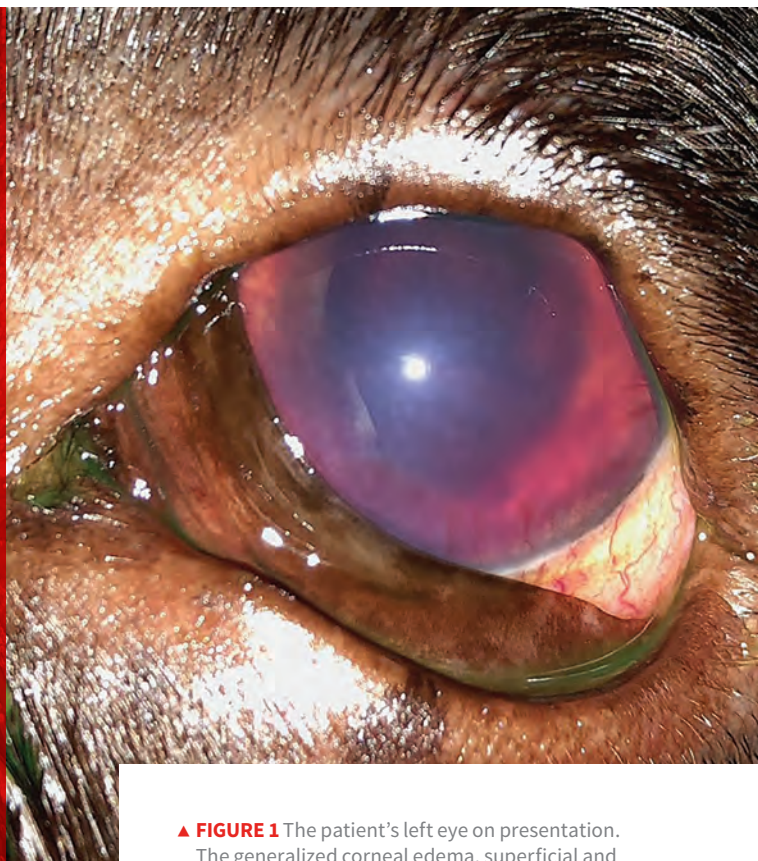


Hemorrhagic Anterior Uveitis in a Labrador Retriever

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▲ **FIGURE 1** The patient's left eye on presentation. The generalized corneal edema, superficial and deep peripheral corneal vascularization, and intraocular hemorrhage, with a visible but difficult to visualize pupil, are evident.

THE CASE

Sammy, a 9-year-old neutered male Labrador retriever, is presented for evaluation of a red, cloudy, painful left eye. The abnormal appearance to the eye was noted by the owners after Sammy had been left to play untended with the other dog in the household for approximately 2 hours. No treatment was administered by the owners, and Sammy was presented 45 minutes after the owners first noted the abnormality.

On examination, Sammy is bright, alert, and responsive. The left eye is blepharospastic, with mild swelling of the eyelids, conjunctival hyperemia, corneal edema, hyphema, and superficial and deep peripheral corneal vascularization (**Figure 1**). The pupil is difficult to visualize but appears miotic as compared with the right eye. Direct pupillary light reflex (PLR) is absent, and consensual PLR in the right eye is present but subjectively decreased. Dazzle reflex (ie, reflex reaction to stimulation of the eye by a bright light) is positive, but menace response is negative in the left eye. Menace response, direct PLR, and dazzle reflex are positive in the right eye, but consensual PLR in the left eye is difficult to visualize

due to hyphema in the left eye. Schirmer tear test shows >15 mm wetting/min in both eyes, fluorescein stain is negative in both eyes, and intraocular pressure (IOP), estimated by applanation tonometry, is 14 mm Hg in the right eye and 6 mm Hg in the left. The remainder of the ocular examination in the right eye, including fundic examination, is normal.

What are the next steps?

THE CHOICE IS YOURS ...

CASE ROUTE 1

To diagnose the patient with presumptive hemorrhagic anterior uveitis secondary to trauma in the left eye and treat for anterior uveitis, go to page 18.

CASE ROUTE 2

To diagnose the patient with hemorrhagic anterior uveitis of unknown etiology in the left eye and perform additional diagnostics, go to page 20.

IOP = intraocular pressure
 PLR = pupillary light reflex

CASE ROUTE 1

You elect to diagnose the patient with presumptive hemorrhagic anterior uveitis secondary to trauma in the left eye and treat for anterior uveitis.

