The Little Bit of Devil in Angel's Eye

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Introduction

Stromal abscessation in the equine patient is a very painful condition which can result in loss of vision if left untreated. The initiation of a stromal abscess begins with a break in the corneal epithelial barrier, allowing foreign materials or pathogens to migrate through to deeper layers of the cornea. Immediate re-epithelialization of the superficial cornea without resolution of foreign material beneath the surface incites an inflammatory reaction within the cornea.[7] While most stromal abscesses form as a result of fungal inoculation, bacterial contamination may also contribute to infection.[6] Diagnosis is primarily based on history and clinical signs, particularly with the presence of a cellular infiltrate. Treatment options include medical management or surgical intervention, depending on the depth and severity of the abscess.[12] The following case will discuss the classic presentation, diagnosis, and treatment of a deep stromal abscess in the equine patient.

History and Presentation

Angel is a 20-year-old Quarter horse mare who presented to Mississippi State University College of Veterinary Medicine equine services on May 21st, 2020. Approximately a week and a half prior to presentation, Angel had excessive lacrimation from her left eye and was seen by her referring veterinarian, who diagnosed a corneal ulcer. She was prescribed a triple antibiotic ointment at that time and was re-examined about 1 week later. The ulcer appeared to be healing at her recheck examination, as it had reduced to about half of its original size. Just a few days later, on Monday May 18th, Angel's owner noted she appeared to be more painful, and her left eye began to look cloudy and blue.

Upon presentation, Angel was bright, alert, and responsive. She weighed 950 pounds, with a body condition score of 5/9, which is ideal. She had a pulse of 36 beats per minute and a respiratory rate of 16 breaths per minutes, however, a rectal temperature was not obtained at this time. Her mucous membranes were pink and moist with a capillary refill time of less than 2 seconds. Cardiothoracic auscultation was within normal limits, with no murmurs, arrhythmias, or abnormal lung sounds appreciated. Gastrointestinal motility auscultated normally in all four quadrants and digital pulses were normal in all four limbs. Additionally, Angel had bilateral clear nasal discharge.

Upon ophthalmic examination, enophthalmos of the left globe was noted in comparison to the right globe. Moderate conjunctival hyperemia, moderate episcleral injection, blepharospasm, and diffuse corneal edema could all be appreciated in and around the left eye. The pupil appeared mitotic and fixed. There was 2+ aqueous flare present in the anterior chamber of the left eye upon examination with the slit beam. A small, tan to yellow, focal infiltrative lesion was present centrally within the left cornea. Angel had a positive menace and dazzle reflex, with appropriate size and motility of the globe. The right eye appeared normal at this time. Based on the history, physical exam, and basic ophthalmology exam, Angel appeared to have a stromal abscess centrally located within the cornea of the left eye.

Diagnostic Approach and Considerations

A few basic diagnostics that may be performed with any ophthalmic examination include the Schirmer tear test, tonometry, and corneal staining. The Schirmer tear test is a quantitative measure of tear production. The strip should be gently placed within the conjunctival fornix over the lower eyelid. The strip is removed and read after 1 minute, with greater than 15 mm/min indicating appropriate tear production. Results of less than 15 mm/min may indicate a tear film

