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CASE REPORT

Intracrystalline Ozurdex®: therapeutic effect maintained for 18 months

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Abstract

Introduction Ozurdex® is a sterile, sustained-release implant of dexamethasone. The device dissolves within the vitreous body and releases dexamethasone. Here we present a clinical case that demonstrates the sustained therapeutic efficacy of Ozurdex® when accidentally injected into the crystalline lens.

Methods Case report.

Results Sixty-three-year-old male in which we decided to prescribe the intravitreal injection of a dexamethasone implant (Ozurdex®) in the left eye because of macular oedema after branch retinal vein occlusion. Best-corrected visual acuity (BCVA) was 0.4. At 15 days post-implantation, the slit-lamp examination revealed the dexamethasone implant was located in the crystalline lens. Given there was no inflammation in the anterior pole, no cataracts had developed, the intraocular pressure (IOP) was normal and the macular oedema had been resolved, we decided to assess the efficacy and safety of the dexamethasone implant located in the crystalline lens. The BCVA improved until 14 months post-accidental injection. At 18 months post-Ozurdex® injection the BCVA worsened until 0.05 because of the cataract evolution. Phacoemulsification and intraocular lens placement in sulcus was performed.

Conclusion Once the complication has occurred, most authors advocate the early withdrawal of the implanted Ozurdex® device by means of crystalline phacoemulsification and then repositioning it in the vitreous body. However, as long as there are no signs of inflammation in the anterior pole, the IOP is within normal limits, the device does not affect the visual axis and there is no cataract development, we can evaluate the potential therapeutic effect of Ozurdex® in this non-indicated, abnormal location.

Keywords Accidental injection of dexamethasone intravitreal implant · Intralenticular dexamethasone implant · Macular oedema · Vein occlusion

This work was performed at Hospital Clínico Universitario Valencia.

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Introduction

Ozurdex® is a sterile, sustained-release, rod-shaped implant with 700 μg of dexamethasone. It measures approximately 0.46 mm in diameter and 6 mm long. The device dissolves within the vitreous body of the eye and slowly releases dexamethasone. It is indicated to treat adults with diabetic macular oedema, macular oedema following branch retinal vein occlusion or central retinal vein occlusion and inflammation of the posterior segment of the eye caused by non-infectious uveitis.

The most common adverse ocular reactions that may appear are an increase in intraocular pressure (IOP) and the onset or progression of cataracts. Other less common negative reactions are sterile or infectious endophthalmitis, ocular hypotonia, retinal detachment or inflammation of the anterior chamber.

The ZERO study (designed to test the safety and efficacy of Ozurdex® intravitreal injections) did not report any intra-operative damage to the lens. However, only a few authors have described the outcome of accidentally injecting Ozurdex® into the crystalline lens [1–8]. This could be the result of the surgeon's lack of experience, the use of an unsuitable surgical technique or an uncontrolled movement of the patient's head during the procedure [1].

Here we present a clinical case that demonstrates the sustained therapeutic efficacy of Ozurdex® when accidentally injected into the crystalline lens. To the best of our knowledge, only a few articles discussing this rare complication have been published. When it does occur, then the most common approach is early phacoemulsification and implant repositioning within the vitreous body [1]. Only one of these articles described a conservative approach in which the authors assessed the therapeutic effect of the device when located in the lens. In that case, phacoemulsification plus intraocular lens implant surgery was delayed by up to 7 months after accidentally injecting Ozurdex® in the crystalline lens [1].

Here we present the case of an accidental intralenticular injection of Ozurdex® that we maintained within the lens for 18 months.

Given that the anterior pole was normal, no cataracts had developed, the Ozurdex® implant's position in the crystalline lens did not affect the visual axis and the macular oedema was disappearing, we decided to follow a wait-and-see approach in order to evaluate the therapeutic efficacy of the implant in this abnormal location.

