

Two Complications Following Intravitreal Dexamethasone Implantation: Desegmentation of The Implant and Retinal Injury

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ABSTRACT

Ozurdex® (Allergan, Inc, Irvine, CA, USA) is an intravitreal sustained-release dexamethasone implant known to be effective in the treatment of macular edema. Common adverse effects of Ozurdex implantation include increased intraocular pressure and cataract progression; however other ocular complications, such as retinal hemorrhage, extra-macular hole, macular hole, desegmentation of the implant, migration of the implant into the anterior chamber might develop. Retinal injury with desegmentation of the implant has not been reported in the literature yet. A 68-year-old woman presented with complaints of decreased visual acuity in her right eye for approximately 1 month. Her medical history included diabetes mellitus that had been present for 10 years. In ophthalmologic examination, her corrected visual acuity was 1/10 in the right eye and 8/10 in the left eye. The patient was diagnosed with macular edema associated with diabetic retinopathy and intravitreal anti-vascular endothelial growth factor injection was performed in the right eye. In spite of three doses intravitreal anti-vascular endothelial growth factor injection, her best corrected visual acuity and cystoid macular edema did not improve. Therefore, intravitreal dexamethasone implant was injected in the right eye due to persistent macular edema. At one month follow up after injection, fundus examination revealed two pieces and one of the pieces was located on the retina. Laser photocoagulation was performed around the dexamethasone implant location. The aim of the case presentation is to discuss the causes and management of these complications after intravitreal dexamethasone implantation.

Keywords: Diabetic retinopathy, Intravitreal injection.

INTRODUCTION

Intravitreal dexamethasone implant (Ozurdex®, Allergan, Inc, Irvine, CA, USA) is a sustained-release agent containing 0.7 mg dexamethasone, which is used in non-infectious uveitis and macular edema. It is also used in several retinal disorders in addition to its use in retinal vein occlusion and treatment-refractory macular edema in diabetic retinopathy.^{1,2} In diabetic macular edema failed to regress despite anti-vascular endothelial growth factor (anti-VEGF) therapy, dexamethasone implant is beneficial in the regression of macular edema by decreasing VEGF release, inflammation and prostaglandin levels. Ozurdex implant (0.46 mm in diameter and 6 mm in length) is implanted by access to sclera using 22 G needled at the tip of applicator. Following implantation, the most common complications include cataract formation and intraocular

pressure (IOP) elevation caused by steroid content of the agent. Rare complications include migration to anterior chamber, retinal hemorrhage, extra-macular hole, implant desegmentation and implantation within lens.^{3,4,5} In our case, there was retinal injury due to implant desegmentation and retinal localization of one of two segments after Ozurdex implantation. We discussed causes and management of complications in the case report.

CASE REPORT

A 68-years old woman presented to our clinic with impaired vision. In her history, it was found out that she had diagnosis of diabetes mellitus over 10 years and was on oral anti-glycemic treatment. Using Snellen charts, best-corrected visual acuity was measured as 1/10 in right eye and 8/10 in the left eye. Biomicroscopic examination revealed

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normal findings in both eyes. In both eyes, there was posterior capsular intraocular lens and posterior capsules of lens were found to be intact. Intraocular pressure (IOP) was measured as 14 mmHg in right eye and 15 mmHg in the left eye. In fundus examination, there were microaneurysms, hard exudates and intraretinal hemorrhages in both eyes. On optical coherence tomography (OCT), cystoid macular edema with central macular thickness (CMT) of 577 nm, subretinal fluid and hyper-reflective dots were in seen the right eye while no macular edema was detected in left eye. Intravitreal anti-VEGF treatment (aflibercept, 3 doses) was recommended for right eye. In the control visit after 3 injections of aflibercept, BCVA was 1/10 in the right eye and 8/10 in the left eye. No pathological finding was detected in biomicroscopic examination. IOP was measured as 14 mmHg in right eye and 15 mmHg in the left eye. Fundus examination revealed findings similar to those before injections in both eyes. On OCT, it was seen that cystoid macular edema and hyper-reflective dots persisted and CMT was measured as 407 nm. Thus, intravitreal dexamethasone implant (Ozurdex®) was recommended to right eye with diagnosis of refractory macular edema. Ozurdex implant was applied under sterile conditions by superficial access to sclera at 4 mm to limbus by 30-45° angle with needle tip oriented upwards. After access to sclera, needle was placed as being perpendicular to application surface and injection was performed. No complication developed during procedure and no leakage was detected at access site. No abnormal finding was detected in biomicroscopic examination on day 3

