

# Results of intravitreal dexamethasone implant 0.7 mg (Ozurdex®) in non-infectious posterior uveitis

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## Abstract

• **AIM:** To evaluate the safety and efficacy of dexamethasone implant in patients with non-infectious posterior uveitis with cystoid macular edema (CME).

• **METHODS:** Retrospective analysis of patients reports with CME secondary to non-infectious uveitis treated with dexamethasone implant. Data included type of posterior uveitis, any systemic immunosuppressive therapy, Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA), central macular thickness (CMT) on optical coherence tomography (OCT) and signs of intraocular inflammation at baseline and then at 2wk postoperatively and monthly thereafter. Follow-up is up to 10mo. Any per-operative and post-operative complications were recorded.

• **RESULTS:** Six eyes of 4 patients with CME due to non-infectious posterior uveitis treated with dexamethasone implant. Diagnosis included idiopathic panuveitis, birdshot chorioretinopathy and idiopathic intermediate uveitis. At baseline mean ETDRS BCVA was 63 letters and mean CMT 556 µm at 2wk postoperatively mean ETDRS BCVA improved to 70 letters and mean CMT decreased to 329 µm. All eyes showed clinical evidence of decreased inflammation. The duration of effect of the implant was 5 to 6mo and retreatment was required in 2 eyes. Two patients required antiglaucoma therapy for increased intraocular pressures.

• **CONCLUSION:** In patients with non-infectious posterior uveitis dexamethasone implant can be a short-term effective treatment option for controlling intraocular inflammation.

• **KEYWORDS:** Ozurdex®; cystoids macular oedema; central macular thickness; posterior uveitis

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## INTRODUCTION

Ozurdex® has been approved by the Food and Drug Administration (FDA) for the treatment of macular oedema and noninfectious posterior uveitis. The implant is manufactured by Allergan which is based in California. National Institute for Health and Care Excellence (NICE) has also recently recommended the dexamethasone implant in the treatment of macula oedema secondary to retinal vein occlusions. It has been reported that the annual incidence of uveitis is approximately 17-52 cases per 100 000 and the prevalence is 38-714 per 100 000. Macular oedema can cause visual impairment in one third of these cases<sup>[1]</sup>.

Corticosteroids are potent anti-inflammatory agents that reduce macula edema by preventing leukocyte migration, reduce fibrin deposition, stabilize endothelial cell tight junctions, and inhibit synthesis of vascular endothelial growth factor, prostaglandins, and proinflammatory cytokines. There are various routes of steroid administration which included topical, local and systemic. Local and systemic corticosteroids have been used for the treatment of intermediate and posterior uveitis. However due to inadequate drug penetration to the posterior segment of the eye, posterior uveitis is often unresponsive to topical administration of steroids. Periocular and intraocular steroid administration have been used while long-term systemic steroid therapy is avoided due to potential side effects<sup>[2,3]</sup>.

Intravitreal corticosteroid such as dexamethasone implant can lead to high local drug concentration in the retina as it bypasses the blood-retinal barrier. Compare to anti-vascular endothelial growth factor (VEGF) treatments, dexamethasone implant has the advantages of being longer lasting not needing the repeated administration of the monthly regimen and cost effective. The drug is slowly released over a period of six months with peak levels occurring at about two months<sup>[4,5]</sup>. The efficacy of Ozurdex® in the treatment of non-infectious posterior uveitis was also reported in a multicentre study known as the HURON (cHronic Uveitis evaluation of the intRavitreal dexamethasone implant)<sup>[6]</sup>.

The dexamethasone implant provides a localised targeted therapy avoiding systemic complications but is associated

with local ocular side effects such as cataract, glaucoma, risk of endophthalmitis and retinal detachment.

We present our cases consisting of 6 eyes in 4 uveitis patients with macula oedema all of whom responded to the dexamethasone implant proven by improvement in Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) and decreased in central macular thickness (CMT). Informed consents were obtained from all the patients. The study was approved by the institution review board and it followed the principles outlined in the Declaration of Helsinki.