Clinical case

Sixty-three-year-old male whose initial complaint was deteriorating visual acuity (VA) and metamorphopsia in the left eye (OS) occurring over a 6 month period. Best-corrected visual acuity (BCVA) was 10/10 in the right eye (OD) and 4/10 in the left eye (OS). The IOP was 13 mmHg in the OD and 15 mmHg in the OS. The anterior poles were normal and the crystalline lens transparent in both eyes (OU). The eye fundus (EF) of the OD was normal, but the OS presented cystoid macular oedema and intraretinal haemorrhage in the region of the superior temporal arcade compatible with branch retinal vein occlusion. Such diagnosis was confirmed performing a fluorescein angiography. Optical coherence tomography (OCT) of the macula revealed a central macular thickness of 548 μm and intraretinal cysts.

We decided to prescribe the intravitreal injection of a sustained-release dexamethasone implant (Ozurdex®). At 15 days post-implantation, the patient complained of myodesopsia and went to our emergency service. The BCVA was 0.15 and a slit-lamp examination revealed the dexamethasone implant was located in the crystalline lens (Fig. 1). The patient did not present cataracts. OCT indicated the macular oedema had been resolved and the IOP was 16 mmHg.

Very few articles have reported this type of complication; the majority of them followed an approach that involved extracting the resulting cataract and repositioning the dexamethasone implant in the vitreous cavity [1]. An intraocular lens was subsequently placed in the capsular bag or the sulcus [1–4]. In the present case, given there was no inflammation in the anterior pole, no cataracts had developed, the IOP was normal and the macular oedema had been resolved, we decided to follow a wait-and-see approach to assess the efficacy and safety of the dexamethasone implant when located in the crystalline lens.

At 2 months post-Ozurdex® implant injection, a slit-lamp examination showed the anterior pole was normal, there was no inflammation and no cataracts had developed. The IOP was 17 mmHg.

At 5 months post-implant injection, the patient had a BCVA of 0.5. Under slit-lamp examination, the Ozurdex® located in the crystalline lens presented no signs of degradation or cataract development (Fig. 2a). OCT confirmed the presence of a normal foveal profile and the absence of macular oedema. The IOP was 19 mmHg. Given this mild increase in IOP with respect to the previous follow-up, we decided to start treatment with brinzolamide eye drops every 12 h although the IOP remained at normal values. Considering the patient's vision had improved, the cystoid macular oedema had not reappeared and IOP values were within normal limits, we decided to continue with a watchful waiting approach.

At 12 months post-Ozurdex® injection, the BCVA continued to have a value of 0.5 and the outer edge of the dexamethasone implant showed signs of slight degradation during the slit-lamp examination (Fig. 2b). There were no signs the macular oedema had reappeared and the IOP was 17 mmHg while under brinzolamide eye drop treatment.

At 14 months post-injection the patient complained of diminishing VA. He had a BCVA of 0.3 and the IOP was 16 mmHg. Slit-lamp examination revealed a posterior subcapsular cataract had developed (Fig. 3). The central macular thickness was normal.

At 18 months post-injection, the BCVA was < 0.05 and the IOP was 15 mmHg. The central macular thickness continued to present normal values, but during examination of the anterior pole we observed that the subcapsular cataract had progressively worsened and the degradation of the temporal end of the dexamethasone implant had accelerated (Fig. 4).

Due to the decrease in visual acuity caused by the rapidly developing cataract noted in previous follow-ups, we decided to perform crystalline phacoemulsification and intraocular lens implantation.

During surgery, despite performing the phacoemulsification at very low intensities, the crystalline lens dislocated to the vitreous chamber with the rest of the remaining Ozurdex® given the posterior capsule had been ruptured previously. This rupture occurred when the dexamethasone implant was accidentally injected into the crystalline lens. Various articles in the literature have described the complications that may arise when extracting cataracts in this special situation in which an implant has been injected into the crystalline lens. This implies a rupture in the crystalline capsule and so the treatment of choice under these circumstances is to implant the intraocular lens (IOL) in the sulcus [2–4]. We therefore envisaged such a situation and accordingly performed a 23-G pars plana vitrectomy (PPV) with extraction of crystalline material and any remains of dislocated Ozurdex® during the same surgical procedure. The anterior capsule was completely intact; in fact it constituted a good anatomical support for an incident-free IOL implantation in the sulcus.

