

Acute Corneal Epithelial Detachment During Lid Speculum Placement Prior to Intravitreal Injection in a Diabetic Patient: A Case Report

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Introduction: Diabetic macular edema (DME) is a vision-threatening complication of diabetic retinopathy. Intravitreal anti-VEGF injections offer effective treatment, but they carry a risk of corneal epithelial detachment, particularly in patients who have recently undergone cataract surgery.

Case Presentation: A 63-year-old male developed bilateral DME following cataract surgery with intraocular lens implantation. His best-corrected visual acuity (BCVA) was 0.15 in the right eye and 0.5 in the left eye. The patient underwent bilateral intravitreal injections of the anti-VEGF agent conbercept. During preparation for the injection in the left eye, corneal epithelial bleb formation was observed. The patient received corneal patching therapy, with complete epithelial healing observed by day 10 post-injection. This case underscores the need for vigilant corneal monitoring during and after intravitreal injections in diabetic patients with prior cataract surgery.

Conclusion: Close observation of corneal epithelial healing is crucial in diabetic patients receiving intravitreal injections, especially those with a recent history of cataract surgery. Careful pre-injection assessment and vigilant post-injection management are essential to mitigate this potential complication.

Keywords: diabetic macular edema, post-cataract surgery complications, corneal epithelial repair, intravitreal injection

Introduction

Intravitreal anti-VEGF injections are the standard of care for DME, providing targeted intervention against the underlying pathology.¹ While generally safe, it is imperative to remain vigilant for potential complications, especially in diabetic patients. Studies have demonstrated increased corneal vulnerability in diabetes, with both the number and density of corneal endothelial cell hexagons decreasing as the stage of diabetic retinopathy advances.² These structural changes, combined with impaired healing and epithelial dysfunction, can increase the risk of complications from such injections. This risk is further heightened in patients who have recently undergone cataract surgery. The surgical wound, coupled with pre-existing alterations in the corneal stroma due to diabetes, can create areas of weakness susceptible to mechanical stress during the injection procedure.³ As clinicians, it is imperative to remain vigilant for potential complications.

This case report presents an exceptionally rare instance of extensive corneal epithelial and basement membrane detachment occurring during an intravitreal injection. The patient's history of diabetes and recent bilateral cataract surgery significantly increased his risk profile.

This case serves as a stark reminder of the critical importance of pre-operative assessment in such high-risk patients. Surgical technique must be meticulous, and close post-operative monitoring is essential to mitigate potential complications. As physicians, we have a responsibility to remain cognizant of these situations and provide our patients with comprehensive and attentive care.

Case Report/Case Presentation

A 63-year-old male presented to our clinic 20 days after cataract surgery in his right eye with complaints of unsatisfactory visual improvement. He had a greater than 20-year history of type 2 diabetes mellitus and had undergone extensive panretinal photocoagulation in both eyes for “diabetic retinopathy with retinal hemorrhage” 5 years prior at another institution. The patient reported undergoing cataract surgery in his right eye on November 12, 2021, followed by cataract surgery in his left eye on November 20, 2021.

Ophthalmologic examination revealed a best-corrected visual acuity (BCVA) of 0.15 in the right eye and 0.5 in the left eye. Intraocular pressure was 15 mmHg in the right eye and 14 mmHg in the left eye. Conjunctivae were clear in both eyes. The corneas were clear bilaterally with well-sealed superior clear corneal incisions. Anterior chambers were deep and quiet. Pupils were round and reactive, and the intraocular lenses were well-positioned. Posterior capsules were clear in both eyes. Fundus examination revealed sharp and well-defined optic nerve heads bilaterally. Both retinas were attached, with multiple old laser scars and scattered hemorrhages visible in the posterior poles. The macular areas exhibited thickening, suggestive of edema, bilaterally. Based on macular OCT imaging (shown in [Figure 1](#)), a diagnosis of bilateral diabetic macular edema (DME) was made, noting the presence of intraretinal fluid in both eyes, more pronounced in the right eye.