**CASE 1**

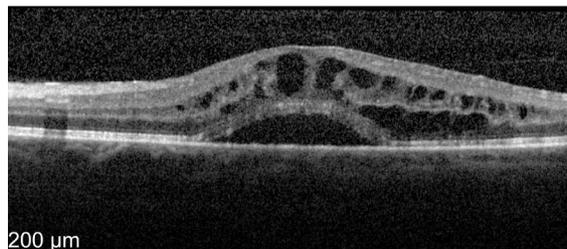
A 52-year-old female who has a history of bilateral panuveitis for 9y presented with left eye pain and redness for 10d waking her up at night. She was on oral Azathioprine but stopped the medications 18mo ago due to elevated liver enzymes. She also had 2 intravitreal triamcinolone injections to her left eye in the past for cystoid macular edema (CME) which responded to treatment but improvement were short acting lasting for 5wk. Decision was made for her to have longer acting agent such as intravitreal steroid implant. Left intravitreal dexamethasone was implanted on 11/1/2012. Two weeks later her left eye vision improved from 63 letters to 76 letters (+13 letters) with decreased in macular thickness (Figures 1, 2).

**CASE 2**

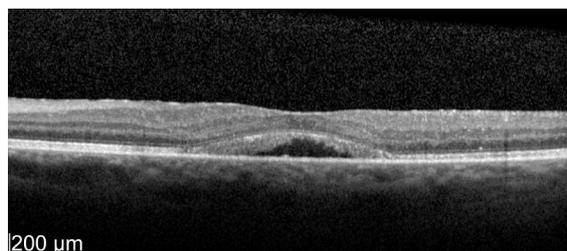
A 49-year-old male patient with a history of birdshot chorioretinopathy with bilateral CME. He complained of visual blurring in the right eye for 3wk. Intravitreal dexamethasone was implanted into the right eye on 29/3/2012. One month later his vision improved 78 to 83 letters with decreased in macular thickness from 621 to 319  $\mu\text{m}$  as shown in Figures 3 and 4. He was a steroid responder with increased in intraocular pressure needing treatment with latanoprost/timolol maleate (Xalacom<sup>®</sup>) eye drops. He was also found to have increased in left macular oedema and was listed for left intravitreal dexamethasone implantation. With 2wk post intravitreal dexamethasone treatment, his left eye vision improved from 72 to 82 letters and macular thickness decreased from 463 to 349  $\mu\text{m}$  as shown in Figures 5 and 6. Five months after the right dexamethasone implantation his right eye vision decreased with recurrence of macular oedema which responded to a second right intravitreal treatment as shown in Figures 7 and 8.

**CASE 3**

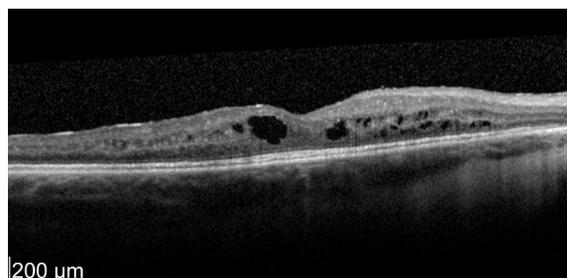
A 51-year-old female patient with history of CME secondary to idiopathic intermediate uveitis presented with decreased in vision both eyes for 2mo despite taking oral prednisolone 30 mg. She was found to have increased in macular thickness both eyes. In view of the need for treatment, she was listed for intravitreal dexamethasone implantation to both eyes.



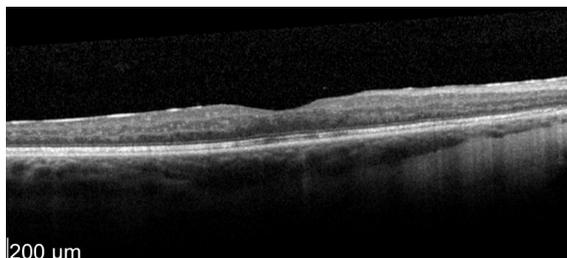
**Figure 1** Pre-treatment OS vision 63 letters optical coherence tomography showed macular thickness of 696  $\mu\text{m}$ .



