Penetrating Keratoplasty in Cicatrizing Conjunctival Diseases

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Purpose: The outcome of successful penetrating keratoplasty (PK) typically is poor in eyes with end-stage chronic cicatrizing conjunctival diseases such as ocular cicatricial pemphigoid (OCP), Stevens-Johnson syndrome, and toxic epidermal necrolysis due to immunologically driven conjunctival inflammation associated with conjunctival cicatrization and lid abnormalities, severe dry eye, and extensive corneal neovascularization. The authors report the results of their experience with PK in 13 patients with OCP, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Methods: The authors reviewed the records of patients with OCP, Stevens-Johnson syndrome, or toxic epidermal necrolysis seen between 1976 and 1992. Patients who underwent PK were examined for the purpose of this study. Initial and final visual acuity, indications for PK, surgical procedure, postoperative therapy, complications, total number of repeat PKs, length of follow-up, and the final outcome were recorded.

Results: Thirty-two PKs were performed in 16 eyes of 13 patients with advanced OCP (6 patients), OCP as a sequela of Stevens-Johnson syndrome (2 patients), Stevens-Johnson syndrome (3 patients), and toxic epidermal necrolysis (2 patients). The indications for the first PK were corneal perforation in six eyes (37.5%) and extensive corneal scarring in ten eyes (62.5%). Preoperative visual acuity was counting fingers in five eyes, hand motions in eight, and light perception in three. Preoperative therapy included systemic chemotherapy (8 patients), mucous membrane grafting (9 eyes), lamellar keratoplasty (2 eyes), superficial keratectomy (1 eye), and corneal dye laser photocoagulation (6 eyes). The mean follow-up period was 4.6 years (3 months–13 years). Eight eyes (50%) had clear grafts, and three eyes (18.7%) had 20/200 or better visual acuity at last visit. The major causes of graft failure were epithelial defect formation/persistence, stromal ulceration, perforation, and graft rejection.

Conclusions: These results indicate that PK may be performed for tectonic reasons, but prospects for restoration of sight in patients with advanced cicatrizing conjunctival diseases, even after extensive preoperative medical and surgical therapy, are limited.
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Ocular cicatricial pemphigoid (OCP), Stevens-Johnson syndrome, and toxic epidermal necrolysis are the bullous oculocutaneous diseases that involve the conjunctiva most frequently and produce severe conjunctival cicatrization and subsequent blinding keratopathy.[1–4]

Ocular cicatricial pemphigoid is a chronic progressive disease characterized by exacerbations of immunologically driven conjunctival inflammation that eventually results in cicatrization with subepithelial fibrosis, symblepharon formation, fornix foreshortening, and lid abnormalities. In the advanced stages of the disease, severe xerosis, along with mechanical factors that also may provoke further inflammation, contribute to the development of profound keratopathy.[1–4] Systemic chemotherapy has been shown to be effective in halting progressive disease in OCP[1–6];

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and adjunctive ocular therapy, including surgical correction of mechanical factors, is an essential part in the care of patients with trichiasis, sicca syndrome, and lid margin keratinization.[1-5,7] Because surgical trauma often reactivates quiescent OCP and leads to rapid deterioration, surgery should not be attempted unless immunologically active inflammation is controlled by immunosuppressive therapy.[2,7,8]

Stevens-Johnson syndrome is an acute vesiculobullous disease of the skin and mucous membranes associated with systemic toxicity.[2-4,9] Toxic epidermal necrolysis is considered a more severe form of Stevens-Johnson syndrome; however, it has distinguishing features, including tenderness and massive denudation of the skin, that support its distinct entity.[2,3,9,10] Ocular involvement during the acute episode and the subsequent complications are similar in both diseases. In severe instances, devastating ocular sequelae develop identical to the advanced stages of OCP.[2,3,11] In contrast to the progressive nature of OCP, however, the typical form of Stevens-Johnson syndrome and toxic epidermal necrolysis is one of chronic remission after an acute episode.[2] Care of patients with chronic consequences of Stevens-Johnson syndrome and toxic epidermal necrolysis involves control or correction of confounding variables that may incite inflammation and provide mechanical insult to the cornea.[2-4,12] Systemic chemotherapy is required only in rare instances, when there are immunologically driven recurrent episodes of conjunctival inflammation unassociated with external aggravants. Conjunctival biopsy shows immune-complex vasculitis in patients with recurrent disease but not in the nonrecurrent form.[13] Linear immune deposits along the epithelial basement membrane zone, characteristic of OCP, are not present in the conjunctiva affected by Stevens-Johnson syndrome or toxic epidermal necrolysis.[13] However, OCP may develop rarely after an acute episode of Stevens-Johnson syndrome, in which case Stevens-Johnson syndrome–induced mucosal injury has been suggested as a precipitating or triggering factor.[14]

