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SHORT COMMUNICATION

Lamellar keratoplasty for the treatment of feline corneal sequestrum

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Abstract

A lamellar keratoplasty was used to treat corneal sequestrum in four Persian cats (six eyes). Following a superficial keratectomy, lamellar corneal allografts (feline corneal tissue) or heterografts (canine corneal tissue) which had been preserved at –20 °C were placed in the recipient cornea. All grafts became optically transparent within 2 months following surgery and no recurrences of the sequestrum have been noted during the follow-up period (4–30 months). We conclude that feline corneal sequestrum may be successfully treated with feline or canine donor corneal tissue using this technique.

Key Words: corneal sequestrum, lamellar keratoplasty, corneal surgery, heterograft, feline

INTRODUCTION

Corneal sequestration (corneal necrosis, corneal nigrum, corneal mummification, or necrotizing keratitis[1]) is a disease unique to the domestic cat characterized by a localized necrosis of the epithelium and anterior stroma in the central or paracentral cornea with associated accumulation of a brown pigment in the affected tissue.[2,3] The lesion is often progressive, extending to the deeper stromal layers of the cornea. Brachycephalic breeds of cats are predisposed to develop this condition, suggesting that it occurs following prolonged exposure of the central, superficial cornea. It has also been reported as a sequel to feline herpes virus (FHV-1).[1,4] While there is some debate on the most effective therapy, most veterinary ophthalmologists treat the condition with a superficial keratectomy with or without secondary placement of a pedicle conjunctival graft. While placement of a conjunctival graft has been reported to lessen the recurrence rate of corneal sequestrum, and provide structural support to the keratectomy site when the depth of the lesion in the cornea requires deep excision, it is characteristically associated with the formation of leukoma of varying density.[5] Conversely, partial-thickness (lamellar) or full-thickness (penetrating) corneal grafts are typically used when an optically clear graft site is desired.[6] The purpose of this study was to investigate the use of a lamellar keratoplasty, using both feline and canine donor tissue, in the treatment of corneal sequestrum.

MATERIALS AND METHODS

Four Persian cats (six eyes) with characteristic corneal sequestrum with vascularization, ulceration, and perilesional corneal edema were treated with lamellar keratoplasty. Two cats developed unilateral sequestrum, while the other two cats had bilateral sequestrum with the opposite eye developing the lesion 2 months and 1 years following keratoplasty in one eye. Associated ocular findings included a mild bilateral meibomitis in one cat, and a low Schirmer I tear test value (7 mm at 60 s), presumably associated with resection of the nictitating membrane which had been performed 4 months previously. No other ocular abnormalities were found in the other two cats (Table 1). Diagnostic testing for FHV-1 was not performed in these four patients due to the absence of history or other clinical signs compatible with viral infection, and the suggested evidence for a breed-related corneal sequestrum.

The cats were anesthetized with ketamine (Imalgène 1000®, Lyon, France) and acepromazine (Calmo Neosan®, Smith Kline Beecham, Madrid, Spain) and maintained on isofluorane (Forane®, Abbott Laboratories, Madrid, Spain). Where necessary, a stay suture with 5–0 nylon was placed in the ventral limbal region to stabilize the globe. A superficial keratectomy was initiated with a corneal trephine (F.C.I Instruments Co., Paris, France) with a diameter 1 mm larger than the lesion, excising to the stromal depth estimated to be required to remove all the brown pigment associated with the sequestrum. Sharp lamellar dissection of the lesion was then completed using a blade constructed from a broken razor blade.

The keratectomy sites were then covered with a lamellar corneal graft of the same diameter and thickness in which the epithelium was removed by gentle scraping with a cellulose sponge. The grafts were harvested at the time of

Table 1 Clinical parameters following lamellar keratoplasty for treatment of corneal sequestrum in four cats

Case no.	Eye	Age (years)	Duration of Sequestrum	Stromal Depth	Trephine Diameter (mm)	Source of donor tissue	Graft clearing (weeks)	Postoperative interval (months)
1	OD	8	3 weeks	75%	8	Dog	1	30
2	OD	4	2 months	75%	5	Cat	1	18
3	OS	–	3 weeks	50%	5	Dog	1	6
4	OD		3 months	75%	7	Cat	4	13
5	OD	2	2 weeks	50%	7	Dog	1	8
6	OS	–	1 week	50%	8	Dog	3	4

surgery from donor globes that had been collected and preserved as described below, using a technique similar to that described for the superficial keratectomy. The grafts were secured to the recipient site using 8–12 simple interrupted sutures using 9–0 nylon.