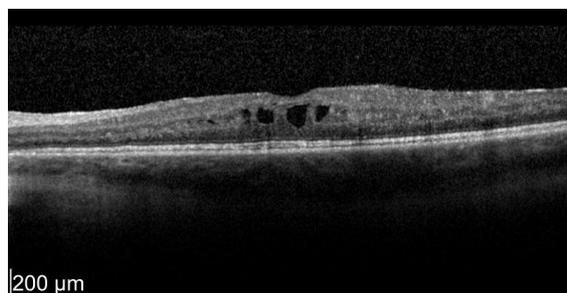
**Figure 2** Two weeks post-treatment OS vision 76 letters with thickness of 365  $\mu\text{m}$ . Even the neurosensory detachment persists.



**Figure 3** Pre-treatment OD vision 78 letters Macular thickness of 621  $\mu\text{m}$ .



**Figure 4** Post-treatment at 4wk OD vision 83 letters with macular thickness of 319  $\mu\text{m}$ .



**Figure 5** Pre-treatment OS vision 72 letters with macular thickness 463  $\mu\text{m}$ .

With 2wk post intravitreal dexamethasone treatment, his right eye vision improved with decreased in macular thickness as shown in Figures 9 and 10. Improvement in the left eye are shown in Figures 11 and 12. Despite having a history of

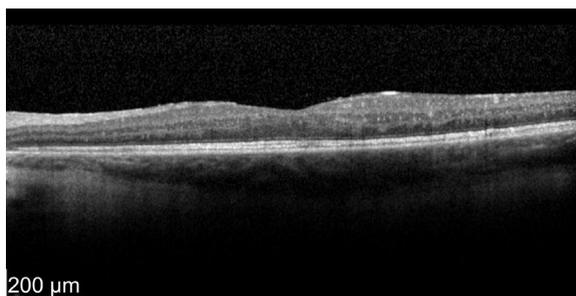


Figure 6 Two weeks post-treatment OS vision 82 letters with macular thickness of 349  $\mu$ m.

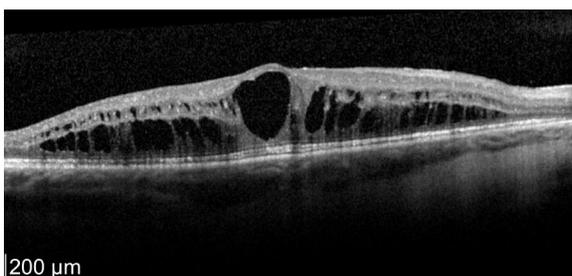


Figure 7 Five months post-treatment OD vision 65 letters.

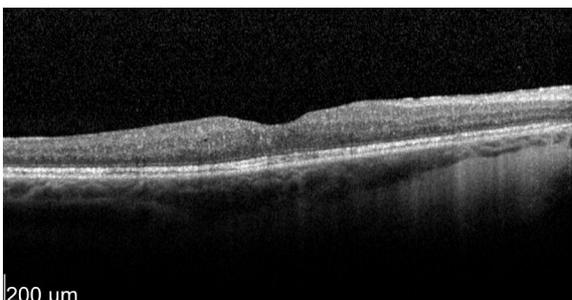


Figure 8 Two weeks later OD vision of 79 letters with macular thickness of 266  $\mu$ m. Right eye with macular thickness of 620  $\mu$ m.