Case Progression

Because of Sammy's acute onset of ocular changes, trauma is suspected as the cause of intraocular bleeding. Because trauma is a one-time occurrence, treatment is targeted toward controlling intraocular inflammation associated with bleeding and managing discomfort. Administration of a topical ophthalmic antibiotic–corticosteroid combination (eg, neomycin–polymyxin B–dexamethasone ophthalmic solution [1 drop in the

left eye q12h]) is initiated to control intraocular inflammation, and analgesia is provided through oral NSAIDs. Recheck examination is scheduled for 3 to 5 days later.

On recheck examination performed 5 days following initial presentation, the owners report that Sammy became significantly more comfortable in the first 1 to 2 days following initial presentation but began squinting and rubbing the left eye a day before the recheck examination. Blepharospasm is present in the eye. The corneal edema has improved, with less free-floating blood and more discrete clotting around the dyscoric pupil (**Figure 2**). The pupil is miotic and irregularly shaped (ie, dyscoric), with irregular bulging and thickening of the surrounding iris. IOP is 43 mm Hg, and menace response, direct PLR, dazzle reflex, and consensual PLR in the right eye (resulting from shining light in the left eye) are absent. The ocular examination remains normal in the right eye.

Clinical diagnoses include hyphema with an intraocular blood clot, secondary glaucoma, and blindness in the left eye. Determining the prognosis for regaining vision is difficult; however, the owners' report of Sammy's squinting and rubbing the eye for at least a day (potentially indicating glaucoma of a day's duration), lack of a consensual PLR in the right eye in response to shining light in the left eye, and lack of dazzle reflex in the left eye are suggestive of a poor prognosis for regaining vision.¹ More aggressive intervention is advised to improve comfort while minimizing the intensiveness of medical therapy.

Clinical Considerations

Options for intervention include evisceration (ie, replacement of the intraocular contents with an implant while preserving the cornea, sclera, extraocular muscles, and adnexa), enucleation (ie, surgical removal of the entire globe), or gentamicin (25–50 mg injected into the vitreous) to destroy



▲ **FIGURE 2** The patient's left eye on recheck examination 5 days after initial presentation. The corneal edema has improved, with less free-floating blood and more discrete clotting around the dyscoric pupil.

the ciliary body, thus decreasing production of aqueous humor and lessening dependence on medications to control secondary glaucoma.

Outcome

Intraocular injections may be contraindicated in eyes with pre-existing ocular hemorrhage due to the potential increase in hemorrhage, and evisceration is primarily performed for cosmetic reasons. Thus, enucleation is elected in this patient and performed under general anesthesia. The globe is submitted for histopathology, and the findings are consistent with intraocular hemorrhage and glaucoma and are identified as secondary to an infiltrative, neoplastic iridal lesion.

Your Choice's Implications

Although treatment with a topical corticosteroid and an oral NSAID is appropriate to control inflammation and pain in cases of presumed traumatic anterior uveitis, additional diagnostic procedures (see **Case Route 2**, next page) should be appropriately performed on any eye with hyphema to rule out other possible causes of bleeding. If performing additional diagnostic procedures is not possible, more aggressive treatment, such as a topical corticosteroid with greater intraocular penetration (eg, prednisolone acetate 1%),² may be more effective in producing a favorable outcome if trauma—or another one-time, controllable condition—is the cause. In addition, because the need for antibiotics is low in patients with intraocular hemorrhage (as represented in the neomycin–polymyxin B–dexamethasone combination), avoiding unnecessary antimicrobial use is recommended. If neomycin–polymyxin B–dexamethasone is the only medication readily available, increasing the frequency of administration (ie, to q6-8h) may be helpful as more aggressive initial treatment. Owner education is also a critical component of the treatment plan, as owners should be aware of the signs (eg, squinting, rubbing, increased cloudiness, increased redness) that would indicate that earlier re-evaluation is necessary.

Treatment with a mydriatic cycloplegic (eg, atropine ophthalmic solution 1%) is indicated in patients with anterior uveitis and low IOP, even if the pupil cannot be visualized due to signs caused by the disease process. Because anterior uveitis produces a miotic, “sticky” pupil, the risk for complete posterior synechiae—and thus secondary glaucoma—is decreased by the use of atropine, which produces pupillary dilation, decreases exudation from the iris, and provides analgesia via cycloplegia. When surgical removal of a globe is advised to treat a painful ocular disease (eg, glaucoma) and the underlying cause of the disease (eg, intraocular tumor) has not been identified, histopathology is appropriate, as the patient’s well-being may be positively impacted if a previously occult disease process is identified.