deficiency, such as keratoconjunctivitis sicca.[1] It is important to note the Schirmer tear test should be performed prior to any stain or topical medication administration into the eye. The Schirmer tear test is always considered part of a normal ophthalmic examination in small animals, however, it is not as consistently performed in horses. In Angel's case, a Schirmer tear test was not performed due to presence of clear nasal discharge and epiphora, indicating that she had obvious adequate tear production. Tonometry is a diagnostic test to measure the pressure within the eye. The two main instruments for measuring intraocular pressure are the TonoVet and the TonoPen. The TonoVet is a rebound tonometer with a magnetized metal probe that is propelled horizontally toward the cornea. The probe measures the "hardness" of the globe as it rebounds back to the tonometer to assess the intraocular pressure. The TonoPen is an applanation tonometer with a small footplate that gently "bounces" off the corneal surface.[(8,10)] Normal intraocular pressure in a horse may be between 15-30 mmHg. Lower pressures could indicate uveitis, while higher pressures are indicative of glaucoma.[8] In Angel's case, the intraocular pressure of her left eye was 6 mmHg, and her right eye was 20 mmHg. The low pressure in Angel's left eye was suggestive of a uveitis secondary to her stromal abscess. A fluorescein stain is the last diagnostic tool that is routinely used to assess the health and condition of the cornea. In horses, the stain is most often applied by spraying a fluorescein liquid through a needle hub onto the surface of the cornea. Any compromise in the corneal surface will result in uptake of the fluorescein stain.[(1,10)] Both Angel's left and right eye were negative for stain uptake, indicating both corneas were fully intact, and the abscess in Angel's left eye was enclosed beneath the surface of the epithelium.

Pathophysiology

The cornea is a transparent barrier that allows refraction and transmission of light through the eye to the retina for visual activity. It is composed of 3 primary layers: the epithelium, stroma, and endothelium. The corneal epithelium is the lipophilic outer layer, consisting of squamous cells superficially, with a deep basal cell layer. The hydrophilic corneal stroma consists mainly of collagen fibers, making up approximately 90% of the overall thickness of the cornea. Descemet's membrane lies between the corneal stroma and innermost layer of the cornea, the endothelium. It is considered the basement membrane of the endothelium, and also consists of collagen fibers.[2,13] The lipophilic endothelium consists of a single layer of cells containing sodium/potassium ATPase pumps that maintain the dehydrated state of the cornea.[2,7]

The formation of a stromal abscess is first initiated after there is a break in the corneal epithelial barrier, such as a traumatic micro-puncture, laceration, or ulceration. This allows the introduction of a pathogen or foreign material into the deeper layers of the cornea. The body often tries to quickly heal this defect by allowing re-epithelialization over the trapped foreign material, inciting a severe inflammatory reaction within the cornea. Fungal organisms are most commonly identified as the cause of stromal abscesses, with Aspergillus, Fusarium, and Candida being the most commonly isolated organisms. Bacteria may also be present along with the fungi, or occasionally these abscesses may be sterile, although it is not as commonly found. Bacteria frequently cultured include pseudomonas, streptococcus, and staphylococcus. The severity of clinical signs, pathogens present, and treatment options may depend on the thickness and invasion of the abscess into deeper corneal tissue. A superficial stromal abscess may be contained within the anterior stroma, where a deep stromal abscess may penetrate through the entire stroma, down to Descemet's membrane. The infection within the stroma stimulates an

inflammatory response, attracting neutrophils and multinucleated giant cells. This inflammation within the cornea will also commonly cause inflammation in the anterior chamber, resulting in a secondary uveitis. A breakdown of the blood-aqueous barrier leads to formation of aqueous flare, hypopyon, and a miotic pupil.[7]

Diagnosis of a stromal abscess is usually based on clinical signs and presence of a focal, white to yellow region of cellular infiltrate within the cornea. Fluorescein stain is often negative due to an intact epithelial surface; however, mild uptake may occur if ulceration is present.[7]

Treatment and Management

Treatment of stromal abscesses may include either medical management or surgical intervention, however, the treatment chosen may depend on the depth and severity of the abscess. A superficial stromal abscess can be successfully treated with medical management and still result in good visual outcome. If the eye is showing no signs of improvement, or worsening uveitis, surgical intervention should be considered. Deep stromal abscesses are typically non-responsive to medical therapy and surgery should be pursued.[(7,9)]

