

TPK. One previous similar case has been documented, occurring in a 65-year-old man.⁶ In this case, the patient underwent a corneoscleral keratoplasty and began prednisolone 1% acetate drops 2 weeks after the procedure. Seven weeks after the corneoscleral keratoplasty, the patient was diagnosed with recurrent *Acremonium* keratitis and ultimately required a second TPK.

In summary, our present case demonstrates the potential for *Acremonium* keratitis to reoccur months after TPK in the absence of clinical signs of persistent infection and encourages clinicians to exercise caution in their use of immunosuppressive medication during postoperative management of this fungal species.

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Late-onset bilateral epithelial ingrowth following rapid corneal decompensation owing to amantadine



Epithelial ingrowth (EI) can occur at the interface between the flap and the stromal bed of the patient's cornea following laser assisted in situ keratomileusis (LASIK) surgery. The introduction of corneal epithelial cells into the interface can happen during surgery or after the procedure owing to loss of contact inhibition and the presence of a pathway to the interface. Epithelial ingrowth is a relatively uncommon complication, with a reported incidence of 3.9% following primary LASIK and up to 12.8% following enhancement with a flap lift.¹ While usually asymptomatic, EI may lead to decreased vision owing to direct intrusion of cells into the visual axis, irregular corneal astigmatism, or melt of the overlying flap. Risk factors for EI have been described; however, systemic drug intake is not reported. We report a case of late-onset bilateral EI induced by acute corneal edema 6 years following primary LASIK in a patient taking amantadine, botulinum toxin (BT) injections, and natalizumab for multiple sclerosis.

In April 2019, a 49-year-old white female patient was referred for acute bilateral corneal edema unresponsive to topical corticosteroids. Her past medical ocular history was notable for uncomplicated bilateral LASIK in 2013, with uncorrected visual acuity (UCVA) of 20/15 in her

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

right eye (OD) and monovision of J1 in her left eye (OS). (Best spectacle corrected visual acuity 20/15 OS with a –1.75 diopter [D] correction). No EI OU. Her past medical history was relevant for multiple sclerosis, diagnosed in 2012 and treated with 200 mg of oral amantadine daily since 2012, BT injections every 3 months for leg spasticity since 2013, and monthly intravenous natalizumab since 2017.

On examination, UCVA was 20/200 OD and 20/150 OS (J8 and best spectacle corrected visual acuity 20/80 OS). Anterior segment was unremarkable OU with only rare cells OS. Slit lamp examination showed moderate corneal edema, no keratic precipitates, normal LASIK flaps, no diffuse lamellar keratitis, no infiltrates, no EI, and no interface haze (Fig. 1A, B). Ultrasound pachymetry revealed a central corneal thickness of 666 microns (μm) OD and 763 μm OS. Digital and tonometer intraocular pressure was normal and fundus examination was unremarkable OU.

Hourly topical prednisolone acetate 1% was continued while sodium chloride 5% drops and ointment were added without improvement. The patient underwent sequential Descemet stripping endothelial keratoplasty (DMEK) grafts OU. Due to a mild head tremor, the patient required rebubbling OU for partially nonadherent grafts and a second DMEK following failed rebubbling OD.

Epithelial ingrowth appeared 20 weeks and 25 weeks after the initial decrease in vision for OD and OS respectively (Fig. 1C, D). The EI occurred before DMEK in OD and after DMEK in OS.