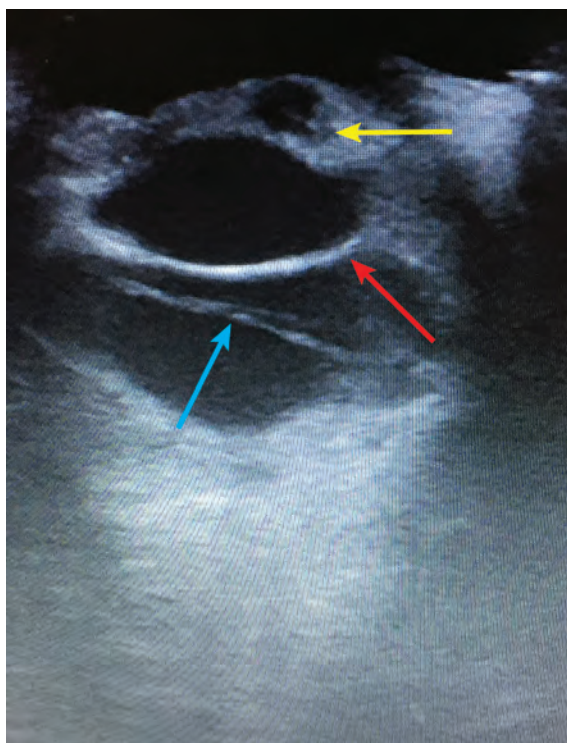
In this case progression, if additional diagnostics—particularly ocular ultrasonography—had been performed at initial presentation, medical management for the intraocular hemorrhage would have been recognized as ineffective treatment for the underlying cause ultimately identified (ie, intraocular tumor). Because ocular ultrasonography may not be performed on all patients with hyphema for various reasons, it is important to consider that more aggressive medical management is appropriate, in the event that anterior uveitis is medically responsive.

Intraocular injections may be contraindicated in eyes with pre-existing ocular hemorrhage due to the potential increase in hemorrhage.

IOP = intraocular pressure
PLR = pupillary light reflex

CASE ROUTE 2

Based in part on the presence of deep peripheral corneal vascularization, you are suspicious of a more chronic intraocular disease process. You elect to diagnose the patient with hemorrhagic anterior uveitis of unknown etiology in the left eye and perform additional diagnostics.



▲ **FIGURE 3** Ultrasonographic image of the patient's left eye obtained on initial presentation. The cornea is near the top of the image, and the sclera is toward the bottom of the image, with the posterior lens capsule (**red arrow**) visible. Retinal detachment (**blue arrow**) is visible as a hyperechoic line in the vitreal space, and the cavitory lesions of the iris (**yellow arrow**) are present anterior to the posterior lens capsule.

Case Progression

Other conditions that may lead to intraocular hemorrhage, such as those localized to the eye (eg, trauma, retinal detachment, intraocular tumor), as well as those with systemic involvement (eg, systemic hypertension, coagulopathy, vasculitis, systemic infections, systemic neoplasia), are considered.³ Thus, based on the diagnosis of hemorrhagic anterior uveitis and the inability to visualize intraocular structures, additional diagnostics are performed to confirm the underlying cause of the bleeding. These diagnostic tests are ordered to noninvasively and cost-effectively provide the most high-yield information based on signalment and clinical signs.

General physical examination parameters are within normal limits. Systemic blood pressure obtained via Doppler averages 110 mm Hg (systolic). CBC, serum chemistry profile, coagulation testing, and urinalysis results are normal. Further tests to evaluate for systemic inflammatory and neoplastic conditions (eg, infectious disease titers, chest and abdominal imaging) are not performed, and further ocular evaluation is pursued.

Following administration of a topical local anesthetic (ie, proparacaine ophthalmic solution [2 drops administered 3-5 minutes apart]), ocular ultrasonography is performed with a 12-MHz transducer placed transcorneally in transverse and sagittal orientations using sterile lubricating jelly.⁴ Although visualization of the anterior segment is less clear with this probe than would be achieved with a higher-frequency probe, multifocal cavitations within the iris architecture, as well as complete retinal detachment (**Figure 3**), are identified.

Based on the signalment, general physical examination findings, and additional diagnostic tests and procedures, diagnoses of hemorrhagic anterior uveitis and retinal detachment secondary to a suspected iridal tumor are made.

Clinical Considerations

Because the likelihood of controlling intraocular hemorrhage and regaining vision are poor based on the underlying disease process, surgical removal of the eye and submission for histopathologic evaluation are recommended.

Outcome

Enucleation of the left eye is performed, and the globe is submitted for histopathologic evaluation. A diagnosis of iridal hemangiosarcoma, with retinal detachment and intraocular hemorrhage, is made. Radiography of the chest and abdominal ultrasonography are performed to determine if metastatic disease is present, and the findings are normal.