The final common pathway to blindness in these ocular mucosal scarring disorders is a hostile corneal environment, which causes corneal epithelial defect formation, ulceration, perforation, and/or extensive neovascularization and opacification. It is acknowledged widely that the prognosis of penetrating keratoplasty (PK) is poor in these eyes due to a host of risk factors, including corneal vascularization, decreased corneal sensation, impaired lid function, and dry eye.[15] Nevertheless, PK may be required for tectonic repair of impending or real perforation, and with the progress that has made in the last 15 years in immunosuppression controlling inflammation and correcting some of the lid and conjunctival abnormalities associated with these diseases,[1,5-7] the temptation to attempt visual rehabilitation in selected individuals with the bilateral blinding consequences of these disorders has become irresistible. The purpose of this article is to report the results of our experience with PK in patients with advanced OCP, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Patients and Methods

We reviewed the records of 203 patients with OCP and 40 patients with Stevens-Johnson syndrome or toxic epidermal necrolysis seen at the Immunology Service of the Massachusetts Eye and Ear Infirmary between 1976 and 1992. Patients who underwent PK were analyzed for the purpose of this study.

The following data for each patient, including sex, age, preoperative diagnosis, disease stage, conjunctival inflammatory activity, degree of keratopathy, conjunctival biopsy information, preoperative systemic and ocular therapy, surgical interventions, initial and final visual acuity, indications for PK, surgical procedure, postoperative treatment, complications, indications for and total number of repeat PKs, length of follow-up, and the final outcome, were recorded.

The diagnosis of OCP was biopsy proven in all patients by demonstration of linear immunoreactant deposition at the conjunctival–epithelial basement membrane zone. Disease staging was done according to Foster's classification.[1] The general management of OCP patients, particularly systemic chemotherapy, followed the guidelines reported previously.[1,5,6] Briefly, dapsone was the initial drug of choice for mild to moderate inflammation. When the therapeutic response was unsatisfactory or when the patient could not tolerate this therapy, methotrexate or azathioprine was added or substituted. Cyclophosphamide was prescribed initially for intense inflammation or sequentially for initial drug failure.

All of the patients with Stevens-Johnson syndrome or toxic epidermal necrolysis had a well-documented history of an acute episode of the disease. Acute care of the ocular manifestations was not analyzed in this study, but the chronic ocular consequences and their treatment were reviewed. Conjunctival biopsies were obtained from the patients who still had inflammation after elimination of external confounding variables such as trichiasis, exposure, entropion, sicca syndrome, and keratinization of the lid margins. Patients who had immune-complex vasculitis, indicating an ongoing immunologically driven mechanism, received immunosuppressive therapy.

In all patients, mechanical factors damaging the ocular surface were treated aggressively. Trichitic and dystichitic lashes were destroyed by cryotherapy. Keratitis sicca was treated with preservative-free ocular lubricants and punctal occlusion. Meibomian gland dysfunction was managed with warm compresses, lid massage, and oral doxycycline. Atopic patients received preservative-free cromolyn drops and systemic antihistamines. Adjunctive topical therapy also included topical retinoids for conjunctival keratinization. Mucous membrane grafting was done in patients with extensive keratinization of the eyelid margins and bulbar conjunctiva and in patients with severe marginal entropion, allowing lash touch or skin/corneal contact. Our surgical procedure for buccal mucous membrane grafting has been described elsewhere.[7] Corneal hypesthesia and lagophthalmos were treated with tarsorrhaphy. Lid or conjunctival surgery was not attempted before ad-

equate control of inflammation with immunosuppressive therapy.

Preoperative procedures to prepare the ocular surface for elective PK also included corneal dye–laser photocoagulation of the new vessels with 577-nm yellow light, superficial keratectomy for extensive corneal vascularization and keratinization, and lamellar keratoplasty for tectonic repair of descemetocele formation and/or extreme thinning of the cornea. Application of tissue adhesives and bandage contact lenses were used for corneal perforation as temporary measures before surgery or therapeutic purposes. The type of bandage contact lens used in this series was the Plano T (polymacon soflens) of 38.6% water content supplied by Bausch and Lomb, Inc (Tampa, FL).

Immunosuppression in addition to elimination of mechanical factors provided a quiet eye before PK, except when PK was performed as an emergency procedure. When the disease was in remission without medication, chemotherapy was started before elective PK. When an emergency PK was required for tectonic reasons on an eye with active OCP, chemotherapy was instituted in the immediate postoperative period.

Surgical Procedure

All surgeries were performed by the same surgeon (CSF). The surgery followed the general principles of PK. The donor corneal button was 0.2 to 0.5 mm larger than the recipient bed. The grafts were sutured with 10–0 monofilament nylon interrupted sutures. Cataract surgery and other procedures were performed concurrently when indicated. The surgery was completed with partial or total tarsorrhaphy with or without bandage contact lens application in most patients.

Postoperatively, 1% prednisolone acetate (4–8 times daily, tapered over 3 months) and polysporin ointment (twice daily for 10 days) were used in addition to the preservative-free lubricating agents. Individual systemic chemotherapy was maintained.

