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CASE REPORT

Application of porcine small intestinal submucosa (Vetrix BioSIS®) for recurrent corneal sequestrum in an American shorthair cat

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Abstract: A 15-year-old, spayed, female American shorthair cat presented with recurrent corneal sequestrum in the right eye. The cat had undergone superficial keratectomy twice for corneal sequestrum treatment 5 and 11 months previously. Two layers of porcine small intestinal submucosa (SIS; Vetrix BioSIS®) were applied to the surgical corneal defect after keratectomy. Thereafter, clinical signs, such as lacrimation, blepharospasm, and corneal ulcer, disappeared 50 days postoperatively. Moreover, the application of SIS with keratectomy prevented recurrence until 651 days after surgery. SIS could be applied as an additional bioscaffold for surgical repair of corneal sequestrum recurring after superficial keratectomy alone in cats.

Keywords: cat, keratectomy, sequestrum, small intestinal submucosa, ulcer

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Feline corneal sequestrum is a common corneal disease in cat breeds such as Persian, Burmese, Himalayan, and Siamese [1]. Although its causes remain unclear, it occurs in chronic corneal ulcer or keratitis caused by feline herpes virus-1 infection, entropion, and trichiasis [1,2]. The clinical signs are characterized by corneal central necrotic degeneration with an amber- or brown-to-black-colored plaque, which is surrounded by an area of corneal superficial ulcer, corneal neovascularization, and corneal edema. It can also cause ocular pain, blepharospasm, and epiphora [1]. Although the necrotic plaque may be sloughed with simple medical treatment for corneal ulcer or anterior uveitis, such treatment would require months or years to complete and causes ocular discomfort [1]. Therefore, keratectomy is recommended for surgically removing the corneal sequestrum plaque [1,2]. In cases of superficial corneal sequestrum, additional grafts are not required [2], but when the lesion spreads to the deep corneal stroma, surgical interventions, such as bulbar conjunctival flap, corneoconjunctival transposition, application of bioscaffold using porcine small intestinal submucosa (SIS; Vetrix BioSIS®), acellular porcine bladder submucosa (UBM; ACell Vet™), or amniotic membrane (AM) are needed after lamellar keratectomy [2-6]. Herein, we report a case of recurrent corneal sequestrum after superficial keratectomy in a cat and describe the effects of a combination of lamellar keratectomy and multilayer porcine SIS implantation for preventing the recurrence of corneal sequestrum.

A 15-year-old, 4.3 kg, spayed female, American shorthair cat presented to the Dana Animal Hospital Eye Center for the surgical repair of recurrent corneal sequestrum in the right eye (OD). An ophthalmic examination including slit-lamp biomicroscope (SL-D7®; Topcon, Japan) revealed clinical signs of mucoid ocular discharge, hyperemia, blepharospasm, corneal ulcer, corneal edema, and corneal neovascularization. The cat had undergone superficial keratectomy twice for the treatment of corneal sequestrum 5 and 11 months previously. However, corneal sequestrum recurred 180 days after the first superficial keratectomy and 124 days after the second one (Fig. 1D and H). As the previous two superficial keratectomies deepened the corneal defects, the corneal stroma layer was expected to be thinner at the third keratectomy. Therefore, additional porcine SIS implantation was considered to prevent the recurrence

