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Case report

Intralenticular Ozurdex injection in an eye with thicker lens and the therapeutic effect maintained for 15 months

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ABSTRACT

Introduction: To report a case of accidental intralenticular Ozurdex injection in an eye with thicker lens. During the follow-up period of 15 months, the therapeutic effect of intralenticular Ozurdex was maintained.

Case description: Ozurdex was accidently injected into the lens of an eye with uveitis, and the lens thickness was measured to be 5.70 mm. The uveitis was under good control, and no significant development of cataract was observed until 7 months after the intralenticular Ozurdex injection. Then due to the outbreak of COVID-19, follow-up was suspended. Fifteen months after the injection, the patient returned to the doctor. At this time, significant cataract development was observed, whereas uveitis was still under good control. Accordingly, cataract surgery and Ozurdex extraction were performed. Two months after surgery, a mild recurrence of uveitis occurred.

Conclusions: A thicker lens might be an important risk factor for accidental intralenticular Ozurdex injections. However, after intralenticular Ozurdex injection, the development of cataract was slow, and Ozurdex could still have a therapeutic effect on uveitis in this case. Thus, immediate surgery might be unnecessary for certain accidental intralenticular Ozurdex injection cases, and a follow-up strategy could be chosen to maintain the effect of Ozurdex.

1. Introduction

Ozurdex (Allergan, Irvine, CA, USA) is a sustained-release dexamethasone implant used to treat macular edema caused by branch or central retinal vein occlusion, diabetic macular edema, or noninfectious posterior uveitis [1]. It will be injected into the vitreous body using a pre-packaged 22-gauge injection device. Ozurdex contains 0.7 mg dexamethasone and targets inflammation/edema by reducing leukostasis, inflammatory cytokines, and vascular endothelial growth factor expression. It has been suggested to be effective for treating macular edema and preventing irreversible changes in retinal glia, with improvement in visual acuity and reduction in macular retinal thickness [2, 3, 4, 5, 6, 7, 8, 9]. As next-generation medications, long-lasting intravitreal drugs have been extensively studied because they demonstrate better and more durable efficacy and less frequent intravitreal injection requirements [9, 10]. Ozurdex is a slow-release drug delivery system that can maintain a stable drug concentration in the vitreous body for up to six months [4].

Since the clinical application of Ozurdex, inadvertent intralenticular injection has been reported [11]. Here, we reported a case of accidental intralenticular Ozurdex injection in a 52-years-old female suffering from noninfectious uveitis. Considering that after the intralenticular injection, there was no significant inflammation in the anterior chamber, the development of cataract was slow, the best corrected visual acuity (BCVA) and intraocular pressure (IOP) were stable, and the uveitis was well controlled, we chose to follow up this patient to evaluate the safety and therapeutic efficacy of intralenticular Ozurdex instead of performing an immediate surgical intervention. The follow-up period was 15 months in this case.

2. Case description

The patient was a 52-years-old female with a history of noninfectious uveitis in both eyes. In addition, the patient had no other significant medical history (e.g., diabetes mellitus, hypertension). The patient had previously been treated with topical and systemic corticosteroids to control uveitis. However, the effect of topical corticosteroids was limited in this patient, and the patient could not tolerate the side effects of long-term systemic corticosteroid application. Thus, considering that the patient's left eye had both uveitis and macular edema (Figure 1), we

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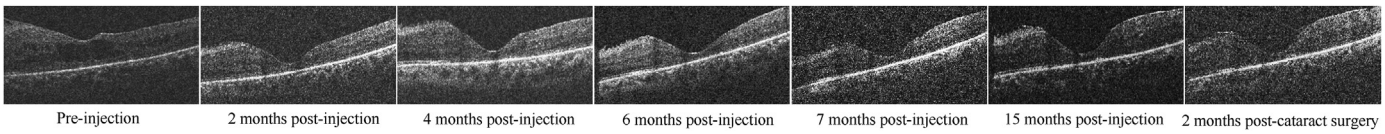