Postoperative examinations were done at day 1, at 1, 2, and 4 weeks, and monthly thereafter for the first 6 months, and then every 6 months. Loose sutures were removed promptly. Patients with epithelialization problems were treated with collagen shields (72-Hour Bio-Cor collagen shields, Bausch and Lomb, Inc) or bandage contact lenses and/or tarsorrhaphy. Conjunctivalization of the cornea was treated with conjunctival resection combined with mitomycin C (0.02% topical solution) either as a single application at the time of surgery or instilled twice daily for 5 days. Microbial keratitis was diagnosed on the basis of a positive Gram stain and/or a positive culture of corneal scrapings and was treated with fortified antibiotics. Sterile corneal ulcers or perforations were treated with tissue adhesives and bandage lenses when they were smaller than 2 mm. A patch graft was placed when the ulcer was large or when other therapies failed. Neodymium:YAG (Nd:YAG) laser transscleral cyclophotocoagulation was performed when increased intraocular pressure could not be controlled by topical beta-blockers and oral acetazolamide. We used the sapphire-tipped Nd:YAG laser, CLMD 50 of Surgical Laser Technologies (Oaks, PA). Corneal graft rejection episodes were diagnosed on the basis of anterior chamber reaction with keratic precipitates on the donor endothelium or by the presence of an endothelial rejection line. Graft rejection episodes were treated with topical 1% prednisolone acetate applied every waking hour. Assessment of graft clarity was based on the central 3.5 mm-diameter region of the graft. A compact graft that allowed visualization of iris and lens details through the central part was considered clear with or without the presence of superficial punctate keratopathy and/or mild subepithelial haze. Grafts with stromal edema, opacity, neovascularization, or keratinization were defined accordingly. Hard contact lens refraction was not performed in testing vision of the patients in this series.

Results

Thirteen patients (16 eyes) underwent 32 PKs. Eight patients had OCP (occurring as a sequela of Stevens-Johnson syndrome in 2 patients), three patients had Stevens-Johnson syndrome, and two patients had toxic epidermal necrolysis. The average age of the patients at the time of surgery was 70 years (range, 51–87 years) in patients with OCP and 29 years (range, 13–43 years) in patients with Stevens-Johnson syndrome–induced OCP, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Nine patients were female, and four were male. The mean follow-up was 4.6 years (range, 3 months–13 years).

The patient characteristics before PK are shown in Table 1. Conjunctival biopsy showed basement membrane zone positivity in all patients with OCP. Perivasculitis with immunoreactant deposition in the vessel walls was found in two patients with Stevens-Johnson syndrome and two with toxic epidermal necrolysis. The conjunctival specimen of one patient with Stevens-Johnson syndrome and a strong history of atopy (case 11) had a large number of eosinophils, mast cells in the epithelium, and degranulating mast cells with granuloma formation, but no perivasculitis.

Of nine eyes with OCP, five had stage III and four had stage IV disease. All of the patients with Stevens-Johnson syndrome or toxic epidermal necrolysis (7 eyes) had extensive subepithelial fibrosis, keratinization of the eyelid margins and conjunctiva, trichiasis, and fornix foreshortening. Symblepharon formation was present in five eyes of four patients (cases 5, 6, 8, and 11). Two patients had glaucoma controlled with medical therapy in both eyes (cases 1 and 2).

The indications for PK were optical in nine patients (10 eyes) with severe corneal scarring and/or neovascularization, and tectonic in six patients (6 eyes) with corneal perforation. Nine of ten optical PKs were performed as a last resort because of profound bilateral blindness or because the fellow eye had been enucleated. Four of six tectonic PKs were performed on an emergency basis because of large corneal perforations, with 8-mm corneal

Table 1. Preoperative Data

Patient No./ Eye	Age (yrs)/ Sex	Disease/ Stage	Indication for PK	Previous Procedures*	Disease Activity	Systemic Medication	Visual Acuity	
							Surgical Eye	*Fellow Eye*
1/OS	43/F	SJS	Tectonic	1	Active	—	HM	20/200
OD		SJS	Optical	1, 2	Inactive	AZA	CF 1 ft	LP
2/OD	62/F	OCP/IV	Tectonic	1	Active	—	LP	CF 1 ft
OS		OCP/IV	Optical	1, 2, 3, 4	Inactive	CYCP	HM	LP
3/OS	72/F	OCP/IV	Optical	1	Inactive	Remission	CF 2 ft	20/60
4/OD	87/F	OCP/III	Optical	1	Inactive	AZA	LP	LP
5/OS	40/M	TEN	Optical	1, 2, 4, 5, 6, 7	Inactive	CYCP	CF 1 ft	LP
OD		TEN	Optical	1, 2, 4, 5, 6, 7	Inactive	CYCP	LP	LP
6/OD	20/M	TEN	Optical	1, 2, 4	Inactive	AZA, Pred CYC A	CF 2 ft	HM
7/OD	25/M	OCP†/III	Optical	1, 2, 5	Inactive	AZA, DAP	HM	HM
8/OS	25/F	SJS	Tectonic	1, 2, 8, 9, 10	Inactive	AZA	HM	LP
9/OS	36/F	OCP*/III	Optical	1, 2, 4	Inactive	MTX	HM	HM
10/OD	51/F	OCP/III	Tectonic	1	Active	—	HM	20/50
11/OD	13/M	SJS	Optical	1, 2, 4, 6, 10, 11	Inactive	Remission	CF 2 ft	Enucleated
12/OS	68/F	OCP/IV	Tectonic	1	Active	—	HM	CF 1 ft
13/OD	80/F	OCP/III	Tectonic	1, 5, 9, 10	Active	—	HM	Enucleated