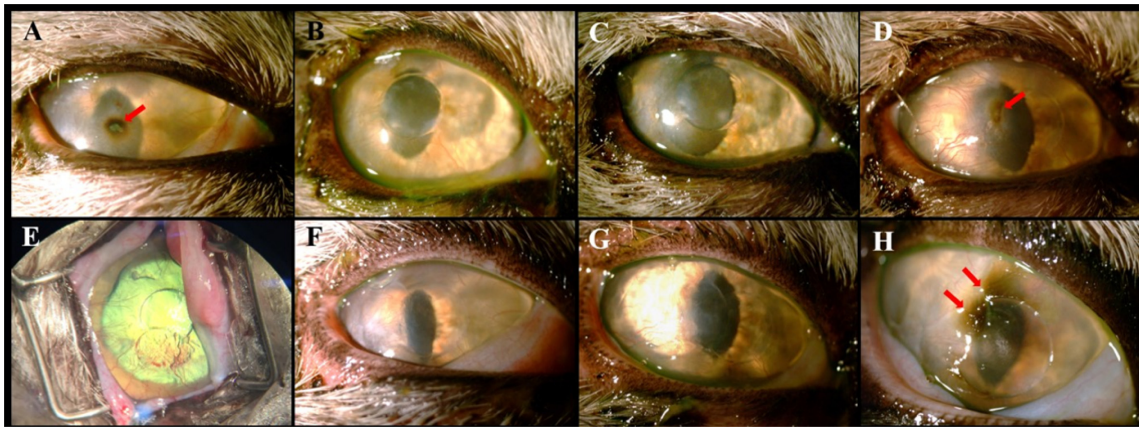

Fig. 1. Preoperative, perioperative, and postoperative appearances of superficial keratectomies performed twice for the treatment of corneal sequestrum in the right eye of the same cat. (A) Central dark brown corneal plaque (arrow) in the right eye before the first superficial keratectomy. (B) Appearance at 22 days after the first superficial keratectomy. (C) Appearance at 79 days after the first superficial keratectomy. (D) Note the recurrent sequestrum (arrow) at the 9 o'clock rim of the first superficial keratectomy site 180 days after surgery. (E) Appearance of the second superficial keratectomy. (F) Appearance at 19 days after the second superficial keratectomy. (G) Appearance at 60 days after the second superficial keratectomy. (H) The second recurrent sequestrum (arrows) at 124 days after surgery.

of corneal sequestrum and to repair the corneal defects.

The cat was premedicated with atropine (Atropine®, Daewon Pharm, Korea) 0.02 mg/kg SC, butorphanol (Butorphan®, Myungmoon Pharm, Korea) 0.2 mg/kg IV, midazolam (Midazolam®, Bukwang Pharm, Korea) 0.2 mg/kg IV, meloxicam (Metacam®, Boehringer Ingelheim, Spain) 0.3 mg/kg SC, and cefazolin (Cefazolin®, Chongkundang, Korea) 20 mg/kg IV, and topical proparacaine 0.5% eyedrop (Alcaine®, Alcon, Belgium) was instilled. General anesthesia was induced using intravenous propofol (Provive®, Myungmoon Pharm) 4 mg/kg and maintained using isoflurane (Isotroy®, Troika Pharm, India) and oxygen. After periocular clipping, the surgical area was disinfected with 0.5% betadine (1:20 diluted with normal saline). All surgical procedures were performed under an ophthalmic surgical microscope. A 6-mm reusable trephine blade with a universal trephine handle (a1 medical, Germany) was used to perform circular keratotomy around the corneal sequestrum area, and the corneal sequestrum was removed using a 2.6-mm crescent microsurgical knife (Kai Medical, Japan). The sequestrated site remaining after the first and second keratectomies was completely removed during the third deep keratectomy. To cover the superficial and central deep corneal defects, two pieces of porcine SIS implants were prepared by cutting a rectangular sheet (4 cm × 7 cm) 1 mm wider than the rim of each defect. The sheet with a coarse side and a smooth side was positioned with its coarse surface facing the corneal defect. Once a deep defect was covered with the appropriate implant, another implant prepared for the superficial defect was overlaid on it. The implant was rehydrated with 0.9% normal saline (Daihan Pharm, Korea) for 1 min before placement and fixation to the cornea by using 8-0 polyglactin 910 (Vicryl®, Johnson & Johnson, Germany) with simple interrupted sutures to avoid excessive tension. The third eyelid flap was sutured using 5-0 nylon (Blue Nylon®, Ailee, Korea), and the bulbar surface of the third eyelid was scarified using a No. 15 surgical blade to cause a hemorrhage. As postoperative care, topical 1% atropine SID (Isoptoatropine®, Alcon Pharmaceuticals, Belgium) for 3 days, 0.5% moxifloxacin QID (Vigamox®, Alcon Pharmaceuticals, Singapore) and 0.5% betadine solution QID for 21 days were instilled onto the third eyelid flap. After removing the flap sutures, 0.15% sodium hyaluronate (Eyelein free®, Kolmar Pharm, Korea) was administered three times a day throughout the follow-up period. Systemic doxycycline 5 mg/kg BID (Unidoxy®, Kukje Pharm, Korea) was prescribed for 21 days. The cat was re-examined 7 days after surgery. The third eyelid flap was well maintained, no ocular pain was noted, and only moderate mucoid ocular discharge was present. The third eyelid flap sutures were removed 3 weeks after surgery. At follow-up on postoperative days 50, 107, and 651, ophthalmic examinations were performed, and these revealed no corneal ulcer or corneal sequestrum.

Porcine SIS, commercialized as Vetrix BioSIS® in veterinary ophthalmology, is composed of three layers: tunica mucosa, tunica submucosa, and tunica muscularis mucosa [7]. Mechanical and chemical removal of the serosa, tunica muscularis, superficial mucosal layer, mesenteric tissues, fibrocytes, and endothelial cell yields non-immunogenic acellular extracellular matrix (ECM) with a rough side (tunica muscularis mucosa) and a smooth side (stratum compactum of tunica mucosa) [3,7]. This ECM has low antigenicity and plays a role in inhibiting matrix metalloproteinases and bacterial infection [8-10]. In addition, the ECM stimulates cell migration and proliferation along with angiogenesis during tissue remodeling [8]. It is also known as a bioscaffold that

helps repair and remodel tissue defects in a structure similar to that of its original tissue histologically [7,11]. Therefore, in veterinary ophthalmology, porcine SIS has been used as a tectonic support for corneal defects secondary to various corneal diseases in dogs, cats, and horses [4,12-15].