Figure 1. The macular optical coherence tomography (Carl Ziess Meditec, Dublin, CA, USA) images of the left eye before and after intralenticular Ozurdex injection.

decided to perform an intravitreal Ozurdex injection in the left eye in May 2019 to control the progression of uveitis and alleviate macular edema. Before the Ozurdex injection, the BCVA was 0.25 (Snellen chart) for the right eye and 0.1 for the left eye, and IOP was 12 mmHg for the right eye and 13 mmHg for the left eye. Both eyes had mild cataract (grade nuclear cataract (NUC)-1, grade cortical cataract (COR)-1, grade posterior subcapsular cataract (PSC)-1 [12]) and anterior chamber inflammation (grade 1+ for anterior chamber flare [13]). The Ozurdex injection site was 4.0 mm behind the limbus.

On the 1st day after the Ozurdex injection, the slit lamp examination revealed that a foreign body was within the lens and was confirmed to be the injected Ozurdex (Figure 2). Although Ozurdex was injected into the lens, the lens showed no significant opacity development (still grade NUC-1, grade COR-1, grade PSC-1), and the BCVA was 0.25 for the right eye and 0.1 for the left eye; the IOP was 15 mmHg in the right eye and 14 mmHg in the left eye. In addition, the anterior chamber inflammation in both eyes was similar to the pre-surgical status (grade 1+ for anterior chamber flare). Thus, since intralenticular Ozurdex did not result in significant cataract development and changes in BCVA and IOP, no immediate surgical intervention was performed, and follow-up observation was chosen. The thickness of the lens was also measured. The lens thickness was 5.70 mm for the left eye (affected eye) and 5.48 mm for the right eye (fellow eye) (IOL master 700, Carl Zeiss, Meditec, Dublin, CA, USA).

The follow-up results are shown below:

Two months after the Ozurdex injection, the BCVA of the left eye was 0.1, and the IOP of the left eye was 16 mmHg. No significant development of cataract (grade NUC-1, grade COR-1, grade PSC-1) was observed in the left eye (Figure 2). The intralenticular Ozurdex was equal to its original size within the lens (Figure 3). Optical coherence tomography (OCT) revealed that macular edema of the left eye was significantly relieved (Figure 1). No inflammation was observed in the anterior chamber of the left eye (grade 0 for anterior chamber flare), whereas anterior chamber inflammation persisted in the right eye (grade 1+ for anterior chamber flare).

Four months after the Ozurdex injection, the BCVA of the left eye was 0.1, and the IOP of the left eye was 18 mmHg. No significant cataract developed (grade NUC-1, grade COR-1, and grade PSC-1). The OCT results showed only slight macular edema in the left eye (Figure 1). The intralenticular Ozurdex presented signs of degradation, reducing to 3/4 of its original size (Figure 3). No inflammation was observed in the anterior chamber of the left eye (grade 0 for anterior chamber flare), whereas anterior chamber inflammation persisted in the right eye (grade 1+ for anterior chamber flare).

Five months after the Ozurdex injection, the patient had a BCVA of 0.1 in the left eye, with an IOP of 19 mmHg. The lens of the left eye showed no significant development of cataract (grade NUC-1, grade COR-1, and grade PSC-1). According to the slit lamp (grade 0 for anterior chamber flare), fundus fluorescein angiography (FFA), and OCT examinations, no signs of uveitis and macular edema (Figure 1) were observed in the left eye. However, uveitis was aggravated in the right eye (grade 2+ for anterior chamber flare), which did not receive Ozurdex treatment.