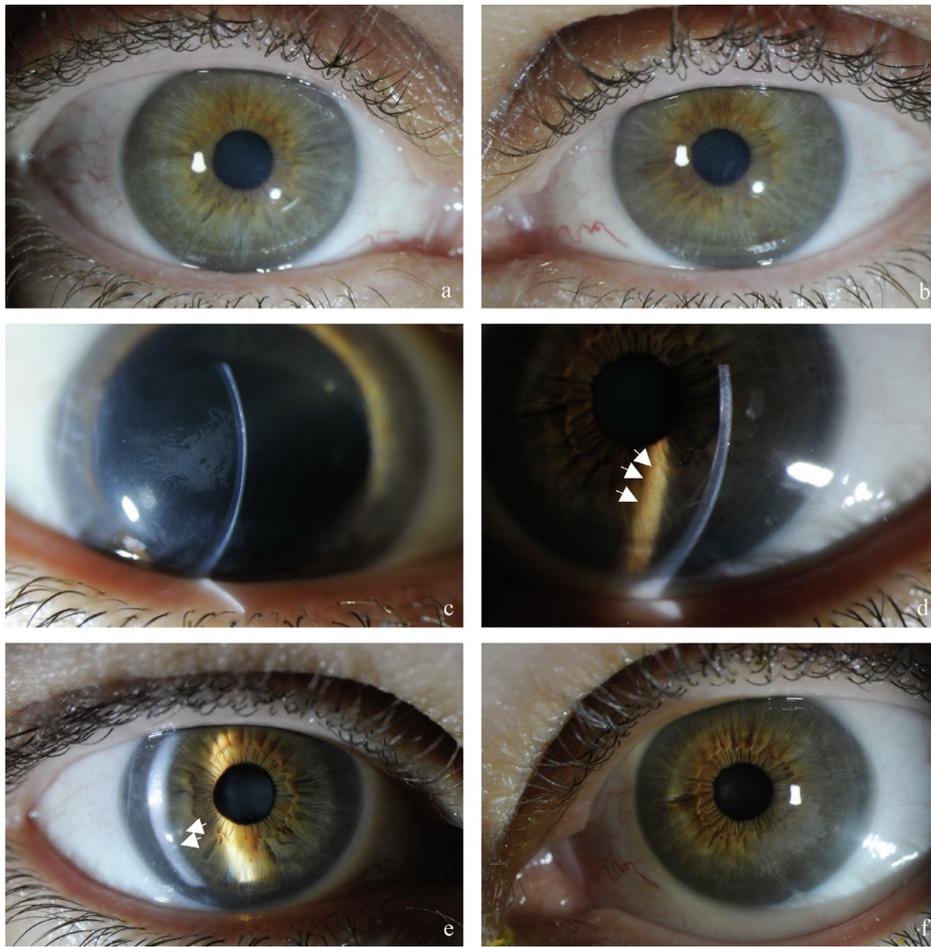


Fig. 1—Initial patient presentation demonstrating moderate corneal edema and no epithelial ingrowth (A) in right eye and (B) in left eye. Presentation at 6 months revealing (C) epithelial ingrowth centrally obstructing the visual axis and in the inferotemporal quadrant in the right eye and (D) epithelial ingrowth in the inferotemporal quadrant of the left eye (arrow). Presentation at 10 months showing (E) small and peripheral epithelial ingrowth recurrence (arrow) following surgical excision with mild residual interface haze in the right eye and (F) stable and non-visually significant epithelial ingrowth in the left eye.

Pathology reported rarified endothelial cells with no inflammation. The diagnosis of rapid and irreversible endothelial decompensation owing to amantadine was emitted. Amantadine was stopped to prevent decompensation of the corneal grafts.

As corneal edema resolved, the size of EI decreased OU but remained central and visually significant in OD with an UCVA of 20/60. Surgical excision of EI was performed OD in January 2020, with resulting UCVA of 20/30 with mild interface haze and peripheral non-visually significant EI recurrence (Fig. 1E). The EI in OS was non-visually significant and remained stable with a UCVA of 20/20 (Fig. 1F). As of May 2020, both eyes remained phakic, with no development of cataract, and did not need further surgery.

To our knowledge, this is the first documented case of late-onset bilateral EI owing to acute bilateral corneal decompensation following BT injection in a patient taking amantadine.