after implantation and IOP was measured as 16 mmHg. Routinely, no fundus examination is performed on day 2 in our clinic. In the control visit on month 1, BCVA was measured as 4/10 in the right eye and 8/10 in the left eye by Snellen charts. No pathological finding was detected in both eyes by biomicroscopic examination. IOP was measured as 15 mmHg in right eye and 16 mmHg in the left eye. In fundus examination, two Ozurdex implant was observed in the right eye. It was seen that one of the implant was localized at vitreal space while other was localized to retina at mid-periphery of retina (ten o'clock position) (Figure 1). On OCT imaging, CMT was measured as 208 nm in the right eye. Three lines of laser photocoagulation were applied to the area where Ozurdex implant caused retinal damage and no complication was observed during laser therapy (Figure 2). In the control visit on month 3, BCVA was 5/10 in the right eye and 8/10 in the left eye by Snellen charts. No pathological finding was detected in both eyes by biomicroscopic examination. In fundus examination, Ozurdex implant localized to supratemporal region of right eye (ten-o'clock position) and surrounding faded laser spots were observed. The other piece of Ozurdex implant could not be observed (Figure 3). On OCT, CMT was measured as 214 nm in the right eye (Figure 3). In the control visit on month 6 after Ozurdex implant, BCVA was 4/10 in the right eye and 8/10 in the left eye by Snellen charts. No pathological finding was detected in both eyes by biomicroscopic examination. IOP was measured as 14 mmHg in right eye and 15 mmHg in the left eye. In fundus examination, laser scars a supratemporal region, micro-

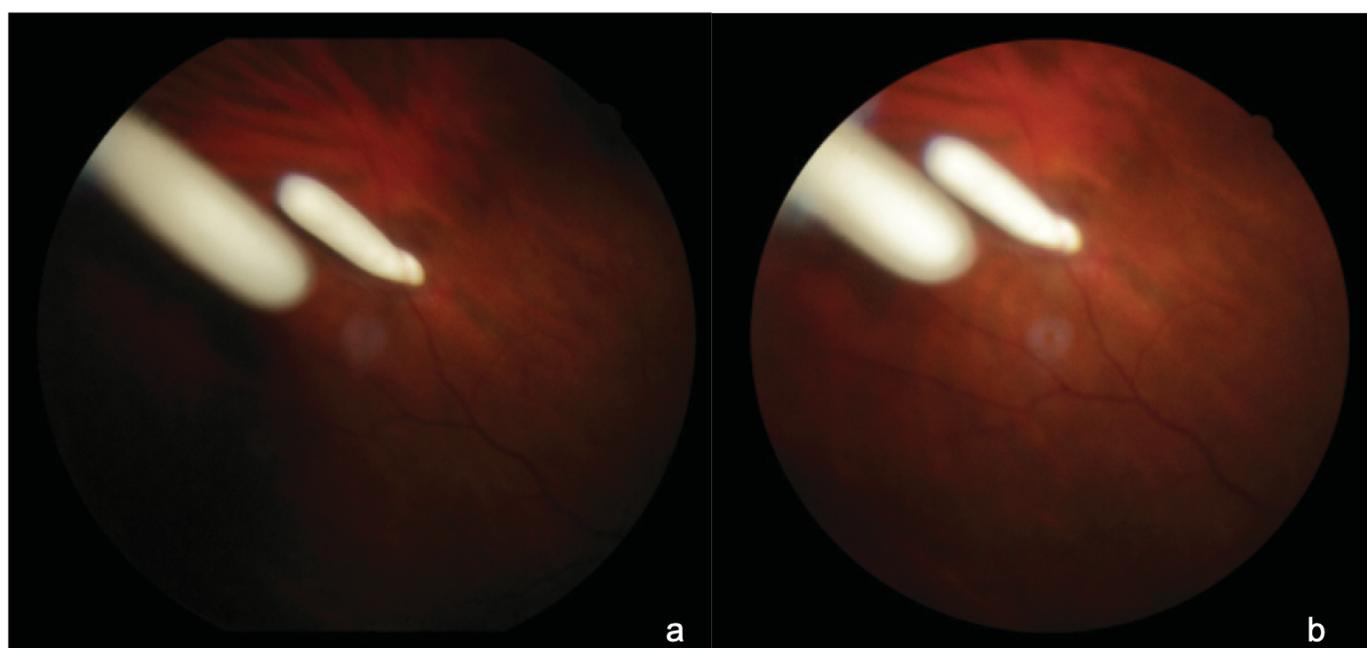


Figure 1: Fundus images on month 1 after dexamethasone implantation; as seen Figures a and b, there was an implant segment within vitreous while other segment was localized to retina at supratemporal region and adjacent to terminal branch of superior temporal retinal vein.