Six months after the Ozurdex injection, the BCVA of the left eye was stable at 0.1, and the IOP of the left eye was still within the normal range (17 mmHg). The uveitis and macular edema (Figure 1) were still under good control, and the lens had no significant opacity development (grade NUC-1, grade COR-1, grade PSC-1) (Figure 2) in the left eye. The intralenticular Ozurdex was absorbed by approximately 1/3 (Figure 3). Significant anterior chamber inflammation differences between the left and right eyes were found (grade 0 for anterior chamber flare in the left eye and grade 2+ for anterior chamber flare in the right eye).

Seven months after the Ozurdex injection, the anterior chamber inflammation was similar to that of the last month in both eyes (grade 0 for anterior chamber flare in the left eye and grade 2+ for anterior chamber flare in the right eye). The BCVA of the left eye remained to be 0.1, and no significant development of cataract was observed (grade NUC-1, grade COR-1, and grade PSC-1) (Figure 2). There was no recurrence of uveitis and macular edema (Figure 1) in the left eye. The intralenticular Ozurdex was significantly smaller and thinner than the original size (Figure 3). Meanwhile, the IOP of the left eye began to rise, fluctuating between 24 and 28 mmHg. To control the elevated IOP, the patient received brinzolamide (q8h) and timolol (q12h) in the left eye. Considering that the lens showed no significant development of cataract, uveitis and macular edema (Figure 1) were under good control, and IOP only had a mild elevation, we chose to continue our follow-up strategy instead of performing the surgical intervention.

Then due to the outbreak of COVID-19 in Wuhan and the subsequent lockdown of Wuhan, the patient suspended her follow-up until 15 months after the Ozurdex injection. Fifteen months after the Ozurdex injection, the patient returned to our clinic and complained of diminishing visual acuity in the left eye, which occurred 2 months ago. BCVA was 0.02 and IOP was 13 mmHg (controlled by brinzolamide and timolol) in the left eye. The lens showed significant opacity development (grade NUC-2, grade COR-3, and grade PSC-3) (Figure 2). Ozurdex was absorbed by about 1/2, reducing to 1/2 of its original size (Figure 3). In the meantime, still no signs of uveitis (grade 0 for anterior chamber flare) and macular edema (Figure 1) were observed in the left eye, while uveitis (grade 2+ for anterior chamber flare) was observed in the right eye.

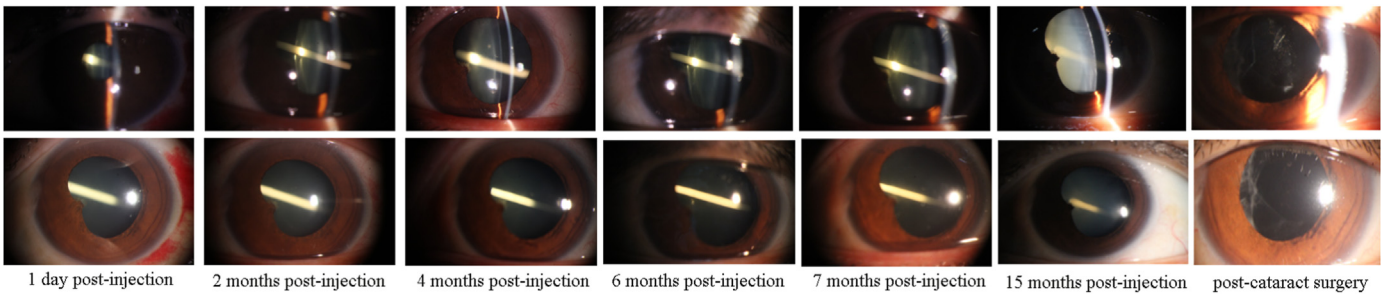

Figure 2. The anterior segment (Keeler Ltd., Windsor, UK) images of the left eye after intralenticular Ozurdex injection.

Figure 3. The scanning laser ophthalmoscopy (Optos, Dunfermline, Scotland) images of the left eye after intralenticular Ozurdex injection.

These results indicated that intralenticular Ozurdex could still have a therapeutic effect on uveitis and macular edema, as in the vitreous body. Meanwhile, after intralenticular Ozurdex injection, the cataract development was slow.