Key components of medical management of a stromal abscess often consists of a topical antifungal, topical antibiotic, topical atropine, and a systemic non-steroidal anti-inflammatory. Polyenes and azoles are both classes of antifungals that may present as options for treatment of mycotic infections. Polyenes, such as natamycin and amphotericin B, are generally effective against a spectrum of fungi, however, they have poor penetration through an intact cornea, and are most effective when the permeability of the cornea is compromised. Azoles, such as miconazole, fluconazole, voriconazole, or itraconazole, have great corneal penetration, with some variability in fungal susceptibility. Voriconazole is often the first choice antimycotic

because of its coverage against the three most common fungi, Aspergillus, Fusarium, and Candida.[6] Although it is not always part of the initial therapy protocol, intrastromal antifungal injections are an additional treatment option that may be used in conjunction with the previously mentioned medical management protocol. An injection of a reconstituted voriconazole solution, typically performed under standing sedation, may be considered if there is little improvement with medical management, but not enough healing with topical medications alone. This injection can directly increase drug concentrations within the cornea, leading to a higher success rate of healing with medical management.[11] Topical antibiotics are used in the treatment and prevention of bacterial invasion in stromal ulceration and abscessation. First line therapy for simple ulceration may include Neomycin-Polymixin B-Bacitracin, tobramycin, or gentamicin. While these may work nicely for an uncomplicated ulcer, there is often resistant organisms to these medications, in which a broader spectrum antibiotic may be indicated.[13] Fluoroquinolones, such as ciprofloxacin, ofloxacin, or moxifloxacin, are generally reserved for deep, severe, or complicated infections.[12] These antibiotics are often a great choice for stromal abscessation because of their ability to easily penetrate the corneal epithelial surface.[3] Topical atropine is indicated in this condition for pupillary dilation for prevention of synechiae formation, as well as reducing ciliary muscle spasm to increase comfort of the horse. Horses on atropine, especially long term, should be monitored closely for ileus. Systemic anti-inflammatories, such as flunixin meglumine or phenylbutazone, should also be included in medical therapy for treatment of pain and inflammation. A prophylactic gastro-protectant is recommended in conjunction with the anti-inflammatory for prevention of gastrointestinal ulceration and irritation.[6]

A subpalpebral lavage system (SPL) is essential for ease of administration of topical medications in medical management of ocular conditions. The system involves a footplate under

the upper or lower eyelid, fastened to a long silicone tube that is draped down the neck of the patient. Medications through the SPL may be delivered without touching the face or eyes of the patient, making treatment simple and feasible for patients in hospital setting, as well as for caretakers at home. This improves efficacy of treatment, safety of personnel handling the patient, and increased compliance with administration of medications. Installation of the SPL begins with proper restraint of the horse in a clean, quiet area, under adequate sedation. The periorbital region should be prepped with povidone iodine/saline solution, and a supraorbital and auriculopalpebral block should be performed for local anesthesia. A trochar is used to carefully puncture the target site in the conjunctiva, adjacent to the orbital rim, and is pushed through the eyelid skin. The trochar and tubing are pulled through the eyelid until a small disc-shaped footplate is properly positioned snug against the conjunctiva. The tubing exiting the eyelid along the face should be sutured in place, and the tubing traversing down the neck may be intertwined with the braided mane for extra security. A catheter is then threaded into the lumen of the tubing, the stylet is removed, and an injection port is secured to the catheter. In neonates and young foals, a section of stockinette over the head and neck may provide more security and protect the tubing from damage. Medication can then be administered through the injection port along the neck, followed by 1.0 to 2.0 mLs of air pushed slowly through the tube. When the medication reaches the eye, horses will often react with a blink or a slight head shake. With multi-drug treatment plans, each medication should be given approximately 5 minutes apart to ensure enough time for absorption and effect without interference from the next drug. The injection port should be wiped with alcohol prior to administration of each drug, as well as use of a new needle each time. A well taken care of SPL may remain intact for days to weeks if necessary. When the SPL is ready to be removed, the tubing is cut just a few centimeters away from the exit site along

the eyelid. A gloved finger may be used to retrieve the footplate carefully from the conjunctiva and pull the short length of tubing through the eyelid.[5]

