Atypical Endophthalmitis Following Artificial Corneal Endothelial Implantation

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Purpose: EndoArt is an artificial endothelial layer device for the management of chronic corneal edema in cases with multiple corneal failed transplants, aiming to restore corneal deturgescence and optical clarity. However, postoperative complications, such as endophthalmitis, remain a significant risk. We report the first case of EndoArt-associated endophthalmitis, although a direct causual link remains uncertain.

Case description: A 75-year-old woman presented with increasing floaters in the left eye 7 months after EndoArt implantation for corneal endothelial dysfunction following multiple graft failures. At presentation, the best-corrected visual acuity (BCVA) was counting fingers, without ocular pain. Slitlamp examination showed non-injected conjunctiva and well-positioned corneal implant with mild corneal edema. B-scan ultrasonography revealed mild vitreous haze, flat retina. Six weeks before, a corneal transfixing single suture was removed. Right eye was unremarkable. The following day, BCVA in the left eye worsened with the appearance of stromal infiltrate, anterior chamber fibrin, and hypopyon, increased vitreous opacification and vitreous strands, leading to diagnosis of endophthalmitis. The patient underwent prompt vitrectomy, revealing purulent vitreous infiltration and hemorrhagic chorioretinitis. The EndoArt was not removed, as not directly involved in the infection. *Staphylococcus epidermidis* was identified in the aqueous and vitreous humors. Postoperative local and systemic antibiotics led to a gradual resolution of inflammation. At 2-month follow-up, the BCVA improved to 20/400.

Discussion: This case describes the atypical clinical appearance and the rapid progression of endophthalmitis in a patient with EndoArt. Prompt vitrectomy and a conservative approach, with EndoArt retention, led to infection resolution and preserved corneal clarity.

Conclusions: Vigilance, early diagnosis, and a tailored surgical approach are crucial to improving outcomes after artificial corneal endothelial implantation. Here the artifcial corneal endothelium implantation may have helped preserve cornea clarity during endophthalmitis, enably timely vitrectomy and contribuiting to a favorable outcome.

Key Words: endophthalmitis, artificial endothelial implant, endothelial keratoplasty, pars plana vitrectomy

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Postoperative infectious complications, including microbial keratitis, interface keratitis, and endophthalmitis (postoperative endophthalmitis), represent serious and potentially sight-threatening events following keratoplasty.[1] In particular, postkeratoplasty endophthalmitis is considered a rare event, with a reported incidence ranging from 0.041% to 0.2%.[2] This clinical entity presents with some specific clinical and diagnostic features, compared with endophthalmitis following other ophthalmic surgeries, including delayed or atypical presentation, graft-associated infiltrates, interface involvement (in endothelial keratoplasty), marked corneal edema, and consequent poor visibility of intraocular inflammation, possible association with donor-derived infections and resistance to standard medical therapy.[3]

A novel artificial endothelial layer device, termed EndoArt (EyeYon Medical, Ness Ziona, Israel), has been recently developed for the management of chronic corneal edema. The hydrophilic and flexible implant is composed of a copolymer of methyl methacrylate and hydroxyethyl methacrylate and is designed to conform to the posterior curvature of the cornea. It measures 50 μm in thickness and has a diameter of 6.5 mm. Upon placement on the posterior corneal surface, the EndoArt functions as a barrier to the influx of aqueous humor, thereby reducing stromal hydration and subsequently alleviating corneal edema, leading to enhanced corneal transparency. Several case series have demonstrated the efficacy of this device in restoring corneal clarity in patients with a history of multiple failed corneal grafts who retain visual potential.[4] However, due to the recent introduction of EndoArt, data on its associated complications remain limited. In this context, we report the first documented case of endophthalmitis following EndoArt implantation, highlighting that the presence of this device may be

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associated with distinct and previously unreported clinical features.