The donor graft was collected from two cats and 4 dogs within 1 of euthanasia. The donor animals were free of obvious systemic disease and the dogs had been screened and found to be free of *Leishmania infantum* by polymerase chain reaction testing. The feline leukemia virus and feline immunodeficiency virus status of the two donor cats was not determined. The globe was removed under sterile conditions, and the entire eye was placed in a sterile vial containing a commercially available ophthalmic antibiotic solution (Gentamicin Ophthalmic Solution, Colircusi Gentamicina 1®, Barcelona, Spain). The vials containing the eyes were then stored at –20 °C for a period of 1 month to 1 years prior to the surgery. The vials were removed from the freezer and allowed to thaw for 30–60 min prior to harvesting the graft for lamellar keratoplasty.

Postoperative treatment consisted of topical 1% atropine ointment (Oftalmolosa Cusi Atropina®, Barcelona, Spain) once a day for 5 days, topical 0.1% dexamethasone (Maxidex®, Barcelona, Spain) three times a day and tobramycin (Tobrex®, Barcelona, Spain) four times a day for 6 weeks, and 0.2% cyclosporine ointment (Optimmune®, Schering-Plough, Madrid, Spain) twice daily for 12 weeks. Fifty per cent of the corneal sutures were removed at 3 weeks postoperatively, and the remainder were removed at 6 weeks. Removing the sutures in this way decreases the amount of blood vessels produced due to the presence of suture material. Corneal healing is slower in nonpenetrating keratoplasties than in penetrating ones and it is better to allow some of the sutures to remain for at least 6 weeks. An Elizabethan collar was used for 3 weeks postoperatively to prevent self-trauma.

RESULTS

The sequestrums were axial in four eyes, and paraxial in two eyes (Fig. 1a). Excision of the sequestrum and harvesting of the graft required corneal trephines of 5–8 mm diameter to a stromal depth of one-half to three-quarters thickness. Residual corneal pigment was present in case 1 and 3 following keratectomy, but this pigment resolved within 4 weeks following surgery.

The cats appeared comfortable by the second postoperative day, and all the graft sites were epithelialized within 5 days postoperatively. The surgical site was fluorescein dye-positive in only one case at the graft-recipient margin at this time. The tear film typically lost its brown color within the first week after surgery. The grafts were mildly edematous, especially in cases 3 and 5, causing an increase in cornea thickness in the surgical site for two weeks following surgery (Fig. 1b). Pre-existing corneal vascularization was typically lessened in the immediate postoperative period, with only one case demonstrating an increase in corneal vascularization associated with one aspect of the suture line. In no case did the vascular response extend into the graft, and the peripheral corneal vascularization resolved in all cases after the final sutures were removed at 6 weeks. Clearing of the grafts begin at $\approx$ 1 week postoperatively, and the graft sites were typically transparent within 4 weeks (Fig. 1c). At 2–3 months postoperative, nonpatent ('ghost') corneal vessels were seen with biomicroscopy (Fig. 1d). Apart from a faint leukoma at the graft/recipient interface, the surgical site was optically clear and without critical biomicroscopic examination, and the graft site was difficult to distinguish from the surrounding normal cornea. Subjectively, no difference was noted in the degree of postoperative edema, the level of associated peripheral corneal vascularization, and the final transparency of the graft between the allografts and heterografts.

A mild superficial corneal ulcer developed in the nongrafted cornea in one case at 5 weeks postoperatively. This was epithelialized within 5 days after temporarily discontinuing the cyclosporine therapy and treating the eye with topical tobramycin and atropine. All six cases maintained transparent corneas with no evidence of recurrence of the sequestrum for the 4–30 month follow-up periods.