Considering that the patient strongly demanded for surgical intervention owing to lens opacity and IOP elevation, cataract surgery and Ozurdex extraction were performed on the 31st of August, 2020. Following the corneal incision was made, medical sodium hyaluronate gel (Healon, Shanghai, China) was injected into the anterior chamber and the space between the lens and the posterior capsule. Subsequently, manual injection/aspiration (I/A) was performed to extract the cataract. During manual I/A, Ozurdex was noted to be located at the lens's posterior pole, completely within the lens. Considering that I/A might smash the fragile Ozurdex to powder, which might potentially damage the endothelium of the cornea, we extracted Ozurdex using manual I/A and microscope forceps. After Ozurdex extraction, we found that the posterior capsule of the lens was complete, and no vitreous was encountered. We then performed phacoemulsification and I/A to extract the remaining lens. After the complete extraction of the lens, an intraocular lens (ZCB00, Abbott Medical Optics, Santa Ana, CA, USA) was implanted (Figure 4).

One day postoperatively, the BCVA was 0.05, IOP was 20 mmHg, IOL was clear and located in the center (Figure 2), and no Ozurdex remained (Figure 3) in the left eye.

Two months after cataract surgery and Ozurdex extraction in the left eye, the BCVA was 0.06, and the IOP was 18 mmHg. Slit lamp (grade 1+ for anterior chamber flare) and FFA examinations showed a mild recurrence of uveitis, while no macular edema was observed by OCT (Figure 1) in the left eye.

3. Discussion

Ozurdex (Allergan, Irvine, CA, USA) is a rod-shaped dexamethasone implant used for intravitreal injections. It is 6 mm in length and 0.46 mm in diameter and is injected into the eye by a 22-gauge needle [1, 11].

A retrospective multicenter study (ZERO study) with 342 eyes that received Ozurdex injections showed that no infection, endophthalmitis, intraoperative lens injury, perioperative hypotension, or retinal detachment were reported by the patients with Ozurdex treatment. The most common complication of Ozurdex injection was elevated IOP, with an incidence of 20%. In general, the Ozurdex-induced increase in IOP required no surgical intervention. Thus, the ZERO study revealed that Ozurdex injection is a therapy with minimal complications. The complication rate would not be higher in the clinical routine application than in registration studies [14]. A study by Mello et al. reported that after an Ozurdex injection, the percentage of an increase of 10 mmHg or more in IOP was 7.4%, that of an increase of 25 mmHg or more in IOP was 6.6%, and that of an increase of 35 mmHg or more in IOP was 1.8%. No cases of endophthalmitis or retinal detachment were observed [5]. Similarly, Iglicki et al. suggested that the application of Ozurdex had an acceptable safety profile [3].

However, in the past few years of Ozurdex application, several cases of accidental intralenticular injection have been reported, and the possibility of the affected eye being the right or left eye was equal [11, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. The underlying reason for accidental intralenticular injection could be the absence of injection experience, inappropriate operation, and accidental head movement of the patient during injection [16]. In addition to the reasons mentioned above, if the patient had a thicker lens, the intravitreal injection might cause injury to the lens because the posterior pole of the thicker lens would be closer to the injection site and the needle tip. However, none of the previous reports of accidental intralenticular Ozurdex injection measured lens thickness. In our case, we performed lens thickness measurement and found that the lens thickness of this patient (5.52 mm for the right eye and 5.70 for the left eye) was much greater than normal lens thickness (reported to be 3.80–4.38 mm) [26, 27, 28, 29]. Thus, in this case, the thicker lens might be a potential reason for accidental intralenticular Ozurdex injection. This report is the first study to measure the lens thickness in patients with intralenticular Ozurdex injection and raise the potential relationship between greater lens thickness and accidental intralenticular Ozurdex injection, suggesting that ophthalmologists should pay more attention to intravitreal Ozurdex injection in patients with thicker lenses.