There are several surgical techniques for treatment of a stromal abscess, with each technique chosen and performed under certain circumstances regarding location and depth of the abscess. A Penetrating Keratoplasty (PK) is a corneal transplantation procedure involving the epithelium, stroma, and Descemet's membrane/endothelium. This full thickness keratoplasty can be used for extensive melting ulcers, deep stromal abscesses, or descemetoceles.[7,9] Because this procedures involves removing a larger portion of the cornea, it is often associated with longer surgery and treatment time, averaging approximately 40-50 days for complete healing.[4] A Posterior Lamellar Keratoplasty (PLK) focuses on only removing and replacing diseased cornea while preserving the healthy corneal tissue. This technique is best utilized for centrally located stromal abscesses that are approximately 12 mm or less. Similar to the PLK, a Deep Lamellar Endothelial Keratoplasty is best utilized on abscesses in the peripheral cornea and is performed through an incision in the limbus.[7,9] The PLK and DLEK are often associated with shorter surgery and recovery times, averaging 30 days and 35 days respectively.[4]

Prognosis for vision in cases of stromal abscesses is usually guarded due to a variety of complications that may arise following both medical management and surgical intervention. The development of glaucoma or secondary cataract formation are common sequelae of any inflammatory disease of the eye, resulting in loss of vision.[4] Corneal scarring is often a sequela to surgery, but is typically small enough to maintain an appropriate field of vision.[8] Other post-surgical complications may include dehiscence, leakage from the incision site, ulceration near or around the incision, graft movement or slippage, or graft failure or rejection. A positive visual

outcome is often achieved following stromal abscessation if treatment occurs without complication.[4]

Case Outcome

Upon initial presentation on May 21st, a subpalpebral lavage system (SPL) was placed over Angel's left eye to begin medical management for her stromal abscess. Angel was started on Voriconazole (0.1 mLs q2h), Ofloxacin (0.1 mLs q2h), atropine (0.1 mL q12h), intravenous flunixin meglumine (1.1 mg/kg q12h), and Gastrogard orally (1 mg/kg q24h). Angel was maintained on this regimen for the next 3 days, and on day 4, her Ofloxacin dosing interval was decreased to every 4 hours, with the remainder of her medications staying the same. On May 26th, Angel's 6th day of medical management, Angel was sedated for another thorough ophthalmology exam. The abscess appeared to be improving, and it was elected to refrain from giving an intraocular voriconazole injection and continue with the same medication regimen. On day 8 of medical management, Angel's voriconazole dosing interval was decreased to every 4 hours, continuing with the other previously prescribed medications. The dosages of all medications were now at appropriate intervals for Angel's owner to continue with medical management at home, and Angel was planning to discharge from MSU CVM the next day, Friday May 29th. Due to travel limitations, Angel's owner was not able to pick her up until the following week, so Angel remained in hospital throughout the weekend.

As Angel was transitioned to oral flunixin meglumine over the weekend, she appeared more painful in her left eye. The abscess itself appeared the same, with no signs of worsening, yet no signs of large improvement. On Monday morning, June 1st, Angel was sedated again for an ophthalmic exam. The abscess appeared slightly larger in size, with worsening corneal edema, and hypopyon now present in the anterior chamber. After the exam, Angel received an extra dose

of atropine to keep the pupil dilated for prevention of synechiae, and the dosing interval of her atropine was increased to every 8 hours. Her voriconazole dosing interval was also increased again back to every 2 hours, and Angel was started back on intravenous flunixin meglumine for adequate pain control. She remained on Ofloxacin and Gastrogard as previously prescribed. Because Angel's eye had become worse again, she remained in hospital for further monitoring and continuation of her medical management. At this time, surgical intervention was discussed with the owner if Angel did not show further improvement in the next few days.