The patient was diagnosed with bilateral diabetic macular edema and was noted to be in a postoperative state following bilateral phacoemulsification with intraocular lens implantation.

Surgical Procedure

Following a standard preoperative assessment and with no contraindications to surgery, the patient underwent bilateral intravitreal injections of Conbercept (1.0 mg/0.05 mL) under topical anesthesia on November 23, 2021. A standard injection technique was employed for the right eye. After sterile draping and placement of a lid speculum, the inferotemporal injection site was marked 3.5 mm posterior to the limbus. The eye was stabilized with forceps, and the medication was injected slowly into the sclera followed by gentle digital pressure to prevent reflux. Retinal artery perfusion was confirmed after injection.

The same technique was planned for the left eye. However, immediately after lid speculum placement and before injection, diffuse bullous elevation of the corneal epithelium was observed, exhibiting a wave-like appearance and colorful sheen (shown in [Figure 2a](#)). After the patient blinked several times, the corneal epithelium flattened and developed wrinkles (shown in [Figure 2b](#)). Given the transient nature of the epithelial elevation, the absence of initially apparent epithelial defects after spontaneous flattening, the cornea’s inherent regenerative capacity, and following communication and shared decision-making with the patient who desired to proceed with treatment, the decision was made to proceed with the intravitreal injection. The injection was performed using the same technique and location as the right eye. Postoperatively, tobramycin-dexamethasone ointment was applied to both conjunctival sacs, both eyes were patched, and the patient was transferred to the recovery room.

Post-Operative Follow-up

Post-Operative Course and Management

On postoperative day 1, the right eye had a visual acuity of 0.15 and an intraocular pressure of 16 mmHg. Mild conjunctival injection was noted. The cornea was clear, with a well-sealed superior incision. The anterior chamber was deep and quiet, with

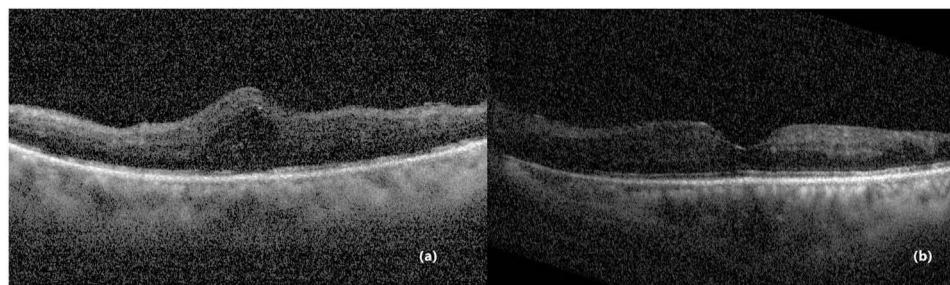


Figure 1 Macular OCT images at the patient's initial visit. (a) Right eye macula demonstrating intraretinal fluid. (b) Left eye macula demonstrating a small amount of intraretinal fluid.