A previous study has demonstrated that by intravitreal injection, for each 0.5 mm the injection site moved further posterior from the limbus, the distance between the needle probe and the lens would increase by about 0.5 mm [30]. However, retinal detachment may occur when the intravitreal injection is made too far from the limbus (>5 mm) [31]. Accordingly, for intravitreal injection in a patient with a thickened lens, the injection site should be placed closer to 5 mm posterior from the limbus, to ensure an adequate distance between the thickened lens and the injection probe and to avoid damaging the retina simultaneously.

Among previously reported intralenticular injection cases, cataract formation and development rates were distinct. In some cases, cataract would be observed shortly after the intralenticular injection of Ozurdex [18, 24, 32, 33], while other cases showed that cataract would only slowly develop after the intralenticular injection of Ozurdex [15, 16, 17, 21, 25]. Thus, the therapeutic strategy for intralenticular Ozurdex injection is also different. The wait-and-see approach can be chosen for cases with no or slow development of cataract. In contrast, when the cataract develops rapidly, immediate surgical intervention is necessary (In addition to the surgical procedure mentioned in this report, the

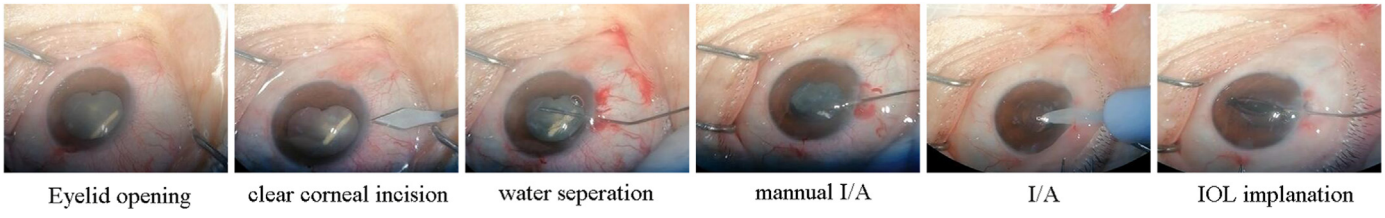

Figure 4. The procedure of cataract surgery and Ozurdex extraction.

sutureless intraocular lens flanged technique [34] might be chosen when the lens capsule is damaged significantly due to intralenticular injection, making the lens capsule unable to support the intraocular lens). Similar to cataract formation and development rate, the therapeutic efficacy of intralenticular Ozurdex is also controversial. Some studies have shown that intralenticular Ozurdex could still have therapeutic efficacy as in the vitreous body [11, 16, 20], while others have reported that intralenticular Ozurdex has little therapeutic efficacy [15, 17, 33].

In the present case, the cataract developed slowly. Therefore, we chose wait-and-see for follow-up. During the follow-up period, the BCVA of the patient remained stable, and the lens showed no significant opacity development in the first 7 months. In the meantime, Ozurdex became shorter and thinner during the follow-up period, and uveitis and macular edema were under good control, indicating that the intralenticular Ozurdex could still be released to maintain the therapeutic effect, although at a relatively slow rate. In our case, from May 2019 to August 2020, Ozurdex was only absorbed by 1/2 in 15 months. This absorption rate is much slower than the normal rate (totally absorbed in 4–6 months, with a peak dose in 2 months) [22].

