Deep, Progressing Corneal Ulcer with Secondary Anterior Uveitis

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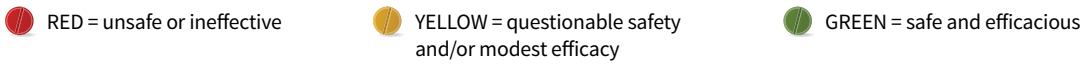
Prince, a 6-year-old neutered male shih tzu, was presented with a 3-week history of blepharospasm of the right eye. Abnormal ocular examination findings were limited to the right eye and included mild blepharospasm, moderate epiphora and mucopurulent discharge, conjunctival injection, diffuse corneal edema, fluorescein-stain–positive paracentral corneal ulceration (6 × 4 mm; estimated depth, 40%), corneal neovascularization, yellow-green corneal infiltrate in the ulcer bed, miotic pupil, intraocular pressure of 5 mm Hg (left eye, 15 mm Hg), and mild aqueous flare. Corneal cytology revealed neutrophils and rod-shaped bacteria. Results of corneal culture and susceptibility testing are pending. Physical examination, including of the left eye, was otherwise unremarkable.

Which of the following drugs would be appropriate in the management of this patient?

Based on the information provided, how would you grade the following drugs and why?



Diclofenac (topical)	RED	YELLOW	GREEN
Atropine (topical)	RED	YELLOW	GREEN
Triple antibiotic ointment (topical)	RED	YELLOW	GREEN
Ofloxacin (topical)	RED	YELLOW	GREEN
Prednisolone (oral)	RED	YELLOW	GREEN
Gentamicin or tobramycin (topical)	RED	YELLOW	GREEN
Autologous serum (topical)	RED	YELLOW	GREEN
Prednisolone Acetate (topical)	RED	YELLOW	GREEN
Doxycycline (oral)	RED	YELLOW	GREEN
Moxifloxacin (topical)	RED	YELLOW	GREEN

TURN THE PAGE AND COMPARE YOUR RESULTS

Did you answer?

The following represents the best responses based on drug metabolism, pharmacokinetics, species, diagnostic differentials, clinical and laboratory data, and other pertinent findings.

Diclofenac (topical)

CORRECT RESPONSE 

Topical NSAIDs are rarely indicated in the treatment of infected corneal ulcers, as they may slow corneal vascularization and epithelialization. In addition, use of some topical NSAIDs has been loosely associated with stromal lysis and corneal perforation in humans, but this has not been reported in dogs.[1]

Atropine (topical)

CORRECT RESPONSE 

A topical cycloplegic such as 1% atropine sulfate is needed to treat pain caused by ciliary muscle spasm (secondary to associated anterior uveitis) and to prevent formation of posterior synechia by dilating the pupil. Because it may cause a mild decrease in tear production, atropine should be administered to effect, then given less frequently as needed.[2]

Triple antibiotic ointment (topical)

CORRECT RESPONSE 

Bacterial infections of the cornea should be empirically treated topically with a broad-spectrum (including against gram-negative rods and gram-positive cocci) bactericidal antibiotic. This patient's corneal ulcer is progressing and has the potential for corneal rupture. Although this medication has relatively good coverage for bacterial keratitis, in general ointments are contraindicated because of their potential for intraocular toxicity if the globe perforates.[3]

Ofloxacin (topical)

CORRECT RESPONSE 

As previously indicated, corneal bacterial infections should be treated empirically with a broad-spectrum topical antibiotic that is specifically effective against gram-negative rods and gram-positive cocci. Although ofloxacin has good coverage for gram-negative organisms, its coverage for gram-positive organisms is not as extensive, and resistance is becoming more common.[4-6] However, studies have shown that fluoroquinolones, including ofloxacin, are a good empirical first-line choice for treating bacterial keratitis.[7] If a potentially resistant organism is suspected or if the infection is severe, use of a fourth-generation fluoroquinolone (eg, moxifloxacin, gatifloxacin) may provide a broader spectrum of activity.[8] Regardless of antibiotic treatment, the ulcer should be rechecked for evidence of progression in 24 to 48 hours, depending on severity.

Prednisolone (oral)

CORRECT RESPONSE 

Control of this patient's anterior uveitis secondary to corneal ulceration and infection would preferably involve a systemic NSAID. However, an anti-inflammatory dose of oral corticosteroid such as prednisolone could also be used. Treatment with oral prednisolone at this dose should have little effect on corneal healing [9,10]; however, the ulcer should be carefully monitored for progression. Anterior uveitis should improve as the ulcer heals. Topical corticosteroids are contraindicated, as they can lead to increased collagenase activity.

Gentamicin or tobramycin (topical)

CORRECT RESPONSE 

Gentamicin and tobramycin are effective against many gram-negative bacteria and some *Staphylococcus* spp; however, a broader spectrum of coverage is desired for empirical treatment of active corneal infections. Combining gentamicin or tobramycin with a first-generation cephalosporin (eg, cefazolin, 50 mg/mL [2 separate drops at each administration]) can provide a broader spectrum of activity and is an excellent choice for treating an infected ulcer.[4]

Autologous serum (topical)

CORRECT RESPONSE 

The depth of this patient's corneal ulcer indicates corneal stromal loss by matrix metalloproteinases (MMPs; ie, collagenases). Degradation of the corneal stroma occurs when the level of MMPs increases beyond the control of naturally occurring proteinase inhibitors. Endogenous proteinases are produced by corneal and inflammatory cells, while exogenous proteinases are produced by infectious organisms. Serum contains inhibitors of MMPs and serine protease and serves as an effective anticollagenase treatment. Protease inhibitors are generally applied topically every 1 to 2 hours for the first several days until the ulcer appears to stabilize and show evidence of healing (eg, decreased pain, epithelialization), when application can be decreased to 3 to 4 times a day.

Prednisolone acetate (topical)

CORRECT RESPONSE 

Topical glucocorticoids are contraindicated in the treatment of infected and noninfected corneal ulcers, as they may activate or exacerbate bacterial infections and increase MMP activity in the cornea, which can lead to rapid corneal stromal lysis (ie, melting).[10]

Doxycycline (oral)

CORRECT RESPONSE 

Oral tetracyclines, including doxycycline, have been shown to decrease collagenase activity in several species, likely by chelation of Zn^{2+}, a cation necessary for enzyme structure and function.[11,12] Because the inhibitory mechanism of doxycycline varies from that of serum, using a combination of serum and doxycycline is likely more effective than using serum alone.

Moxifloxacin (topical)

CORRECT RESPONSE 

As a fourth-generation fluoroquinolone, the gram-positive spectrum of moxifloxacin is significantly increased over earlier fluoroquinolones. Moxifloxacin can be used as monotherapy for empirical treatment of bacterial keratitis. Development of resistance to fourth-generation fluoroquinolones is much less common than with earlier generations but can occur.[8] Use of this class of drug should be reserved for treatment of severe bacterial corneal infections.

MMP = matrix metalloproteinase

NSAID = nonsteroidal anti-inflammatory drug

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