PK = penetrating keratoplasty; OS = left eye; SJS = Stevens-Johnson syndrome; HM = hand motions; OD = right eye; AZA = azathioprine; CF = counting fingers; LP = light perception; OCP = ocular cicatricial pemphigoid; CYCP = cyclophosphamide; TEN = toxic epidermal necrolysis; pred = prednisone; CYC A = cyclosporine A; DAP = dapsone; MTX = methotrexate.

* 1 = cryotherapy of trichitic lashes; 2 = mucous membrane grafting; 3 = conjunctival transplantation; 4 = corneal photocoagulation; 5 = tarsorrhaphy; 6 = conjunctival resection; 7 = lamellar keratoplasty; 8 = fornix reconstruction; 9 = gluing with tissue adhesive; 10 = bandage contact lens; 11 = superficial keratectomy.

† Occurring as a sequela of SJS.

melt and vitreous in the wound in one eye (case 2, right eye), and with a subluxated lens in one eye (case 12). In the tectonic group, one eye with a perforated descemetocele (case 8) was treated with cyanoacrylate adhesive and bandage contact lens before PK.

Preoperative surgical modalities that aimed to control mechanical factors included cryotherapy of trichitic lashes (15 patients; 16 eyes), mucous membrane grafting (8 patients; 9 eyes), fornix reconstruction (1 eye), tarsorrhaphy (3 patients; 4 eyes), and conjunctival transplantation (1 eye). Previous therapy also included conjunctival resection and superficial keratectomy for extensive conjunctivalization of the cornea in one eye (case 11). One of the patients with toxic epidermal necrolysis (case 5) had extensive peripheral corneal thinning bilaterally, and he underwent 360° perilimbal conjunctival resection and tectonic lamellar keratoplasty before vision restoring PK in both eyes (Fig 1). Corneal dye-laser photocoagulation of the new vessels was performed before PK in five patients (6 eyes).

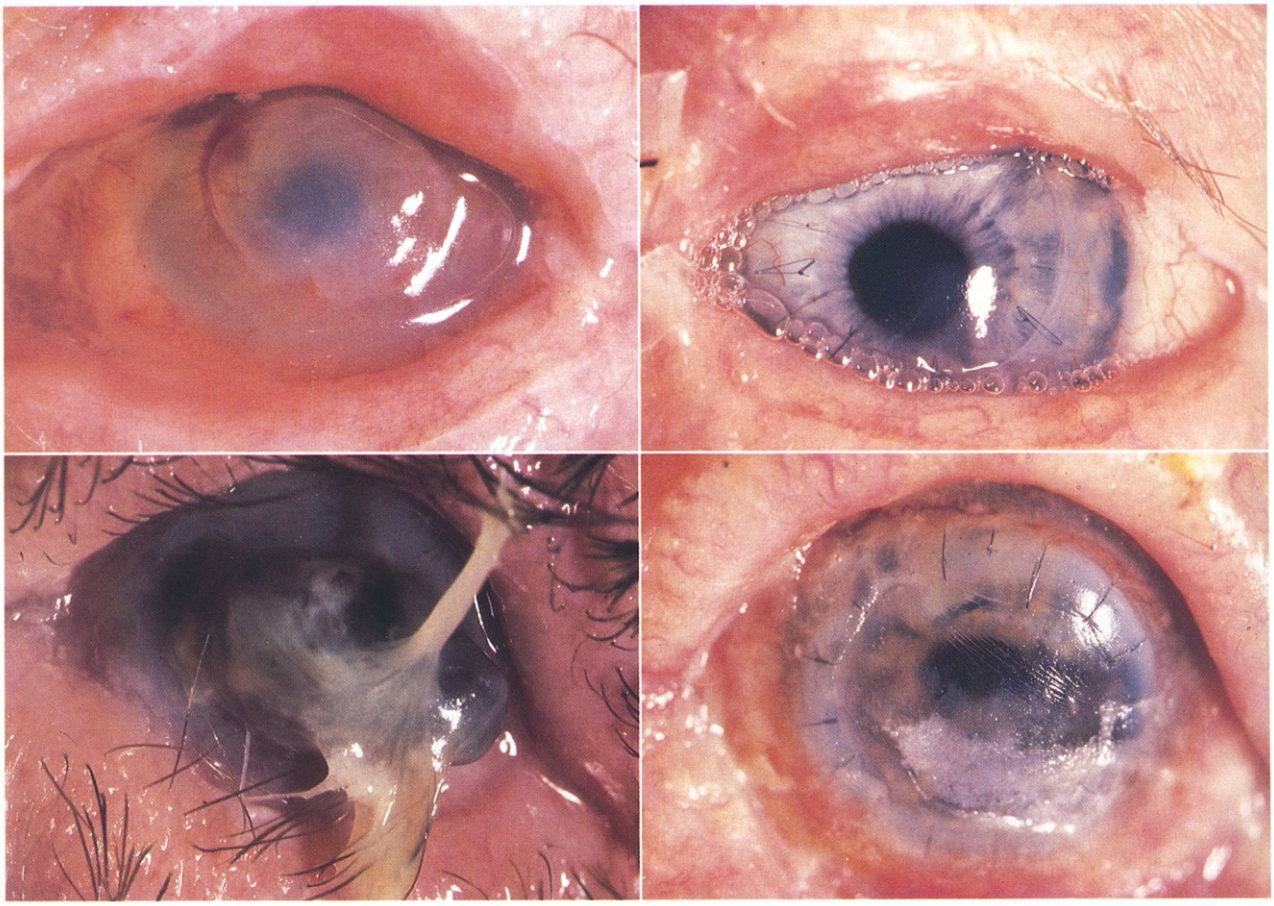
Preoperative visual acuity was counting fingers in five eyes (31.2%), hand motions in eight eyes (50%), and light perception in three eyes (18.7%).