Although the absorption rate of intralenticular Ozurdex was slower than that under normal conditions (intravitreal Ozurdex), Ozurdex still seems to affect uveitis. During the follow-up period, we performed slit-lamp, FFA, and OCT examinations to evaluate the uveitis status in both eyes of the patient. The results showed that the right eye (without Ozurdex injection) had persistent uveitis and the left eye (with Ozurdex injection) had no uveitis, indicating that intralenticular Ozurdex was still effective for uveitis and the effect duration of intralenticular Ozurdex was much longer than normal (4–6 months). A previous study indicated that, after the discovery of intralenticular injection of Ozurdex, immediate cataract surgery might increase the posterior capsule stress and tear the posterior capsule [23]. When we chose the wait-and-see strategy, the posterior capsule rupture might become fibrosed and recover during the follow-up period. After the fibrosis of the posterior capsule rupture, the subsequent surgical intervention would be safer. Thus, when the lens with intralenticular Ozurdex showed no significant opacity, follow-up may be recommended instead of immediate surgical intervention.

The therapeutic effect of intralenticular Ozurdex is controversial because, within the lens, Ozurdex would not be directly exposed to the aqueous humor or blood circulation [16]. However, to be inserted into the lens, Ozurdex must penetrate the lens capsule and cause potential rupture on the capsule. Thus, a portion of Ozurdex may be in contact with the vitreous body and produce a therapeutic effect [11]. In addition, previous studies have indicated that the anatomical and functional efficacy of Ozurdex was equal in both non-vitrectomized and vitrectomized eyes [35, 36], indicating that Ozurdex might not require the vitreous body as a substrate to work [6, 35]. Thus, intralenticular Ozurdex could still have a therapeutic effect, even if it was not in the vitreous body. In addition, another evidence of the therapeutic efficacy of intralenticular Ozurdex was the size reduction of Ozurdex during the follow-up course, even at a relatively slow rate (reduced by 1/2 in 15 months).

OCT can provide clear images and precise measurements of individual layers of the retina [37, 38]. Different OCT models may have different advantages (e.g., enhanced-depth imaging OCT could display the connection between the schisis cavity in the retina and the gap in the lamina cribrosa, and long horizontal OCT could display the macula and optic disk for detection of connectivity) [37]. Thus, OCT is an important examination method in diagnosing and managing various fundus lesions, and baseline OCT measurements have been suggested to be the predictive biomarkers for certain fundus lesions [8, 37, 38, 39, 40, 41]. In terms of diabetic macular edema (DME) treated by Ozurdex, absent disorganization of retinal inner layers, submacular fluid, absent hyperreflective foci, and continuous inner segment-outer segment layer were reported to be OCT biomarkers for the better treatment effect of Ozurdex on DME [8, 38]. In terms of DME treated by surgical interventions, early surgical performance and the presence of subretinal fluid on OCT could be biomarkers for better visual prognosis [39]. In addition to DME, central serous chorioretinopathy has also been suggested to have OCT biomarkers. Singh et al. indicated that changes in both central macular thickness and subfoveal choroidal thickness, as well as subfoveal ellipsoid zone injury, could be OCT biomarkers for central serous chorioretinopathy resolution [40]. Thus, these OCT biomarker studies may provide retinal specialists and ophthalmologists with clues for proper treatment timing selection and disease prognosis prediction. In addition to OCT, other examination methods (e.g., scanning laser ophthalmoscope, FFA) could also be useful in the diagnosis and management of fundus lesions [42, 43, 44, 45]. In this study, we used scanning laser ophthalmoscope to record changes in the length of Ozurdex and FFA to evaluate the status of uveitis. The combination of various ophthalmic examination methods can assist ophthalmologists to make proper diagnoses and treatment options.

In conclusion, a thicker lens could be an important risk factor for accidental intralenticular Ozurdex injections. When accidental intralenticular injection occurs, not all cases will cause immediate cataract formation or rapid cataract development. A wait-and-see approach can be used for cases with slow cataract development. In addition, intralenticular Ozurdex could still have a long-term therapeutic effect. However, we should also note that this study was only a case report; thus, no data analysis was performed, which might lead to study bias due to the lack of statistical evidence. Thus, to further verify our conclusions, more observations and statistical analyses are required.

Declarations

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

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Data included in article/supp. material/referenced in article.

Declaration of interest's statement

The authors declare no competing interests.

Additional information

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