triamcinolone for macular oedema in CRVO. Corticosteroids have been shown to inhibit the expression of VEGF and other pro-inflammatory mediators. The advantage of intravitreal steroids over anti-VEGF agents includes their longer duration of action up to six months.

Usage of triamcinolone for macula oedema has been complicated by a high rate of elevated IOP and cataract. Intravitreal dexamethasone or Ozurdex™, on the other hand,
possesses an increased potency compared to triamcinolone with a much better IOP profile. Ozurdex™ is a sustained release intravitreal implant consisting of 700µg dexamethasone. It has been shown to be particularly effective for CMO due to CRVO.4

Persistent macular oedema or reoccurrence of macular oedema despite treatments do occur in some cases. Possible causes include resistance to one anti-VEGF agent or vitreomacular traction (VMT). The OCT finding and good treatment response to steroid in this case excluded VMT. One of the studies has mentioned a subset of patients who do not have resolution of macular oedema after treatment with intravitreal bevacizumab may respond to treatment with an intravitreal dexamethasone implant.5 Elevation of IOP did occur three months after Ozurdex™. This is consistent with a previous study where the peak incidence of high IOP (16%) occurred on day-60 post implantation. This was well controlled with topical antiglaucoma medications.

**LEARNING POINTS**

This report documents a new era of safe and efficacious usage of short acting corticosteroids for intravitreal administration which can be delivered in depot form and obviates the risks and need of repeated intravitreal injections.

- Intravitreal dexamethasone implant (Ozurdex™) is a safe and efficacious treatment option for recalcitrant macular oedema secondary to CRVO that had been resistant to repeated anti-VEGF therapy with a single agent.
- Close monitoring for elevation of IOP is mandatory after intravitreal dexamethasone.
- Increased IOP can be well controlled with topical antiglaucoma medications.
- A patient can enjoy improvement in vision and a long injection-free period after receiving an intraocular dexamethasone implant.

**REFERENCES**