Perioperative management of high-risk corneal transplantation using basiliximab and mycophenolate mofetil

Corneal transplantation has a low failure and rejection rate due to the avascular nature and immunologic privilege status of the cornea. The acute endothelial rejection rates for a penetrating keratoplasty (PK) and endothelial keratoplasty (EK) are around 21%−31% and 0.1%−5%, respectively.[1] Yet patients who have had prior rejection and multiple grafts are at additional risk for decreased longevity of future grafts. Corticosteroid-sparing systemic immunosuppressive agents such as cyclosporin A (CsA), tacrolimus, and mycophenolate mofetil (MMF) are current options for patients with high-risk keratoplasties, but these agents do require monitoring for adverse effects.[2] While basiliximab is used for induction to prevent early acute graft rejection in solid-organ transplants, its use in ophthalmology is limited. Herein we present a case of a high-risk keratoplasty in a patient who received immunosuppression therapy with basiliximab induction and MMF to minimize subsequent graft rejection.

A 35-year-old male with a history of keratoconus OU presented with blurry vision. There was a history of hard contact lens wear but with increasing intolerability. Past medical history was significant only for kidney stones and smoking.

On initial examination, the patient's best-corrected visual acuity (with hard lenses) was 20/60 OD and 20/25 OS. Slit-lamp examination revealed a prominent cone, old hydrops, and a deep stromal scar OD without obvious corneal edema. There also was a prominent cone and mild stromal scarring OS. Otherwise, the rest of the slit-lamp examination was unremarkable, and corneal sensation was intact OU. Posterior examination was unremarkable OU.

The patient desired to proceed with a keratoplasty, so an unremarkable manual deep anterior lamellar keratoplasty was performed OD. Despite no double anterior chamber postoperatively, there was persistent, diffuse corneal edema and count fingers vision at 2 months, so a PK was subsequently performed. The patient's medication regime following the PK included prednisone 60 mg tablet daily, topical difluprednate 0.05% qid, topical CsA 0.05% bid, and topical antibiotic. Despite the graft clearing postoperatively, there was corneal edema at the 6-week follow-up, and acute rejection was suspected and treated. Without improvement, a second PK combined with cataract surgery and iridoplasty was recommended.

After a year of improving vision and no signs of rejection (acuity of uncorrected 20/125 with pinhole 20/50) postoperatively, the patient was noted to have acute rejection for the second time OD. Examination revealed hand motions vision, an edematous PK graft, and nasal neovascularization. Because of the history of multiple episodes of graft rejection, it was decided to proceed with a Descemet's stripping endothelial keratoplasty (DSEK) under the PK with a systemic immunosuppression regimen including basiliximab perioperatively and MMF. The patient was instructed to start on 1000 mg MMF bid 1 month prior to surgery. The patient received 1 infusion of basiliximab just prior to surgery and a second infusion of basiliximab 5 days after the surgery (due to scheduling because this is usually performed 4 days later). Topical difluprednate qid, brimonidine-timolol 0.2%−0.5% qid, CsA bid, and levofloxacin qid also were started. MMF was tapered about 2 months postoperatively and discontinued after 31 months. By 1 year postoperatively, vision improved to 20/70 (pinhole 20/40) following a YAG laser capsulotomy. Visual acuity and the graft remained stable until about 3 years following the DSEK, when signs of mild endothelial failure with 2+ edema were detected. There were no signs of graft rejection, that is, keratic precipitates, conjunctival injection, and anterior-chamber reaction. Instead, this graft demonstrated endothelial failure/exhaustion. The patient's medication regime at the time of the noted failure included difluprednate qid and MMF (1000 mg). At last follow-up at 3.5 years following DSEK, visual acuity has been maintained at 20/70 (pinhole 20/30).

Basiliximab is a chimeric monoclonal antibody targeted against the interleukin 2 receptor antibody and more specifically the interleukin 2 receptor α-chain (also known as *CD25 antigen*), thus inhibiting T-cell proliferation. In the past, while basiliximab was used primarily for prophylaxis of acute rejection in renal transplants, it has been shown to be efficacious in increasing the long-term survival of the corneal xenografts.[3]

Basiliximab also has been used preoperatively in combination with oral CsA for immunosuppressive treatment in human keratoplasty patients. In a case series of 7 patients with high-risk PKs, only 1 graft developed endothelial rejection (which was reversible) during the mean 18 months of follow-up. One patient did have side effects linked to CsA, but basiliximab appeared to be well tolerated.[4] A separate study compared 10 patients receiving basiliximab with 10 patients receiving oral CsA for high-risk keratoplasty. There were 4 basiliximab patients that showed corneal immune reactions and 2 in the CsA group. Basiliximab demonstrated similar efficacy to CsA, but no patients demonstrated side effects, while 2 of those treated with the CsA had to be counselled to discontinue taking it owing to adverse effects.[5]

We used basiliximab in conjunction with MMF for this high-risk graft in our patient, particularly to decrease the chance of early acute rejection because this had occurred previously. We acknowledge that EK has a lower chance of

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rejection and likely helped in improving the longevity, yet we have not seen an immune reaction over the 3.5-year follow-up. During follow-up, the patient in this study did not experience any adverse drug events related to basiliximab. There was some degree of nonadherence to regular follow-up visits in this patient, and systemic immunosuppression requires regular follow-up visits and laboratory monitoring for safe continued administration. Basiliximab has high pharmaceutical compliance because of perioperative and outpatient administration, which poses a solution for noncompliant patients who are at high risk of graft rejection and failure.

There is a paucity of high-risk keratoplasty cases in the literature that have used basiliximab. To our knowledge, this is the first case using a regimen of combined basiliximab with MMF for the peri- and postoperative management of high-risk keratoplasty. This case demonstrated a longer graft survival, although it did succumb to endothelial-related failure without graft rejection. Nevertheless, 3.5 years was a longer period of corneal clarity than that provided by previous grafts at least in part due to the combination therapy of basiliximab and MMF in preventing graft rejection. Our standard systemic immunosuppression regimen, especially for limbal stem-cell transplantation, often involves initial 3-agent immunosuppression (i.e., tacrolimus, MMF, and prednisone). The use of basiliximab induction along with maintenance MMF could reduce rejection-related failure and help avoid the use of calcineurin inhibitors such as cyclosporine or tacrolimus for long-term immunosuppression in high-risk patients. Additional studies are needed to further study perioperative immunosuppression regimens.

Cameron B. Reinisch,[*] Asma M. Azam,[†] Albert Y. Cheung,[†,‡] Amit Govil,[*] Edward J. Holland[*,§]

[*]University of Cincinnati, Cincinnati, Ohio; [†]Eastern Virginia Medical School, Norfolk, Va.; [‡]Virginia Eye Consultants/CVP Physicians, Norfolk, Va.; [§]Cincinnati Eye Institute, Edgewood, Ky.

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Correspondence to:
Edward J. Holland, MD; eholland@holprovision.com.

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Footnotes and Disclosure

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