In nine patients (10 eyes) who underwent optical PK and in one patient (1 eye) who underwent tectonic PK (case 8), there was no conjunctival inflammation at the time of surgery. The inflammation was controlled with systemic chemotherapy in eight patients (9 eyes); and the disease was in remission without chemotherapy in two patients (2 eyes). Five patients (5 eyes) who underwent emergency PK had active conjunctival inflammation preoperatively.

Systemic chemotherapy was instituted in the immediate postoperative period in these five patients. One patient received systemic prednisone (60 mg daily) perioperatively as an adjunct to induction of therapy with methotrexate.

Grafts ranged in size from 7.5 to 14.0 mm (mean, 9.3 mm). Two grafts were corneoscleral (case 2 [right eye] and case 11). Surgical procedures performed at the time of PK were extracapsular cataract extraction (4 eyes), intracapsular cataract extraction (1 eye), intraocular implantation (3 eyes), anterior vitrectomy (3 eyes), synechialysis (1 eye), conjunctival flap (2 eyes), and partial or complete tarsorrhaphy (8 eyes).

During the postoperative follow-up, azathioprine was the drug used most commonly (6 patients), followed by dapsone (3 patients), cyclophosphamide (2 patients), and methotrexate (2 patients). One patient with inactive Stevens-Johnson syndrome did not receive systemic chemotherapy throughout the follow-up. One patient with OCP was started on chemotherapy 1 year after the primary PK because she had a flare-up of inflammation. None of the remaining pa-



Top, Figure 1. **Top left,** case 5 with toxic epidermal necrolysis. Slit-lamp photograph of the vascularized left cornea 2 months after annular lamellar keratoplasty that was performed for extreme thinning of the peripheral cornea. **Top right,** same eye 2 months after the first penetrating keratoplasty with clear graft and partial tarsorraphy.

Bottom, Figure 2. **Bottom left,** case 9 with ocular cicatricial pemphigoid, left eye. Slit-lamp photograph of the patient with extensive corneal perforation and iris prolapsus. **Bottom right,** same eye 1 month after tectonic penetrating keratoplasty. Notice the patchy keratinization on the inferior cornea.

tients had acute exacerbation of the disease during the postoperative follow-up.