Higher daily dosage of amantadine (400 mg daily) was found to induce greater changes in endothelial parameters than a long-term intake.² Subsequent corneal edema is a

rare but serious side effect that can occur any time during treatment with a dose-dependent increase in risk and can be reversible if amantadine is stopped early.³

While a case report of a patient acquiring a necrotising retinopathy secondary to varicella zoster while on natalizumab was described in the literature,⁴ no cases of corneal endothelial damage were described. One case report described acute anterior uveitis activated subsequent to BT injection in a patient with Behçet's disease, which was attenuated by infliximab.⁵ However, no ocular side effects have been described from the combination of BT injections and intravenous natalizumab. It is possible that the BT injection inducing the myasthenic syndrome also induced a bilateral anterior uveitis, left undiagnosed owing to the long delay between the decrease in vision and the first eye exam (1 month). The anterior uveitis could have led to a rapid and permanent corneal edema in a patient with an already weakened endothelium from the amantadine.

In conclusion, patients taking amantadine on a long-term basis should be referred in ophthalmology for

monitoring and referred quickly if vision decreases after BT injection, as it can lead to visual complications. Endothelial cell count should be monitored, and amantadine stopped if endothelial cell change occurs to avoid irreversible damage. In the rare event of a rapid and irreversible corneal decompensation occurring in a patient with previous LASIK, prompt endothelial graft should be considered before epithelial ingrowth further complicates restoration of vision.

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Intrastromal voriconazole for refractory infectious crystalline keratopathy associated with *Candida parvulus*



Infectious crystalline keratopathy (ICK) is an infrequent complication of long-term topical steroid use following penetrating keratoplasty,¹ classically caused by *Streptococcus viridans*.² It has been reported in association with local immunosuppression after any ocular surgery (lamellar keratoplasty, cataract surgery, trabeculectomy, corneal cross-linking, and laser in situ keratomileusis), as well as in contact lens wearers, herpetic and *Acanthamoeba* keratitis, and corneal anaesthesia.^{3,4} Besides α -haemolytic streptococci,² multiple additional microorganisms have been causally linked to ICK, including Gram-positive or -negative bacteria, atypical mycobacteria, and fungi,³ most of them bearing biofilm-forming capacity. We hereby report an association between ICK and a rare *Candida* species, highlight some of the major challenges in diagnosis and treatment of ICK, and demonstrate effectiveness of intrastromal antifungal treatment for refractory keratitis.

A 60-year-old man complained of left ocular pain. He had presented 10 months previously with impending corneal perforation owing to descemetocoele secondary to recurrent herpes simplex virus (HSV) keratitis. At that time, following consideration of treatment options,⁵ the patient underwent left phacoemulsification and intraocular lens implantation combined with penetrating keratoplasty. He had no additional ophthalmic or medical history. He was on

topical preserved dexamethasone 4 times daily OS and oral aciclovir 400 mg twice daily *per os*. At presentation, best-corrected visual acuities (BCVAs) were 20/30 OD and 20/40 OS. The right eye was normal. Examination of the left eye showed a stellate branching opacity within the paracentral donor corneal stroma (Fig. 1A, 1B) with no overlying epithelial defect. There was marked left anterior chamber inflammatory activity (3+ cells) with no hypopyon. Clinical findings were suggestive of ICK. A suture associated with the lesion was removed, dexamethasone discontinued, and intensive topical ciprofloxacin and teicoplanin treatment initiated. Of note, left intraocular pressure (IOP) was 45 mm Hg, requiring treatment with a short course of oral acetazolamide and topical dorzolamide and timolol. Nine days later, IOP decreased to 5 mm Hg and subsequently normalized without requiring further treatment for the duration of follow-up period.

Serial corneal impression membrane sampling failed to uncover a causative microorganism, and the patient was empirically treated for several months with various combinations of antimicrobial, antifungal, and antiviral agents, which included oral aciclovir and doxycycline, and topical aciclovir, chloramphenicol, ciprofloxacin, teicoplanin, and voriconazole. The patient remained comfortable during this period and reported satisfactory compliance to prescribed treatment. Clinical findings remained stable with above treatments until 19 weeks later when there was evidence of progression (Supplementary Fig. 1A, available online). This prompted a corneal biopsy and intrastromal injection of vancomycin and cefuroxime. Culture and genomic analysis (the latter for 16S and 18S ribosomal RNA, and HSV) of