CASE DESCRIPTION

A 75-year-old woman presented to our eye emergency department (EED) with complaints of progressively worsening blurred vision and floaters in the left eye for about 10 hours. Her ocular history was significant for multiple corneal graft failures followed by the implantation of EndoArt device in the left eye 7 months prior. In particular, the patient underwent 2 Descemet stripping automated endothelial keratoplasty (DSAEK) procedures for endothelial corneal decompensation in 2009 and 2015, followed by 8.25 mm penetrating keratoplasty (PK) for corneal perforation due to HSV-related keratitis in 2018. Following cataract surgery in 2020, the patient developed a progressive graft failure, leading to the implantation of the EndoArt device in July 2024. Six weeks before EED presentation, a corneal transfixing single suture was removed due to loosening by cutting the external portion and withdrawing it completely. Notably, the most recent follow-up before presentation, 1 week prior, had documented a clear cornea with a best-corrected visual acuity (BCVA) of 20/63.

At presentation, the patient did not report any ocular pain. Ophthalmic examination of the left eye revealed a BCVA of counting fingers and an intraocular pressure of 14 mm Hg. Noninjected conjunctiva, with well-positioned corneal transfixing sutures and proper placement of the EndoArt implant, with mild corneal oedema, vitreous opacity, and flat retina (confirmed on B scan) with no signs of retinal hemorrhage or chorioretinal inflammation. At the time of presentation, her ongoing treatment regimen included topical dexamethasone 1 mg/mL (3 times daily), topical chloramphenicol 5 mg/mL (4 times daily), artificial tears (4 times daily), and oral acyclovir 400 mg (twice daily). Prolonged topical corticosteroid use was warranted due to the patient's history of multiple graft failures and the need to minimize interface inflammation; systemic acyclovir was prescribed prophylactically based on the patient's history suggestive of herpetic etiology in earlier graft failures. Based on the aforementioned clinical findings, the patient was initially diagnosed with vitreous hemorrhage and discharged.

The patient returned to the EED the following day due to a further progressive decline in visual acuity. At this time, left BCVA had deteriorated to hand motion. Slitlamp examination revealed a stromal infiltrate in the superotemporal quadrant, near the previously removed suture, anterior chamber fibrin, and a 1-mm hypopyon. The corneal sutures and the EndoArt device remained well-positioned (Fig. 1). B-scan ultrasonography showed vitreous opacification and thick vitreous strands. Based on these clinical findings, a diagnosis of endophthalmitis was made and an urgent pars plana vitrectomy was scheduled on the same day. Concurrently, blood tests, including blood cultures, were performed.

After the AC washout using ceftazidime 2.2 mg/mL and vancomycin 1 mg/mL and the mechanical removal of fibrin and hypopyon, the patient underwent 23-gauge pars plana vitrectomy, ceftazidime 2.2 mg/mL, and vancomycin 1 mg/mL injection in the vitreous cavity, heavy silicone oil (HSO) (Densiron Xtra, Fluoron GmbH, Ulm, Germany). During the procedure, which was particularly difficult due to the vitreous being densely infiltrated with purulent material, the retina was observed to be completely affected by hemorrhagic exudative chorioretinitis, making it impossible to visualize the optic disc.

A therapeutic contact lens was applied at the end of the procedure. Aqueous and vitreous humors were sampled for microbiological analysis.

Blood tests and blood cultures returned negative, whereas *Staphylococcus epidermidis* was isolated from both aqueous and vitreous samples.

Postoperative therapy included topical cefazolin 50 mg/mL and tobramycin 14 mg/mL every 2 hours after the loading dose, atropine 10 mg/mL twice a day, betamethasone 2 mg/mL and chloramphenicol 5 mg/mL 6 times a day, and brinzolamide/timolol 10/5 mg/mL twice a day. Systemic doxycycline 100 mg once a day for 6 weeks, systemic acyclovir 400 mg twice a day for 6 months, and intravenous ceftriaxone 2 g once a day for 7 days were also prescribed.

During the hospitalization period, corneal infiltrate decreased in intensity, intraocular inflammation, retinal exudations, and hemorrhages gradually resolved. The right eye remained clinically stable, with the absence of any infectious or inflammatory signs. At discharge, the therapy remained unchanged except for the 2 fortified antibiotic eye drops, which were reduced to 6 times daily. The systemic therapy was also switched to oral trimethoprim-sulfamethoxazole 160/800 mg 3 times a day for 2 weeks; systemic doxycycline 100 mg once a day for 6 weeks, and aciclovir 400 mg twice a day for 6 months were continued.