Postoperative complications are shown in Table 2. The most common postoperative complication was epithelial defect formation (10 patients; 11 eyes, 68.7%). Therapeutic intervention with tissue adhesive (for 1 eye with descemetocele), bandage contact lenses, or collagen shields (5 patients; 6 eyes) and/or tarsorrhaphy (5 patients; 5 eyes) was done in patients with persistent epithelial defects, but did not prevent the ensuing perforation in six patients (6 eyes). Wound dehiscence was a major complication in two patients (2 eyes), occurring 2 and 7 months postoperatively. This resulted in perforation with spontaneous lens extrusion in one patient and repeated dehiscence, despite resuturing twice in the other patient. Four patients (5 eyes) had postoperative intraocular pressure (IOP) elevation, which was controlled with topical timolol in one patient (1 eye), timolol and oral acetazolamide in two patients (3 eyes), and Nd:YAG laser transscleral cyclophotocoagulation in one patient (1 eye). Conjunctivalization of the peripheral graft was treated with conjunctival resection followed by topical mitomycin C therapy in one eye (case 6). Graft rejection developed in two patients (2 eyes, 12.5%), which could not be reversed, despite vigorous steroid treatment. The result of primary PK in 13 patients (16 eyes) is summarized in Table 3. Only one of six tectonic grafts (16.6%) remained stable with patchy keratinization; three of ten optical grafts (30%) remained clear; 12 grafts failed. Nine of the 11 patients with failed grafts underwent repeat PK: 7 patients for tectonic reasons (stromal ulcer perforation in 5 eyes, wound dehiscence in 2 eyes), and 3 patients (3 eyes) for optical reasons. In one of the remaining two patients with failed grafts, a keratoprosthesis was placed 3 years after primary PK (case 2, right eye); this eye later became phthisical. The other patient with a perforated graft was treated with a tectonic lamellar graft 4 months after the primary PK (case 8), and the lamellar graft later became vascularized and scarred.

Postoperative complications encountered after the second PK in nine patients (10 eyes) are shown in Table 4. Three patients (3 eyes) had bacterial keratitis, resulting

Table 2. Postoperative Complications and Outcome of Primary Penetrating Keratoplasty

Patient No./ Eye	Epithelial Defect/ Persistence	Stromal Ulcer/Melt Perforation	Wound Dehiscence	Bacterial Keratitis	IOP Elevation	PAS	Neovascularization/ Conjunctivalization	Exposure Keratopathy	Rejection	Phthisis	Outcome
1/OS*	+				+	+	+		+		Optical regraft
OD					+						Stable
2/OD*										+	Keratoprosthesis
OS	+				+						Stable
3/OS	+	+ (2×)									Tectonic regraft
4/OD					+						Stable
5/OS	+						+	+			Optical regraft
OD	+	+					+				Tectonic regraft
6/OD	+		+ (2×)				+				Tectonic regraft
7/OD	+	+					+				Tectonic regraft
8/OS*	+	+		+			+				Lamellar keratoplasty
9/OS	+	+									Tectonic regraft
10/OD*			+ (3×)								Tectonic regraft
11/OD	+				+				+		Optical regraft
12/OS*											Stable
13/OD*	+	+									Tectonic regraft

IOP = intraocular pressure; PAS = peripheral anterior synechiae; OS = left eye; OD = right eye.

* Tectonic penetrating keratoplasty.

Table 3. Outcome of Primary Penetrating Keratoplasty

Outcome	No. of Eyes
Stable/clear graft	4
Tectonic regraft	7
Optical regraft	3
Keratoprosthesis	1
Lamellar keratoplasty	1
Total	16

in failure of the graft in two patients. Elevation of IOP in two patients (2 eyes) was controlled with topical antiglaucomatous therapy. The regraft perforated in case 9 and was rejected in case 1 (left eye). Overall, five (50%) of ten regrafts remained stable until the final visit.

A third PK was performed in four patients (for optical reasons in case 1 [left eye] and case 7; for tectonic reasons in cases 9 and 13). Case 1 (left eye) had secondary glaucoma postoperatively, and she underwent cyclodialysis, cyclocryotherapy, and Nd:YAG laser transscleral cyclophotocoagulation in succession; her third graft failed with extensive PAS and retrocorneal membrane formation. The third graft of case 7 was rejected. Case 9 had postoperative glaucoma controlled with Nd:YAG laser transscleral cyclophotocoagulation, and later she had corneal perforation treated with corneoscleral patch graft. Case 13 who underwent repeat PK combined with vitrectomy and intravitreal antibiotic injection for endophthalmitis, had an uneventful postoperative course with no recurrence of infection.

A fourth PK was performed in two patients (case 1 [left eye] and case 7). Case 1 (left eye) had sterile stromal ulcer postoperatively which was treated by tarsorrhaphy, but subsequent rejection led to loss of the regraft. A suture abscess developed in the fourth graft of case 7 and was treated with fortified antibiotics. Later, this regraft also was rejected.

Total number of PKs in each eye, outcome of last PK, final visual acuity, causes of poor vision, and length of follow-up since last PK are shown in Table 5. Penetrating keratoplasty was performed on six eyes once (37.5%), six eyes twice (37.5%), two eyes three times (12.5%), and two eyes four times (12.5%). Twelve (75%) of 16 primary grafts and 10 (62.5%) of 16 regrafts failed. At the time of last evaluation, the graft was clear in eight eyes (50%), had patchy keratinization in two, was scarred in three, and edematous in two. One eye was phthisical. Ultimately, in 15 (93.7%) of 16 eyes in this series, the structural integrity of the globe was preserved. Final visual acuity was 20/200 or better in three eyes (18.7%), counting fingers in six (37.5%), and hand motions or worse in seven (43.7%).