Two months after extracting the cataract and intracrystalline Ozurdex®, we observed a recurrence of the cystoid macular oedema as it returned to pre-dexamethasone implant injection values. We therefore decided to insert a new Ozurdex® implant and once again we observed that it resolved the macular oedema, even at 8 days post-injection.

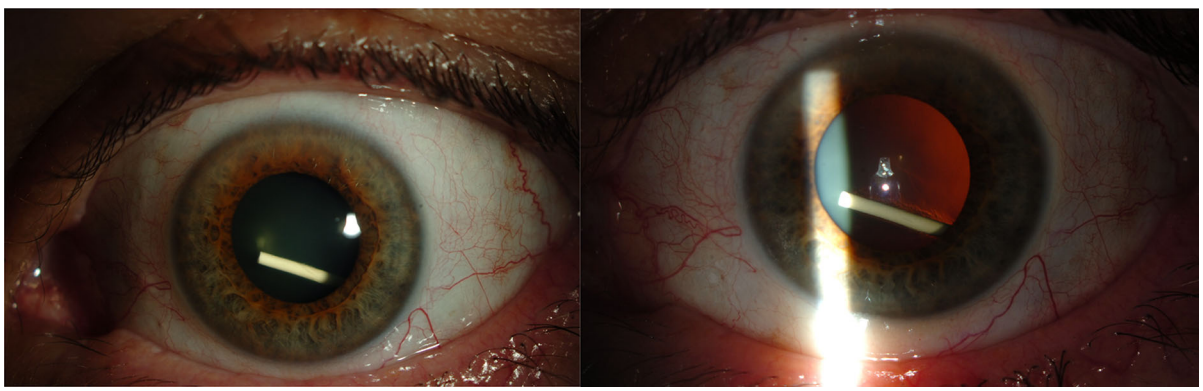

Fig. 1 Anterior pole 15 days after Ozurdex® implant injection. The dexamethasone implant was located in the crystalline lens. Entry was from lower temporal quadrant (left). Retroillumination shows the path drawn by the implant as it passes through the lens (right)

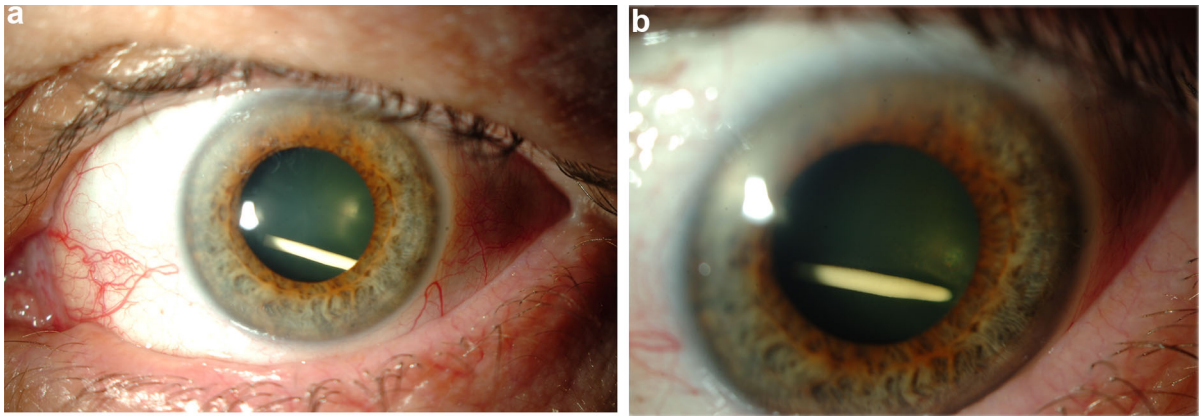

Fig. 2 **a** 5 months post-Ozurdex® accidental injection: the implant located in the crystalline lens presented no signs of degradation neither the nasal nor temporal side. There was no cataract development. **b** 12 months post-Ozurdex® accidental injection: the outer edge of the dexamethasone implant showed signs of slight degradation