In this case, superficial keratectomy was performed twice to treat corneal sequestrum in an American shorthair cat, but it recurred at 180 days and 124 days after each keratectomy (Fig. 1D and H). In another study, recurrence was confirmed in 11 (25%) out of 44 cats that underwent superficial keratectomy alone [15]. Therefore, to prevent the recurrence of corneal sequestrum at the time of admission for the third surgery, a surgical method involving the application of conjunctival grafts or porcine SIS as a scaffold in addition to keratectomy was considered. Conjunctival grafts provide sufficient conjunctival tissue containing fibroblasts and collagens to help treat corneal defects, as well as leukocytes, α_2-macroglobulin, and serum through conjunctival vessels to help remodel and strengthen corneal tissue [3]. However, a disadvantage of corneal grafts is that they cause vision impairment owing to permanent corneal scarring [3,12]. In the case of porcine SIS implantation, scar formation was minimized enough to preserve clear vision after surgery [12]. Featherstone et al. [12] reported that the simultaneous application of keratectomy and porcine SIS in five cats with corneal sequestrum resulted in no recurrence or complications up to 10 months after surgery. Therefore, we decided to perform combined keratectomy and porcine SIS implantation in this case.

At the time of the third surgery, a necrotic plaque remained after superficial keratectomy. Since the remaining stromal sequestrum was a major risk factor for recurrence [15], deep keratectomy was additionally performed to complete the dissection of the brown necrotic stroma (Fig. 2A and B). Because the corneal defect deepened, porcine SIS implants were mounted in two layers (Fig. 2C and D). Moderate mucoid ocular discharge was observed 7 days after surgery, but the depth changes of the corneal defect and anterior chamber were not observed on a high-resolution ocular ultrasound examination. According to the owner's feedback, ocular discharge decreased until 21 days after surgery. After the removal of the third eyelid flap sutures, disposable 0.15% sodium hyaluronate eyedrops without epitheliotoxic benzalkonium hydrochloride was continuously instilled for the entire follow-up period. Sodium hyaluronate improved wound healing, enhanced corneal epithelialization and tear film stability, and suppressed tear evaporation [1,2]. At the last follow-up visit on postoperative day 651, a brown periocular discharge was observed without any clinical signs such as ocular discomfort, ocular pain, blepharospasm, or corneal ulcers. The corneal sequestrum did not recur and vision was well maintained. The limitation of this case report was that we could not compare the long-term prognosis and recurrence rates of this treatment to those of other surgical options, such as porcine UBM, AM, conjunctival pedicle flap, and conjunctival transposition flap with keratectomy.

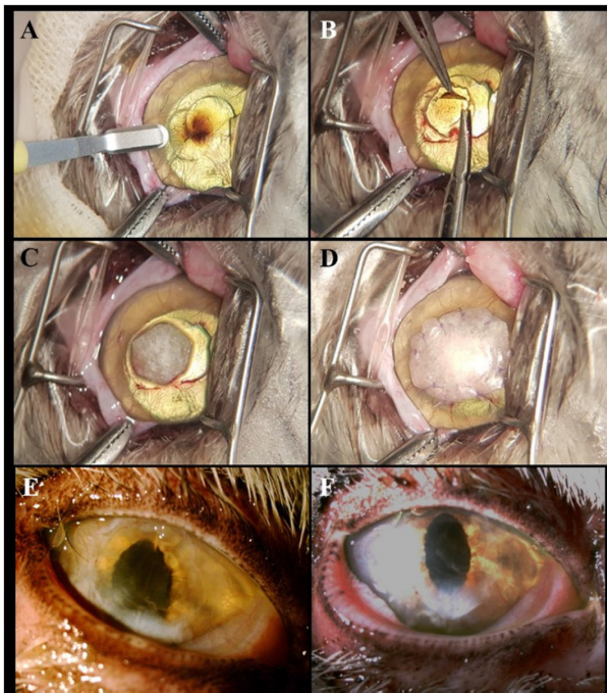

Fig. 2. Preoperative and postoperative appearances of the third superficial keratectomy and application of porcine SIS (Vetrix BioSIS®) in the same cat. (A) The third superficial keratectomy with a crescent microsurgical knife. (B) Additional deep keratectomy for the complete removal of necrotic areas remaining after the third superficial keratectomy. (C) Placement of the first SIS graft cut to the size of the deep stromal defect. (D) Suturing of the second SIS graft with 8-0 polyglactin 910 onto the corneal defect margin. No recurrence of corneal sequestrum is observed at 50 days (E) and 651 days (F) after surgery. SIS, small intestinal submucosa.

In conclusion, this case report suggests that the application of keratectomy with porcine SIS would be an effective surgical intervention to prevent corneal sequestrum recurrence in cats.

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