Ten eyes underwent elective PK for attempted visual rehabilitation. Three of these eyes achieved a remarkable, stable improvement in vision (case 2 [left eye], case 5 [left eye], and case 11 [right eye]). Two additional eyes had an improvement in vision, which the patients declared to be meaningful (case 1 [right eye] and case 4 [left eye]). Vision worsened from hand motions to light perception in two eyes (case 7 [right eye] and case 9 [left eye]) in the attempt to regain sight.

Case Reports

Case 2. A 62-year-old woman with OCP stage IV and primary open-angle glaucoma in both eyes had a perforated ulcer with vitreous in the wound and 8-mm corneal melting in the right eye in June 1982. A 14-mm tectonic corneoscleral graft combined with anterior vitrectomy, conjunctival flap, and lateral tarsorrhaphy was performed. Conjunctival biopsy disclosed basement membrane zone positivity for IgG. Postoperatively, cyclophosphamide (75 mg daily) was instituted. In September 1985, failure of this graft resulted in placing a keratoprosthesis in the right eye. Conjunctival transplantation and mucous membrane grafting were performed in the left eye in 1982 and

Table 4. Postoperative Complications after Second Penetrating Keratoplasty in Nine Patients (10 eyes)

Patient No./ Eye	Epithelial Defect/ Persistence	Perforation	Bacterial Keratitis	Endophthalmitis	IOP Elevation	PAS	Neovascularization/ Conjunctivalization	Rejection	Outcome
1/OS					+	+		+	Optical regraft
3/OS	+		+						Clear graft
5/OS									Clear graft
5/OD	+						+		Scarred graft
6/OD	+				+		+		Mild vascular graft
7/OD	+		+			+	+		Optical regraft
9/OS	+	+							Tectonic regraft
10/OD									Clear graft
11/OD							+		Clear graft
13/OD			+	+					Tectonic regraft

IOP = intraocular pressure; PAS = peripheral anterior synechiae; OS = left eye; OD = right eye.

Table 5. Total Number of Penetrating Keratoplasties in Each Eye and the Outcome of Last Penetrating Keratoplasty

Patient No./ Eye	Total No. of PKs	Outcome of Last PK	Final Visual Acuity		(+)*	Follow-up since Last PK (mos)
			Surgical Eye	*Fellow Eye*		
1/OS†	4	Edematous (rejected)	LP	CF 5 ft		24
1/OD	1	Clear	CF 5 ft	LP	G	5
2/OD†	1	Phthisis	LP	20/200		11 yrs
2/OS	1	Clear	20/200	LP	G	20
3/OS	2	Clear	CF2 ft	CF6 ft	A	34
4/OD	1	Clear	CF 2 ft	LP	A	3
5/OS	2	Clear	20/80	LP		3
5/OD	2	Scarred	LP	20/80		8
6/OD	2	Mild neovascularization patchy keratinization	CF 2 ft	20/200		20
7/OD	4	Edematous (rejected)	LP	LP		3
8/OS†	1	Scarred (lamellar graft)	CF 2 ft	LP		22
9/OS	3	Scarred	LP	LP		20
10/OD†	2	Clear	HM	20/40	T	17
11/OD	2	Clear	20/70	Enucleated		4
12/OS†	1	Patchy keratinization	CF 2 ft	CF 5 ft		3
13/OD†	3	Clear	LP	Enucleated	R	1

PK = penetrating keratoplasty; OS = left eye; LP = light perception; CF = counting fingers; OD = right eye; HM = hand motions.

* Causes of visual acuity of 20/200 or worse in eyes with clear grafts; G = glaucomatous optic nerve damage; A = irregular astigmatism; T = tarsorrhaphy; R = retinal pathology.

† Primary tectonic PK.

1989, respectively. Visual acuity deteriorated to hand motions due to extensive keratopathy and cataract formation in the left eye in 1991. An 8-mm PK combined with pupillary membrane excision, extracapsular cataract extraction, and anterior vitrectomy was performed in July 1991. At the time of surgery, the patient was receiving a tapering dose of cyclophosphamide (50 mg daily). Postoperative IOP elevation was controlled with Nd:YAG laser transscleral cyclophotocoagulation 6 months after the corneal transplantation. At the time of the last visit in March 1993, the patient's visual acuities were light perception in the right eye with a phthisical globe and 20/200 in the left eye with a clear graft. She continued receiving cyclophosphamide (25 mg daily) when the disease became inactive.