At 1-month follow-up, the fortified antibiotic eye drops were switched to tobramycin 3 mg/mL and levofloxacin 5 mg/mL 4 times daily. The remaining therapy was unchanged. At last follow-up (2 months after pars plana vitrectomy), left eye showed a BCVA of 20/400, intraocular pressure 14 mm Hg, mild diffuse corneal edema, with limited superonasal and inferior EndoArt detachment, well-tensioned sutures, no sign of infection or intraocular inflammation, retina flat with resolved hemorrhage (Fig. 1). At final follow-up, all topical antibiotics were discontinued due to complete resolution of inflammation. In the light of the favorable clinical course, the patient was listed for HSO.

DISCUSSION

We described the first case of endophthalmitis following EndoArt implantation. Notably, our case showed a combination of atypical findings, including time of onset, causative pathogen, and clinical course, which collectively differentiate it from more typical presentations of postkeratoplasty endophthalmitis. The recent introduction of EndoArt device for the treatment of specific ocular conditions offers promising therapeutic benefits.[4] However, despite its increasing use, there is a significant lack of evidence about the potential short-term and long-term complications, highlighting the need for further long-term monitoring to understand its safety profile. If confirmed by subsequent reports, this set

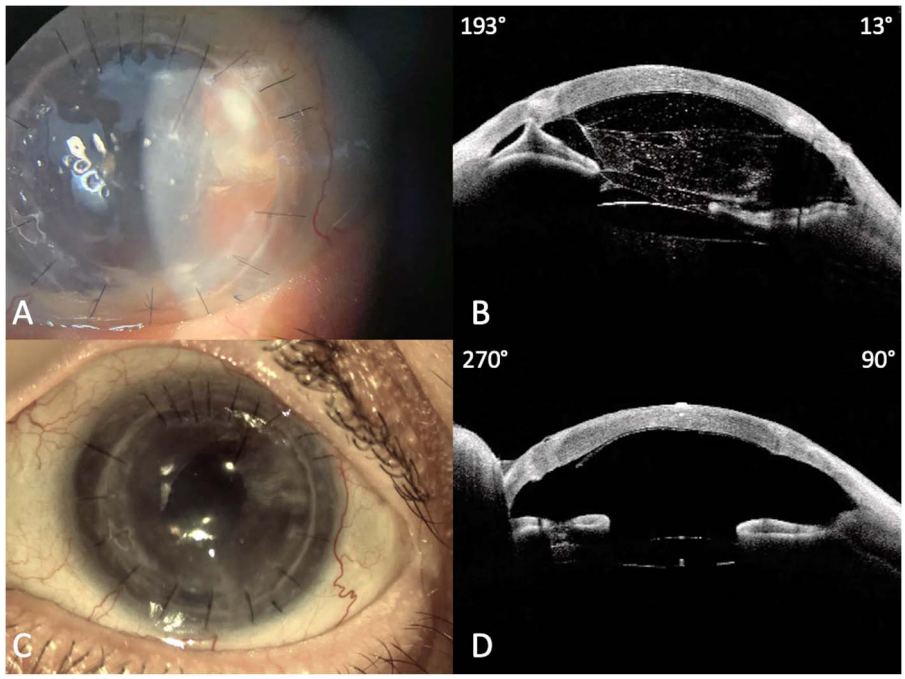

FIGURE 1. Anterior segment appearance before and after vitrectomy. Slitlamp photographs (A) and AS-OCT (B) of the left eye at day 2 showing noninjected conjunctiva, with a stromal infiltrate in the superotemporal quadrant, anterior chamber fibrin, and a 1-mm hypopyon. Slitlamp photographs (C) and AS-OCT (D) at 2-month follow-up showing a mild diffuse corneal edema with EndoArt limited detachment and no signs of AC active inflammation.

of signs and symptoms may configurate a peculiar clinical scenario.