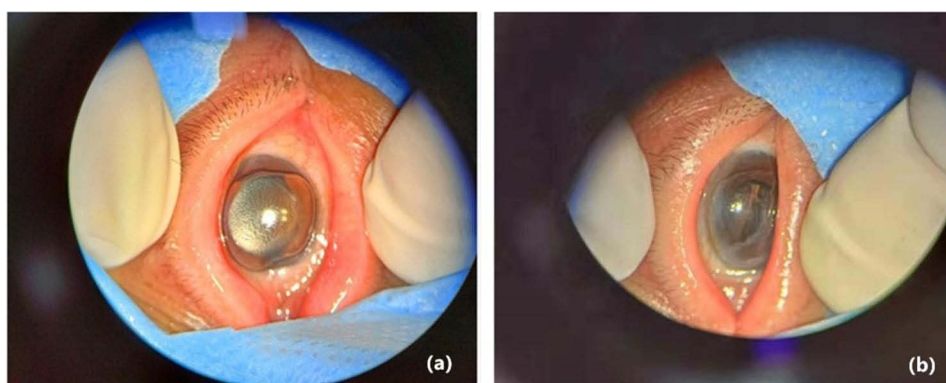


Figure 2 Images of the patient's eyes with eyelids retracted during the intravitreal injection procedure. (a) Left eye demonstrating diffuse bullous corneal epithelial elevation. (b) Left eye demonstrating flattening and wrinkling of the corneal epithelium after several blinks.

a round pupil and a well-positioned IOL. Fundus examination was unremarkable compared to the initial presentation. The left eye had a visual acuity of hand motions at 30 cm and an intraocular pressure of 14 mmHg. Conjunctival injection was observed. The cornea exhibited diffuse edema with epithelial haze and Descemet's membrane folds visible. While the superior incision remained well-sealed, detailed visualization of intraocular structures was not possible.

Postoperative Management

The patient was started on levofloxacin ophthalmic solution four times daily and tobramycin/dexamethasone ophthalmic solution four times daily in both eyes. Recombinant human epidermal growth factor ophthalmic solution was also administered four times daily in the left eye.

By postoperative day 4, visual acuity in the left eye had improved to counting fingers at 50 cm. Partial corneal epithelial healing was observed, though Descemet's membrane folds persisted. Anterior segment OCT revealed a hyporeflective cleft filled with fluid between the corneal epithelium and endothelium, accompanied by endothelial folds (shown in Figure 3). A bandage contact lens was placed on the left eye, and topical medications were continued.

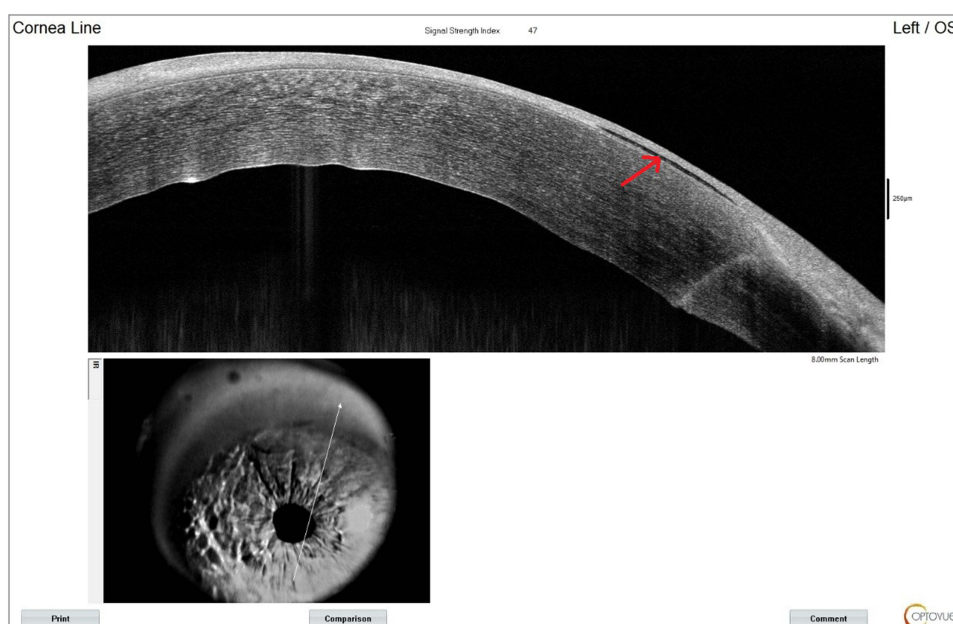


Figure 3 Anterior segment OCT image of the left eye on postoperative day 4, showing a hyporeflective area (red arrow) between the corneal epithelial layers and Descemet's membrane folds.