DISCUSSION

Surgical treatment for feline corneal sequestrum typically includes lamellar excision of the lesion through a superficial keratectomy. Depending on the surgeon's preference and depth of the keratectomy site, other secondary grafting procedures, such as pedicle conjunctival graft, or corneoscleral transposition, may also be used.[1,7] The use of a pedicle conjunctival graft has been suggested to reduce the incidence of recurrence of the sequestrum, compared with keratectomy alone. Because stromal regeneration requires a period of weeks to months and is often incomplete following keratectomies extended to the deep stroma level, use of a

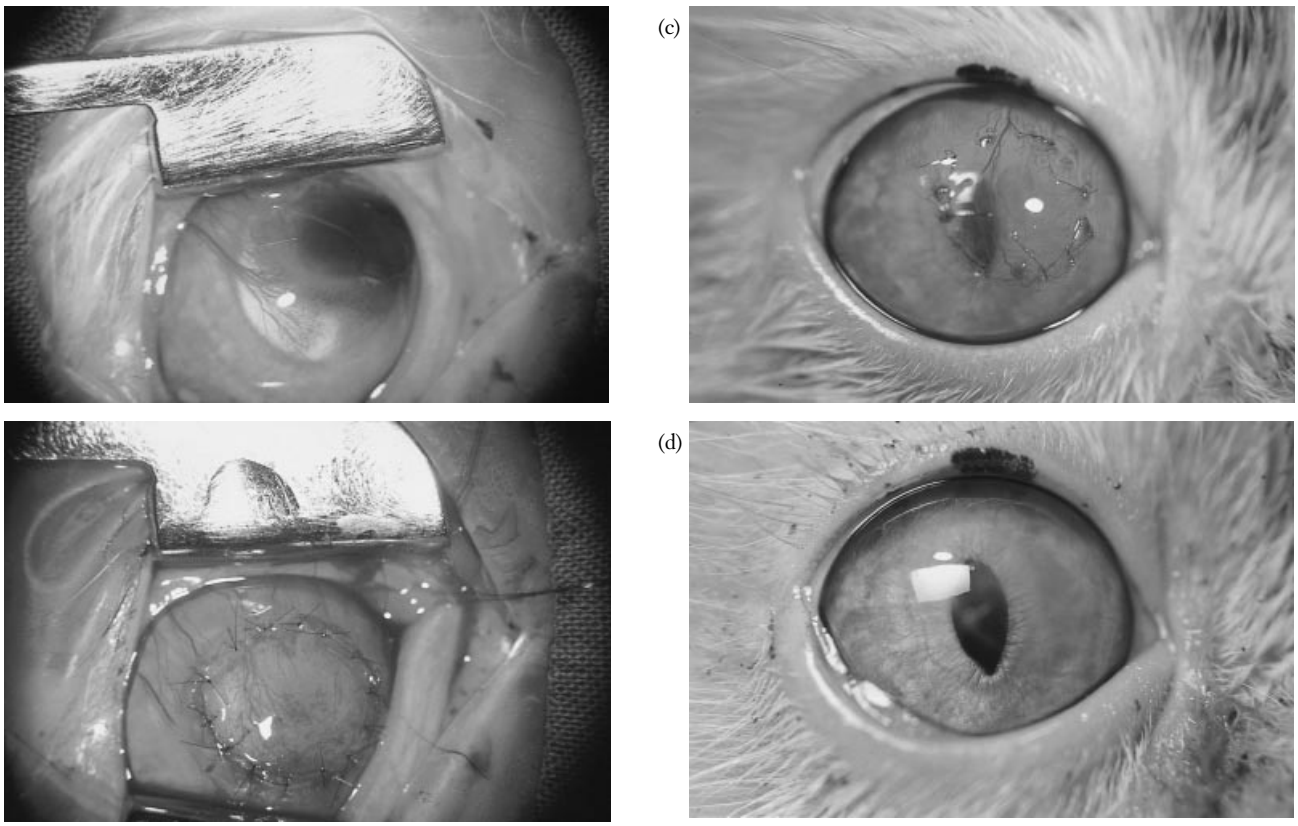

Figure 1. (a) Preoperative appearance of the corneal sequestrum in case 5. (b) Immediate postoperative appearance of lamellar graft from a canine donor eye. The graft is edematous, and a peripheral corneal vascular response and vascularization of the deep stroma in the keratectomy site may be seen. (c) Appearance of the eye 3 weeks postoperatively. Substantial clearing of the graft and resolution of the pre-existing corneal vascularization is noted. (d) Appearance of the eye 6 weeks postoperatively. The graft site is transparent and optically clear. Without bimicroscopy, it is difficult to distinguish the grafted from nongrafted cornea.