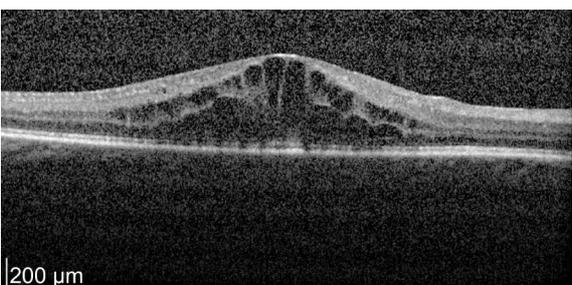


Figure 9 OD vision 43 letters and macular thickness of 675  $\mu$ m.

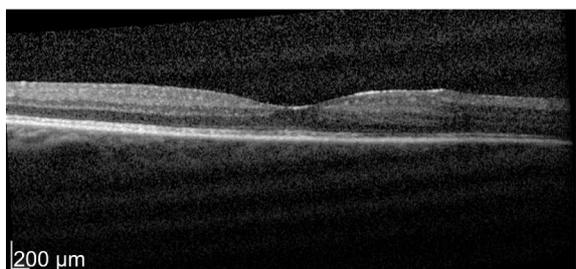


Figure 10 Two weeks post treatment OD vision 49 letters with decreased in macular thickness to 224  $\mu$ m.

being a steroid responder, her intraocular pressure remained stable with topical antiglaucoma treatment not needing surgical intervention.

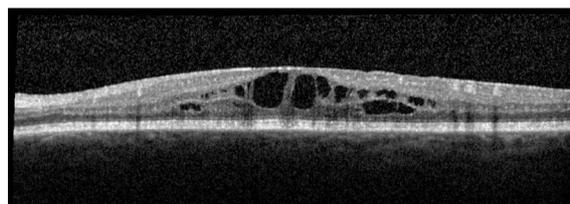


Figure 11 OS vision 63 letters with CMT of 446  $\mu$ m despite 2mo on oral prednisolone.

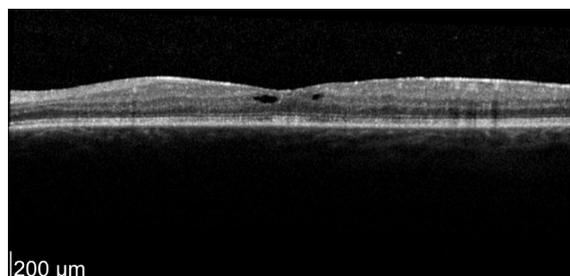


Figure 12 Two weeks post-treatment OS vision improved to 78 letters with macular thickness of 333  $\mu$ m.

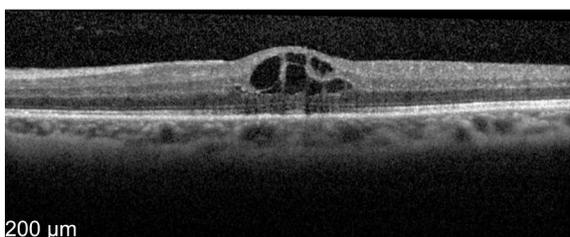


Figure 13 Pre-treatment OS vision 61 letters with central macula thickness of 496  $\mu$ m.

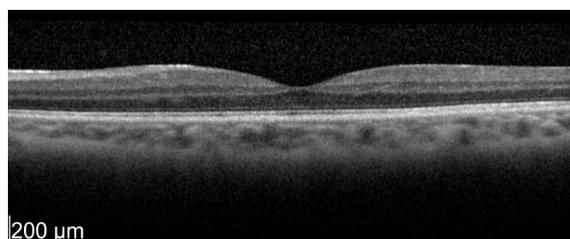


Figure 14 Two weeks later OS vision improved to 72 letters with CMT of 230  $\mu$ m.

#### CASE 4

A 30-year-old female patient with a history of recurrent panuveitis presented to the eye clinic with left visual blurring for 3wk. She also has a history of autoimmune polyendocrinopathy with posterior non-granulomatous uveitis affecting both eyes for the past 2y. Her uveitis episodes frequently flared up when she tapered topical steroids. Due to the recurrent uveitis and secondary complication of cystoid macular oedema resulting in worsening visual morbidity, she underwent intravitreal dexamethasone implantation to her left eye. Two weeks later her left eye vision improved with decreased in macular thickness as shown in Figures 13 and 14.