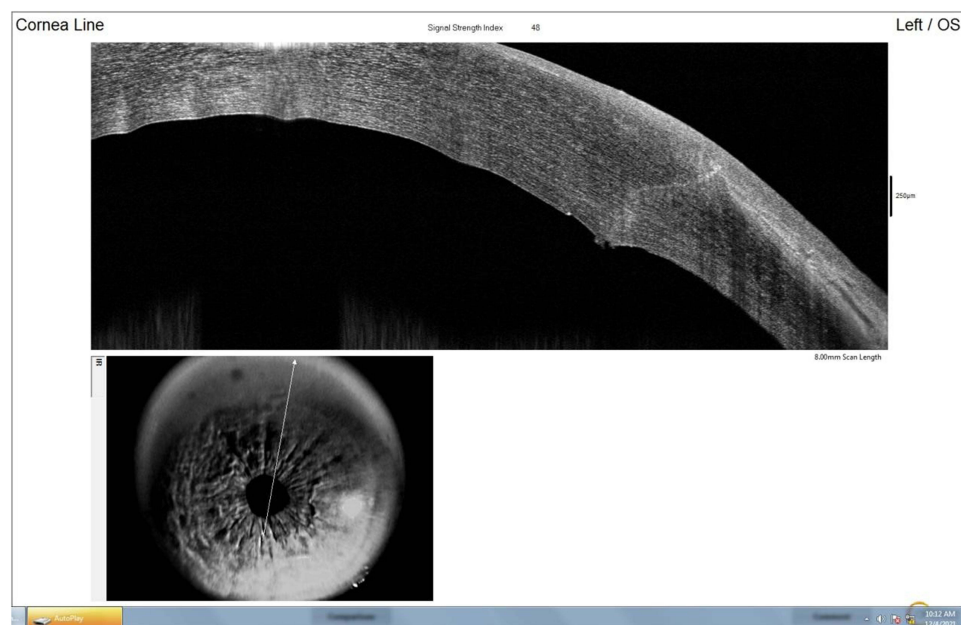


Figure 4 Anterior segment OCT image of the left eye on postoperative day 10, showing resolution of the hyporeflexive area between the corneal epithelial layers and mild residual endothelial folds.

On postoperative day 10, visual acuity in the left eye had further improved to 0.3. The corneal epithelium was intact, and Descemet's membrane folds were reduced. Anterior segment OCT demonstrated normal corneal epithelial contours, and mild residual endothelial folds (shown in Figure 4).

Discussion

The corneal epithelium is composed of four distinct layers, from superficial to deep: the superficial cell layer, wing cell layer, basal cell layer, and basement membrane. The basement membrane is anchored to the basal cells by hemidesmosomes.⁴ Critically, the corneal epithelium exhibits a remarkable capacity for regeneration.⁵ Cell-to-cell adherence, mediated by tight junctions, and the structural integrity between the basement membrane and basal epithelial cells, provided by hemidesmosomes, are essential for maintaining epithelial barrier function.⁶

Diabetic patients often exhibit abnormalities in the corneal epithelial basement membrane, including reduced subbasal nerve density and decreased corneal sensitivity, impacting the normal healing processes of the corneal epithelium.⁷ Studies using confocal microscopy have revealed a significant reduction in nerve fiber density within the corneal basement membrane and Bowman's layer in these patients.⁸ Additionally, basement membrane thickening and compromised adhesion between the basement membrane and basal epithelial cells have been observed, potentially contributing to persistent corneal epithelial defects. Hyperglycemia itself can disrupt the corneal epithelial surface, leading to irregularities such as a reduction in microvilli and microplicae, decreased epithelial cell layers, and cellular degeneration.⁹

In this case, the patient's advanced age, 20-year history of type 2 diabetes, and recent bilateral cataract surgeries are likely contributing factors to the observed epithelial detachment. The combined effect of these factors could have led to compromised corneal integrity and impaired wound healing. Diabetes is known to reduce corneal sensitivity due to abnormalities in the corneal nerves, impacting epithelial healing.¹⁰ Advanced age is also associated with reduced limbal stem cell proliferative capacity, further hindering epithelial healing.¹¹ The close proximity of the left eye cataract surgery to the intravitreal injection may also have contributed to inadequate sealing of the corneal incision, increasing the risk of epithelial separation during the injection.