conjunctival or corneoconjunctival graft may also be necessary to provide structural support to the cornea.[1,2,7,8] Conjunctival pedicle grafts and corneoconjunctival pedicle flaps are autografts and therefore donor tissue is readily available, but both have the disadvantages of a residual leukoma or scar in the graft site.[7,8] While the density of this leukoma often diminishes with time, especially in the feline cornea, in the authors' experience, some degree of clinically detectable corneal fibrosis is usually permanent. Here we have demonstrated that a lamellar corneal graft may be successfully used to treat corneal sequestrum and have the additional advantage of allowing a transparent, optically clear graft site. This is particularly desirable with feline corneal sequestrum, which are typically located in the central or paracentral cornea, along the visual axis. In the cases reported in this study the grafts were epithelialized within 5 days and the patients developed a transparent graft site within 1–4 weeks following surgery and no recurrence of the sequestrum was noted. Similar to a previous report on feline corneal sequestrum with conjunctival graft placement, incomplete removal of the deep stromal pigment was of no long-term consequence in the two cases in which it was present in this study.[9]

The donor tissue was harvested using a modification of a relatively simple and inexpensive procedure previously described for full-thickness corneal grafts.[10] The storage medium was a commercially available ophthalmic antibiotic solution and the tissue was stored in a freezer section of a standard refrigerator for up to 1 year. Because lamellar grafts were used in this study, and not full-thickness grafts in which endothelium cell viability is of concern, storage in this fashion was possible for extended periods at –20 °C. We collected and stored entire globes rather than corneal buttons to facilitate harvesting of the graft to the correct stromal level at the time of the keratectomy in the recipient cornea. The donor animals used in this study were screened with a physical and ophthalmic examination prior to euthanasia and tissue collection. However, because infectious disease transmission has been reported with corneal grafts in humans, we would recommend screening donor cats for feline leukemia and feline immunodeficiency viruses, and donor dogs for any common endogenous infectious diseases (such as leishmaniasis in Europe or rabies in most parts of the world) which have the potential, albeit slight, for transmission to the host.

Importantly, we found no obvious difference between the level of peripheral corneal vascularization, edema, or final

transparency of the graft site between canine corneal grafts (heterografts), and feline corneal grafts (allografts) in patients in this study. Heterografts were used in lieu of allografts in some cases in this study according to the availability of donor tissue at the time of surgery.[10] Full-thickness grafts, or penetrating keratoplasties, have been previously used in veterinary ophthalmology in dogs, cats and horses,[10,11] primarily to provide structural support to diseased sections of excised corneas (tectonic grafts) rather than in an effort to regain corneal transparency (optical grafts). The likelihood of immunologic recognition and graft rejection (which manifests as opacity in the graft) by the host is enhanced with pre-existing corneal vascularization, which is common in veterinary ophthalmology with most corneal diseases which require grafting. Additionally, the immunologic recognition is directed predominately against the corneal endothelium and epithelium.[12] As a result, penetrating grafts, especially those with epithelium, pose a greater risk of graft rejection than lamellar grafts. The absence of corneal epithelium and endothelium in the grafts used in the study were probable factors that allowed for an optically clear graft, despite the presence of pre-existing corneal vascularization directed against the sequestrum. In no cases reported here did the corneal vascular response extend into the graft, suggesting that immunologic recognition of stromal tissue, even of that from a different species, is low in the cat. The use of topical corticosteriods and cyclosporine after lamellar keratoplasty is recommended to lessen the probability of corneal vascularization and subsequent graft rejection.

In conclusion, breed-related feline corneal sequestrum may be successfully treated with lamellar keratoplasty using canine or feline donor tissue. The procedure avoids the need for expensive and limited storage of donor corneal tissue, is technically not difficult, and in these cases was associated with an transparent graft with no recurrent of the sequestrum.

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