First, our case showed an atypical combination of time of onset and causative pathogen. Indeed, the endophthalmitis manifested about 7 months after EndoArt implantations and *S. epidermidis* was the only pathogen identified. *S. epidermidis* is commonly responsible for postoperative endophthalmitis, accounting for about 30% of cases; however, bacterial postoperative endophthalmitis usually presents early after surgery, with a median time to diagnosis of 4.5 to 14 days.[5] In addition, Borkar et al[6] demonstrated that bacterial endophthalmitis is more common with perforating keratoplasty, whereas fungi are the primary cause in endothelial transplantation. However, although *S. epidermidis* is more commonly associated with acute-onset endophthalmitis, it has been implicated in delayed presentations.[7] Notably, the potential link between suture manipulation and delayed postkeratoplasty bacterial endophthalmitis has been already suggested after reporting a case of occurring 2 days after suture removal, performed 10 months postkeratoplasty.[8] However, in this patient a corneal transfixing single suture was removed due to loosening about 6 weeks before the diagnosis of endophthalmitis.

Second, the clinical course appeared unusual for several aspect. Indeed, the primary symptoms reported by the patient were vitreous floaters and decreased visual acuity. The absence of ocular pain, along with minimal anterior segment inflammation, the reduced visibility associated with the corneal edema and the lack of evident corneal infiltrates, represented confounding factors that contributed to an initial misdiagnosis. It is important to note that, due to her history of multiple grafts failures, the patient was receiving ongoing topical corticosteroid therapy, which may have attenuated the inflammatory response and masked classic signs of infection. Despite this initially insidious presentation, the patient's condition deteriorated rapidly, requiring urgent surgical intervention. Moreover, the intraoperative findings of dense vitreous infiltration and hemorrhagic chorioretinitis contrast starkly with the subtle early clinical signs, further highlighting the aggressive nature of the infection.

One of the most critical aspects of this case was the surgical management and, in particular, the choice to retain the EndoArt device. Indeed, in the management of endophthalmitis, the decision to remove intraocular medical devices, such as intraocular lenses, is contingent upon factors including the infection's onset, severity, and response to initial treatments.[9] Our choice to leave the EndoArt in place was based on several considerations, including the absence of direct involvement of the implant and its critical role in preserving corneal clarity (and thus intraoperative visualization). More specifically, despite the development of evident stromal infiltration, there was no sign of interface keratitis and the EndoArt device was not directly involved; moreover, the removal of the EndoArt would have caused a sudden loss of corneal transparency with potential dramatic consequences on intraoperative visibility and, thus, surgical performance. On the contrary, retaining the artificial device resulted in the preservation of corneal transparency allowing a smooth surgical procedure and an appropriate visualization both intraoperatively and during the follow-up to monitor the clinical condition. In addition, the premature removal of the device and the secondary stromal edema could have made the tissue more vulnerable to damage, leading to further additional complications. We acknowledge that PK could have been a viable alternative and frame our decision as a carefully weighed, patient-specific approach. However, to optimize infection control, a meticulous anterior chamber washout was

performed using intracameral antibiotics. Topical postoperative antibiotics were prescribed and discontinued at 2-month follow-up due to the favorable clinical course. While some clinicians advocate for long-term prophylactic topical antibiotics in artificial corneal implants, in this case, a tailored, stepwise withdrawal was deemed appropriate based on the patient's favorable response.

Finally, HSO was used as ocular endotamponande. The use of silicone oil and HSO as an intraocular tamponade in endophthalmitis cases is well-documented.[10] Silicone oil has demonstrated antimicrobial properties, and it has been suggested that HSO might be more effective than conventional silicone oil in against endophthalmitis-causing agents, including *S. epidermidis*.[11] Its use not only aids in infection control but also reduces the risk of postoperative retinal detachment, especially in instances of undetected retinal breaks, and helps prevent severe postoperative hypotony.[5]

Our conservative surgical approach ultimately proved to be successful, as the infection was effectively controlled while maintaining corneal transparency and integrity. The potential for infection and the presence of a biofilm is an interesting issue about the role of bioengineered corneal implants in the pathogenesis of ocular infections. Further investigations are needed to better understand the potential resistance of the EndoArt device to pathogen colonization.

CONCLUSION

In conclusion, we described for the first time the atypical manifestation of an EndoArt-associated endophthalmitis. In the absence of evident infectious involvement of the device, a conservative approach was effective in controlling the infection while maintaining corneal stability. This case highlights the importance of vigilance and individualized treatment in complex postkeratoplasty patients.

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