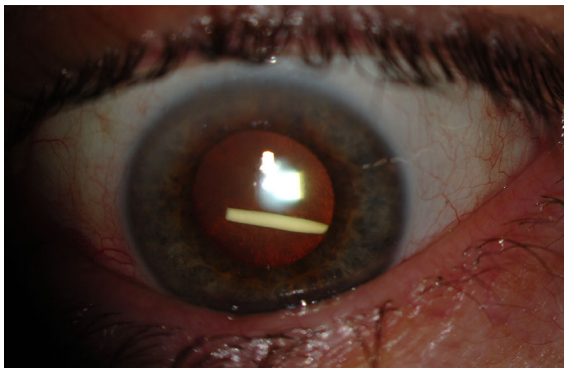

Fig. 3 14 months post-Ozurdex® accidental injection: retroillumination revealed a posterior subcapsular cataract

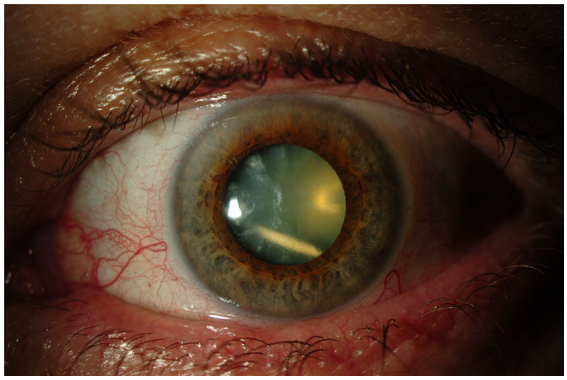

Fig. 4 18 months post-Ozurdex® accidental injection: acceleration in the development of the cataract. Best-corrected visual acuity was < 0.05

Discussion

As far as we are aware, very few published articles discuss this rare complication that arises when Ozurdex® is inadvertently injected into the crystalline lens [1–8]. Of all the articles we reviewed, only one described a wait-and-see approach where the authors assessed the medium/long-term therapeutic effect of the implant when injected into the crystalline lens [1]. Most articles recommend early phacoemulsification of the crystalline lens, repositioning the dexamethasone implant in the vitreous body and the introduction of an IOL. Through the present article, we have demonstrated the therapeutic effect of Ozurdex® when situated intralenticularly since it resolved macular oedema, IOP values remained normal, VA improved and there was no cataract development for the first 14 months; at which point a rapidly evolving posterior subcapsular cataract started to develop. The cataract was extracted 18 months after the inadvertent intracrystalline injection. This means the implant was maintained in an intralenticular location for more than twice as long as the next longest case published in the literature, wherein the implant was in place for 7 months [1]. Besides this, another significant difference compared to the previous publication is that the macular oedema resolved in the present case actually translated into increased VA for 14 months because the crystalline lens remained transparent. That is why we did not consider crystalline lens phacoemulsification with intraocular lens implantation until 18 months after injecting the Ozurdex® device, which

is when the BCVA fell below 0.05 due to the cataract's rapid progress, because OCT still revealed an anatomically suitable foveal profile.

The therapeutic effect of Ozurdex® when located in the crystalline lens is questionable because it does not come into direct contact with either the aqueous humour or the blood circulation [1]. However, the fact that the device crossed, and therefore ruptured, the posterior crystalline capsule in order to become inserted within the posterior cortex of the crystalline lens must be taken into account. Hence, a portion of the Ozurdex® implant was in contact with the vitreous humour and thus produced the desired therapeutic effect and resolved the macular oedema. Throughout the entire follow-up period, the dexamethasone device's shape remained practically unchanged and there were no signs of degradation until 1 year after it had been injected into the crystalline lens. At which point we observed slowly progressing decomposition on the outer edge of the device that started to accelerate at 14 months post-implant injection. The accelerated degradation of the Ozurdex® implant coincided with the accelerated development of the subcapsular cataract and therefore we consider both events are directly related to each other.

In conclusion, accidentally inserting Ozurdex® into the crystalline lens when injecting the intravitreal implant is a very rare complication, but it must be borne in mind during the procedure so that it may be averted. However, the present article demonstrates that once the implant injection has been misplaced, then so long as there are no signs of inflammation in the anterior pole, the IOP is within normal limits, the device does not affect the visual axis and there is no cataract development; then, we can follow a wait-and-see approach while evaluating the potential therapeutic effect of Ozurdex® in this non-indicated, abnormal location.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Human rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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