After 15 days of being in hospital, moderate blepharospasm, epiphora, and corneal edema were still present from Angel's left eye. At this time, the owner elected to pursue surgical intervention, so routine bloodwork was performed prior to surgery. A complete blood count showed a mildly elevated segmented neutrophil count and a large animal chemistry profile showed no significant abnormalities. On Thursday June 4th, Angel underwent a posterior lamellar keratoplasty (PLK) using synthetic Swine Intestinal Submucosa (SIS). Pre-operatively, a catheter was placed in Angel's left jugular vein, and she received procaine penicillin G (22,000 IU/kg IV) and gentamicin (6.6 mg/kg IV).

Angel was placed under general anesthesia and positioned in right lateral recumbency. Her left eye and eyelids were clipped and prepped with a betadine solution. The stromal abscess was measured with Jameson calipers to be 8mm in diameter. Using a 64 beaver blade, a three sided rectangular incision, approximately 1/3-2/3 stromal thickness, was made into the cornea over the stromal abscess. The fourth side of the rectangle was left uncut as a hinge, and the flap was undermined with the 64 beaver blade and Martinez corneal dissectors to make a superficial flap overlying the abscess. An 8mm biopsy punch was used to outline the abscess to the depth of Descemet's membrane around the abscess. A keratome was used to make a stab incision into the

anterior chamber, and viscoelastic was used to maintain the anterior chamber throughout the procedure. Corneal section scissors were used to remove the affected corneal tissue. The tissue was submitted for culture and sensitivity, as well as histopathology. An 8mm disc of swine intestinal submucosa was placed and sutured into the defect. The corneal flap was laid over the defect and sutured in a simple interrupted pattern. Angel had also managed to pull out her subpalpebral lavage system the night before surgery on June 3rd, so her SPL was replaced while she was under anesthesia. Surgery was without complication and Angel recovered from anesthesia uneventfully.

Samples taken during surgery for culture and histopathology were returned with results in the following few days. Aerobic culture and sensitivity revealed growth of staphylococcus haemolyticus from enrichment broth only, which was sensitive to all medications tested. Fungal culture resulted in growth of Cladosporium. On histopathology, the corneal stroma was markedly expanded by edema, fibrovascular proliferation, degenerate neutrophils, necrosis, and fibrin. The center of the sample did contain fungal hyphae, and overall, the sample was consistent with a deep corneal stromal abscess.

Angel's left eye began healing well just after surgery. She remained on voriconazole (0.1 mLs through SPL q4h), Ofloxacin (0.1 mLs through SPL q4h), atropine (0.1 mLs through SPL q12h), flunixin meglumine (1.1 mg/kg IV q12h), and Gastrogard (1/4 tube PO q24h). On June 9th, just 5 days after surgery, Angel was transitioned to oral flunixin meglumine (1000 lbs dose PO q12h) to assess her comfort level before being approved for discharge. On June 12th, 2020, Angel was discharged from MSU CVM. At the time of discharge, her graft appeared to be healing nicely with minimal corneal edema. Angel was also showing signs of regaining vision

and she was sent home on all previously described medications, as well as an equivizor to protect her eye and lavage system.

Angel returned on June 25th for her a recheck examination after she had been recovering at home for 2 weeks. Her left cornea appeared clear, with neovascularization still present over the area of the previous stromal abscess. Several sutures were still present, however overall, the cornea appeared to be healing well since the graft was placed. The left pupil was still slightly miotic, with a fibrin strand present along the endothelium. The anterior chamber contained trace amount of aqueous flare, with no hypopyon seen. Angel appeared to have good vision at this time, with a present dazzle reflex and menace. With very minimal inflammation and no signs of infection, the atropine, voriconazole, and ofloxacin were discontinued at this time, and Angel's subpalpebral lavage system was removed. Angel was also switched to Firocoxib (57 mg, 1 tab PO q24h) at this visit to continue keeping her comfortable while she recovers.

At Angel's final recheck examination on August 4th, 2020, her cornea had completely healed and a corneal scar had formed. At this point, Angel had good vision in that eye and no longer needed any further medical examination regarding her left eye.

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