#### DISCUSSION

In our study 2 of the 6 eyes needed antiglaucoma treatment and 1 of the 6 eyes needed cataract surgery within 1y. Results in Table 1 summarised the reduction in retinal thickness and

**Table 1 Results of non-infectious posterior uveitis following two weeks of dexamethasone intravitreal administration. Change in VA (ETDRS letters) and foveal thickness (CMT  $\mu\text{m}$ )**

Patient	Eyes	Age	Sex	Diagnosis	Systemic immuno suppression prior to Ozurdex®	Baseline VA	Post treatment VA	Baseline CMT ( $\mu\text{m}$ )	Post treatment CMT ( $\mu\text{m}$ )	Frequency of Ozurdex® treatment	Duration of follow up (mo)
No.1	OS	52	F	Bilateral panuveitis	Y	63	76	696	365	Once	18
No.2	OD	49	M	Birdshot chorioretinopathy	N	78	83	621	319	Twice	16
No.2	OS	49	M	Birdshot chorioretinopathy	N	72	82	463	349	Once	16
No.3	OD	51	F	Idiopathic Intermediate uveitis	Y	43	49	675	224	Once	14
No.3	OS	51	F	Idiopathic Intermediate uveitis	Y	63	78	446	333	Once	14
No.4	OS	30	F	Panuveitis	N	61	72	496	230	Once	12

VA: Visual acuity; CMT: Central macular thickness.

increased in letters read with intravitreal dexamethasone treatment in our group of patients. The complication rates for glaucoma and cataract are slightly higher compared to previous studies. Intravitreal treatment with dexamethasone implant also meant that the systemic complications of immunosuppressants or anti-tumour necrosis factor (TNF) administrations can be prevented. Limitation of our study included it being a retrospective analysis and small patient group of 6 eyes in 4 patients.

In bilateral noninfectious uveitis, the corticosteroids tend to be administered orally rather than locally (bilateral panuveitis, birdshot chorioretinopathy) starting at a high dose followed by a slow taper. Ozurdex® is reported to be effective in short term results, but the side effect profile of multiple implants is not yet clear and further data are needed. Complications of treatment such as cataracts and ocular hypertension increases much as the number of injections.

In the Huron study, 229 patients with intermediate and posterior uveitis were randomised into 3 groups: a single administration with dexamethasone implant 0.7 mg ( $n=77$ ) or dexamethasone implant 0.35 mg ( $n=76$ ) or a sham procedure ( $n=76$ ). Results showed clear benefits of intravitreal dexamethasone in controlling the inflammation, improving the vision and decreasing macular thickness. The proportion of patients with a vitreous haze score of zero at 8<sup>th</sup> week was 47% in patients with dexamethasone implant 0.7 mg and 36% in the 0.35 mg dexamethasone when compared to the sham group.

The proportion of patients with BCVA gain of 15 letter was significantly greater in both active treatment groups compared with sham. There was also a greater decrease in mean CMT at 8<sup>th</sup> week in the treatment group compared with sham. Twenty-three percent of patients with dexamethasone treatment required IOP-lowering medications and the

incidence of cataracts were 15% in the 0.7 mg dexamethasone implant patients, 12% in patients with 0.35 mg and 7% in the sham treatment [6]. Myung *et al* [7] reported good outcomes of dexamethasone implantation to control intraocular inflammation on non-infectious posterior uveitis patients with effect lasting 3-4mo.

In conclusion, from the results analysed with improvement in vision and decreased in macular thickness we advocate the use of dexamethasone implant in patients with non-infectious posterior uveitis. It is an effective treatment for controlling intraocular inflammation especially in resistant uveitis macular oedema.

**ACKNOWLEDGEMENTS**

**Conflicts of Interest:** Yap YC, None; Papathomas T, None; Kamal A, None.

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