Figure 2: Fundus image of right eye after laser photocoagulation.

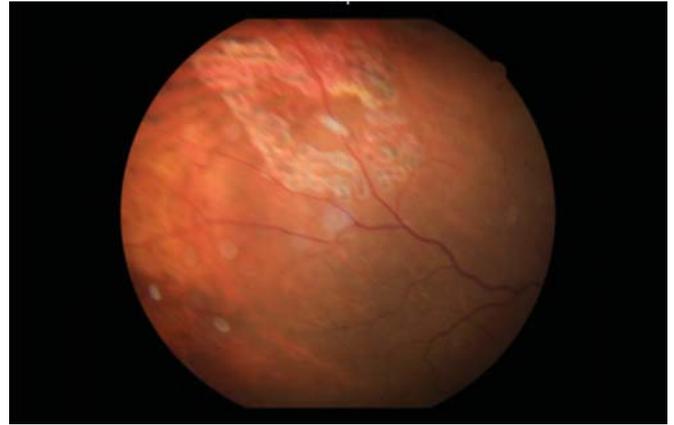


Figure 3: Laser spots can be seen easily in fundus images on month 1.

aneurysms and hard exudates were observed in the right eye while micro-aneurysms and hard exudates in the left eye. On OCT, CMT was measured as 214 nm in the right eye. Throughout follow-up, no edema was detected in left eye; thus, no treatment was given.

DISCUSSION

The most common complication is IOP elevation after Ozurdex implant; however, it is temporary and generally recovers with medical treatment without need for filtering surgery.¹ Moreover, migration to anterior segment has been reported in addition to complications that leads retinal injury such as retinal hemorrhage or extra-macular hole. The retinal injury caused by one segment of agent localized to retina after desegmentation has never been reported so far.

Ozurdex implant desegmentation is a very rare condition with a few reports in the literature. No retinal complication occurred in reported cases and no difference was detected regarding treatment efficacy.^{6, 7} In our case, implant desegmentation occurred as two pieces; one piece caused retinal injury while other piece was observed to be free in vitreous. As similar to those reported in the literature, no difference was detected in the efficacy of Ozurdex implant and it was seen that macular edema was regressed on OCT obtained on month 1.

It was detected that, Ozurdex implant leading retinal injury was localized adjacent to terminal branch of superior temporal retinal vein at mid-periphery of retina (ten o'clock position). The tip of implant had contact with retina but we failed to determine how much of implant was localized within retina. As known, Ozurdex implant is applied into eye at 4 mm distance to superiotemporal limbus. Sclera at 4 mm distance to limbus is projection of pars plana region of ciliary body and is defined safe localization for

intraocular access preferred in vitreoretinal surgeries and other intravitreal injections. Previously, ejection velocity and impact energy applied by Ozurdex implant applicator on retinal surface were tested in in vitro study.⁸ In the study, based on Gullstrad schematic eye (23.89 mm) the distance between needle tip of applicator and retinal surface was accepted as 15 mm when Ozurdex implant placed perpendicular to surface and 6 mm when placed by an angle of 30°. Ozurdex implant applications were repeated in water and vitreal gel media and it was found that implant output velocity was higher in water media than gel media (820±350 mm/second vs. 817±350 mm/second). Although 5 implants covered distance of 15 mm in 8 applications performed in water media, no implant was able to cover distance >4 mm in 8 applications performed in vitreal gel media. In a previous in vitro study, it was reported that the force needed to be applied on retinal surface in order to cause retinal injury is 0.1 to 0.2 N for an intraocular foreign body.⁹ In another in vitro study, it was reported the force applied by Ozurdex implant in case of retinal contact was extremely below than the force required for retinal injury.¹⁰ In our case, there was no history of previous vitreoretinal surgery. Based on these data, it could be thought that intravitreal implantation will not cause retinal injury; however, we think that implant desegmentation might change output velocity and force applied on retina. In addition, implant desegmentation might have caused to change in direction of segments and reduced distance from exit point and retinal surface. The implant pieces moving different directions after implantation can cause implant migration to anterior chamber in patients with zonular weakness and anterior chamber lens. In patients with implant at anterior chamber, implant can be forced to move posterior chamber by surgical treatment or positioning.^{11,12} However, such complication is unexpected in our case due to presence of intraocular lens within capsule and lack of zonular weakness. There is no in

vitro or in vivo study on changes in ejection dynamics by implant desegmentation. In addition, pressure applied on application surface during implantation may decrease distance between applicator needle and retinal surface. It is thought that this may be a promoting factor for implant access to retina in vitrectomized eyes and hypotonic eyes. Although it is avoided to apply pressure on application surface during Ozurdex implantation in our facility, it becomes inevitable to apply some degree of pressure due to patient complication. Although it is less likely, we think that this may be a risk factor for the complication encountered.