Several mechanisms may explain the observed detachment. One possibility is that during surgical preparation, the irrigation of the conjunctival sac with saline, coupled with potential pressure fluctuations from blinking or inadvertent

pressure on the eyelid, may have caused transient gaping of the corneal incision. This could create a negative pressure, drawing air in and forming a bleb-like elevation of the corneal epithelium, as described in similar cases.¹² Alternatively, intraocular pressure fluctuations during the procedure could have led to the passage of aqueous humor from the anterior chamber into the potential space beneath the corneal epithelium. The anterior segment OCT findings of an open internal aspect of the incision support this possibility. Trauma from lid speculum application could also be a contributing factor to the observed detachment.

While the exact sequence of events remains unclear, this case highlights the vulnerability of the corneal epithelium in patients with diabetes, especially following recent cataract surgery. It underscores the importance of meticulous attention to corneal health in these patients, particularly when intravitreal injections are performed soon after cataract surgery. The duration of diabetes, glycemic variability, and the severity of diabetic retinopathy are positively correlated with reduced corneal sensitivity and impaired epithelial healing, highlighting the complexity of managing these patients.¹⁰

In this case, although corneal epithelial detachment was observed prior to the injection, the decision to proceed with the injection was made based on a variety of considerations. Firstly, the epithelial elevation was transient and spontaneously flattened upon blinking, indicating a likely superficial and not initially full-thickness detachment. Secondly, upon flattening, there were no immediately apparent epithelial defects, and we considered the cornea's robust regenerative capacity. Thirdly, the urgency to address the bilateral DME was paramount, given the patient's already compromised visual acuity following recent cataract surgery. Delaying the injection would have prolonged the visual impairment stemming from the DME. Furthermore, it is pertinent to note that the anti-VEGF medication had already been drawn and prepared prior to lid speculum placement. Abandoning the injection would have necessitated discarding the pre-drawn medication, which is often unacceptable in most clinical settings due to medication cost and availability. Crucially, upon observing the corneal epithelial event, we immediately communicated the situation to the patient. The patient, fully informed of the corneal finding, explicitly requested to proceed with the scheduled intravitreal injection to treat their DME. This case also provides a valuable learning point, suggesting that in patients at higher risk of corneal epithelial complications, a more cautious approach might involve deferring the preparation of the injection medication until all preparatory steps, including lid speculum placement, are completed and corneal integrity is confirmed.

Ideally, an anterior segment OCT immediately or on postoperative day 1 would have provided further insights into the initial corneal changes. However, due to clinical workflow and the evolving nature of the corneal findings, the first anterior segment OCT was obtained on postoperative day 4.

Further research is needed to better understand the mechanisms underlying these complications and to develop strategies for prevention and management. Prospective studies evaluating corneal epithelial integrity and wound healing in diabetic patients undergoing cataract surgery and subsequent intravitreal injections would be valuable. The development of standardized protocols and improved surgical techniques could help minimize the risk of such complications.

Abbreviations

VEGF, Vascular endothelial growth factor; OCT, Optical coherence tomography; DME, Diabetic macular edema; BCVA, Best-corrected visual acuity.

Data Sharing Statement

The data supporting the conclusions of this article are included within the manuscript. Further inquiries regarding the data can be directed to the corresponding author.

Study Approval Statement

As this is a case report and retrospective in nature, formal institutional review board approval was not required at our institution. The study adhered to the tenets of the Declaration of Helsinki.

Consent to Publish Statement

Written informed consent for publication has been obtained from the patient described in this article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare in this work.

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