Case 9. A 36-year-old black woman who had had a classic episode of Stevens-Johnson syndrome was first seen at Massachusetts Eye and Ear Infirmary 2 years after the acute episode. After the acute episode was resolved, chronic conjunctival inflammation developed, which led to progressive cicatrization and lid complications. At the first evaluation, results of slit-lamp examination disclosed 2+ conjunctival inflammation, keratinization of the lid margins, and severe keratopathy in both eyes. A conjunctival biopsy was performed, showing basement membrane zone positivity for IgG. Ocular cicatricial pemphigoid as a sequela of Stevens-Johnson syndrome was diagnosed, and the patient began treatment with dapsone (50 mg twice daily). However, the patient could not tolerate the drug because of development of hemolysis. Methotrexate (15 mg weekly) then was started. After the conjunctival inflammation was controlled, mucous membrane grafting was performed in both lids in the right eye and lower lid in the left eye. The first PK was performed in the left eye in March 1990. The graft perforated and a regraft was done 1 month after the primary PK. The second graft also failed due to stromal ulceration and a third PK was performed in June 1991. The patient still was receiving methotrexate (10 mg weekly), and the inflammation was controlled. The patient's visual acuity was counting fingers at 6 feet immediately after surgery; however, 1 month later, a corneal perforation developed, and a corneoscleral patch graft was performed for tectonic reasons (Fig 2). The elevation of IOP was controlled with Nd:YAG laser transscleral cyclophotocoagulation. The patient's final visual acuity was LP in both eyes in February 1993, and the patient still was receiving methotrexate (10 mg weekly) with inactive disease.

Discussion

Eyes with impaired lid function, severe conjunctival cicatrization, poor tear production, decreased corneal sensitivity, or extensive corneal neovascularization are at high risk for corneal transplant failure.[15] In patients with advanced OCP, Stevens-Johnson syndrome, and toxic epidermal necrolysis, in addition to the underlying immunologic pathology, successful PK is unlikely. Therefore, we have performed PK as a last resort on a select few patients with extensive attempts to control the primary immunologic process and to reduce the risk factors.

The major postoperative complication after both optical and tectonic PKs was persistent epithelial defect formation that eventually led to perforation requiring repeat

tectonic PK. Nobe et al[16] reported similar results after PK in six eyes with corneal melting and perforation due to immunologic disorders and associated ocular surface abnormalities. Further corneal melting and perforation occurred in all of their patients independent of the timing of initial PK after perforation. On the other hand, Killingsworth et al[17] achieved an 80% success rate in restoring the structural integrity of the eye after therapeutic PK for corneal perforation secondary to persistent epithelial defects from a variety of causes, including Stevens-Johnson syndrome, and 87% of those grafts remained clear. However, their visual results were uniformly poor in patients who underwent PK for large corneal perforations secondary to persistent epithelial defects caused by severe keratoconjunctivitis sicca associated with Sjögren syndrome. Previous studies have shown that emergent PKs in perforated eyes, keratoplasty a chaud, had higher rates of graft failure than did those performed after treatment of perforations with temporizing measures (i.e., tissue adhesive, bandage contact lens, conjunctival flaps, lamellar patch grafts, and tarsorrhaphy).[16,18] Nine (56.2%) of 16 regrafts in our series were performed for tectonic reasons, because temporizing measures failed to restore anatomic integrity in most of the patients.

The cause of graft clouding was multifactorial in most eyes. Surface failure recurred in the majority, resulting in vascularization and scarring of the graft. Five episodes of bacterial keratitis occurred in this series; one was suture-related. Fong et al[19] analyzed the predisposing factors for bacterial keratitis in 68 corneal graft infections and reported that the prevalence of mucosal scarring disorders was 4%. Ormerod et al[20] analyzed corneal infection in mucosal scarring disorders and Sjögren syndrome, and found that corneal surgery was a potential predisposing factor in 11 of 56 patients. They reported that the rate of corneal infection was reduced in patients with OCP that was satisfactorily controlled with immunosuppressive therapy. This also may be why we did not encounter bacterial keratitis as a major postoperative complication in this series. Frequent follow-up visits, prompt removal of loose sutures, and avoidance of prolonged topical steroids also may have helped in reducing the rate of this complication. However, three of five episodes of bacterial keratitis resulted in failure of the graft, and one was associated with endophthalmitis that required emergent surgical intervention.

Irreversible graft rejection developed in 2 (2.5%) of 16 primary grafts and 4 (25%) of 16 regrafts in this series. These figures are lower than the reported rates of corneal graft rejection (50%–70%) in high-risk eyes.[15] This is due to the failure of most of the grafts in our series from ocular surface problems.

Our results indicate that control of underlying immunologic pathology through aggressive preoperative and postoperative anti-inflammatory therapy does not yield a high rate of graft success; and once advanced conjunctival cicatrization develops, extensive attempts at preparing the environment for a more hospitable acceptance of a corneal graft do not usually result in long-lasting changes sufficient to allow survival of a clear corneal graft. Glaucoma or corneal ulceration or perforation after elective PK even may result in further loss of vision. We must be careful not to allow success in control of inflammation and partial restoration of reasonably good lid–lash–globe relations to encourage pursuit of visual rehabilitation through keratoplasty in most of these patients. Because we are not yet able to surgically rehabilitate patients with OCP once stage III or IV disease is reached, prevention of disease progression and of blinding keratopathy by early aggressive treatment is of critical importance.

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