It has been proposed that implant ejection velocity may differ based on applicator in addition to application angle and media dynamics. In a previous case, it was seen that retinal hemorrhage was developed after retinal contact of implant in vitrectomized eye underwent Ozurdex implant application. It was thought that implant ejection more powerfully than required by applicator.¹³ In our case, we think that the complication in our patient could be due to same reason as there was no risk factor for implantation in our patient.

Although it has been proposed that extra-macular holes caused by Ozurdex implant are stable requiring no laser photocoagulation, there is one case report of extra-macular hole in which prophylactic laser photocoagulation was preferred.¹⁴ Authors reported that prophylactic laser photocoagulation was applied since the hole was wide and caused traction. In another case, Ozurdex implant with retinal localization was detected after Ozurdex implant applied to a vitrectomized eye and prophylactic laser photocoagulation was preferred in the patient.¹⁵ Given cases reported in the literature, we preferred laser photocoagulation in our patient. No vitreous hemorrhage was detected in our patient as there was no injury in vascular structure; thus, we were able to apply effective prophylactic laser photocoagulation at early period. Although vitreous hemorrhage was observed in 3.4-4.1% of patients underwent Ozurdex implant injection in previous studies, no significant difference was detected between bevacizumab and control groups.^{16,17} In the vitreous hemorrhage attributed to Ozurdex implantation, management is not changed unless a retinal injury occurs. In a case with vitreous hemorrhage with retinal localization of implant, prophylactic laser photocoagulation was preferred due to history of vitrectomy and previous panretinal photocoagulation at implant localization.¹³ Given that vitreous hemorrhage related to Ozurdex implantation is a rare complication, the management can show individual variation.

In conclusion, although Ozurdex implantation is performed in accordance to procedure, one should be careful regarding complications that may develop after implantation. Applicator should be placed perpendicular to application surface and it should be avoided to apply pressure on ocular surface during application. Thus, risk for injury at retinal surface can be decreased by maintaining distance between needle tip and retinal surface. In addition, it is warranted to attempt to observe implant in control visits and to ascertain appropriate localization of implant.

REFERENCES

- Haller JA, Bandello F, Belfort R Jr, et al. OZURDEX GENEVA Study Group. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. *Ophthalmology*. 2010;117:1134-46.
- Chiang A, Haller JA The dexamethasone drug delivery system: indications and evidence *Adv Ther* 2011;28:351-66.
- Fassbender Adeniran JM, Jusufbegovic D, Schaal S. Common and Rare Ocular Side-effects of the Dexamethasone Implant. *Ocul Immunol Inflamm*. 2017;25:834-40.
- Schmitz K, Maier M, Clemens CR, et al. German Retinal Vein Occlusion Group. Reliability and safety of intravitreal Ozurdex injections. *The ZERO study Ophthalmology* 2014;111:44-52.
- Christensen L, Sanders R, Olson J. "Magic Bullet": Eccentric Macular Hole as a Complication from Dexamethasone Implant Insertion. *Case Rep Ophthalmol Med*. 2016;2016:1706234.
- Agrawal R, Fernandez-Sanz G, Bala S, et al. Desegmentation of Ozurdex implant in vitreous cavity: report of two cases. *Br J Ophthalmol*. 2014;98:961-3.
- Donmez O, Parlak M, Yaman A, et al. Splitting of a Dexamethasone implant (Ozurdex) following the injection. *Case Rep Ophthalmol Med*. 2013;2013:247949.
- Meyer CH, Klein A, Alten F, et al. Release and velocity of micronized dexamethasone implants with an intravitreal drug delivery system: kinematic analysis with a high-speed camera *Retina*. 2012;32:2133-40.
- Ernst B.J, Velez-Montoya R, Kujundzic D, et al. "Experimental measure of retinal impact force resulting from intraocular foreign body dropped onto retina through media of differing viscosity," *Clinical & Experimental Ophthalmology*, 41;5:471-5, 2013.
- Christensen L, Sanders R, Olson J. "Magic Bullet": Eccentric Macular Hole as a Complication from Dexamethasone Implant Insertion. *Case Rep Ophthalmol Med*. 2016;2016:1706234.
- Stefano C, Enrico B, Giorgio M. Retinal and vitreous hemorrhage after traumatic impact of dexamethasone implant in a vitrectomized eye. *Eur J Ophthalmol* 2016; 26: e55-e57