Your Choice's Implications

Evaluating the patient for disease processes potentially associated with intraocular hemorrhage was appropriate to determine the prognosis and effective therapies. Ocular ultrasonography was the most informative diagnostic procedure performed and allowed for appropriate intervention to be performed at an early stage in the ocular disease process. Radiographic imaging (eg, chest radiography, abdominal ultrasonography or radiography) may also be considered preoperatively to determine the overall systemic condition prior to surgical intervention. If not performed preoperatively, as in this case, radiographic imaging can be performed postoperatively if histopathology results indicate. ■■■

References

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Mirataz™ (mirtazapine transdermal ointment)

For topical application in cats only. Not for oral or ophthalmic use.

CAUTION: Federal law (USA) restricts this drug to use by or on the order of a licensed veterinarian.

Before using this product, please consult the product insert, a summary of which follows:

INDICATION: Mirataz™ is indicated for the management of weight loss in cats.

DOSAGE AND ADMINISTRATION: Administer topically by applying a 1.5-inch ribbon of ointment (approximately 2 mg/cat) on the inner pinna of the cat's ear once daily for 14 days. Wear disposable gloves when applying Mirataz™. Alternate the daily application of Mirataz™ between the left and right inner pinna of the ears. **See Product Insert for complete dosing and administration information.**

CONTRAINDICATIONS: Mirataz™ is contraindicated in cats with a known hypersensitivity to mirtazapine or to any of the excipients. Mirataz™ should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz], as there may be an increased risk of serotonin syndrome.

HUMAN WARNINGS: Not for human use. Keep out of reach of children. **Wear disposable gloves when handling or applying Mirataz™ to prevent accidental topical exposure.** After application, dispose of used gloves and wash hands with soap and water. After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally. However, negligible residues are present at the application site and the body of the cat at 2 hours after dosing. In case of accidental skin exposure, wash thoroughly with soap and warm water. In case of accidental eye exposure, flush eyes with water. If skin or eye irritation occurs seek medical attention. In case of accidental ingestion, or if skin or eye irritation occurs, seek medical attention.

PRECAUTIONS: Do not administer orally or to the eye. Use with caution in cats with hepatic disease. Mirtazapine may cause elevated serum liver enzymes (See **Animal Safety** in the product insert). Use with caution in cats with kidney disease. Kidney disease may cause reduced clearance of mirtazapine which may result in higher drug exposure. Upon discontinuation of Mirataz™, it is important to monitor the cat's food intake. Food intake may lessen after discontinuation of mirtazapine transdermal ointment. If food intake diminishes dramatically (>75%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz™ has not been evaluated in cats < 2 kg or less than 6 months of age. The safe use of Mirataz™ has not been evaluated in cats that are intended for breeding, pregnant or lactating cats.

ADVERSE REACTIONS: In a randomized, double-masked, vehicle-controlled field study to assess the effectiveness and safety of mirtazapine for the management of weight loss in cats, 115 cats treated with Mirataz™ and 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an ointment containing the same inert ingredients as Mirataz™ without mirtazapine. The most common adverse reactions included application site reactions, behavioral abnormalities (vocalization and hyperactivity), and vomiting. **See Product Insert for complete Adverse Reaction information.** To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Kindred Biosciences, Inc. at 888-608-2542. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

EFFECTIVENESS: The effectiveness of Mirataz™ (mirtazapine transdermal ointment) was demonstrated in a randomized, double-masked, vehicle-controlled, multi-site field study involving client-owned cats of various breeds. Enrolled cats were ≥ 1 year of age and had existing documented medical history of ≥ 5% weight loss deemed clinically significant. The most common pre-existing conditions included renal insufficiency, vomiting, and hyperthyroidism. Some cats had more than one pre-existing condition. Cats were randomized to treatment groups in a 1:1 ratio of Mirataz™ to vehicle control. A total of 230 cats were enrolled and received either Mirataz™ (115 cats) or a vehicle control (115 cats) containing the same inert ingredients without mirtazapine. The cats were 2.8-24.6 years of age and weighed 2.1-9.2 kg. The dosage was a 1.5-inch ribbon (approximately 2 mg/cat) mirtazapine or vehicle ointment administered topically to the inner pinna of the cat's ear. A total of 177 cats were determined to be eligible for the effectiveness analysis; 83 cats were in the Mirataz™ group and 94 cats were in the vehicle control group. The primary effectiveness endpoint was the mean percent change in body weight from Day 1 to the Week 2 Visit. At Week 2, the mean percent increase in body weight from Day 1 was 3.94% in the mirtazapine group and 0.41% in the vehicle control group. The difference between the two groups was significant (p<0.0001) based on a two-sample t-test assuming equal variances. A 95% confidence interval on the mean percent change in body weight for the Mirataz™ group is (2.77, 5.11), demonstrating that the mean percent change is statistically different from and greater than 0.

STORAGE: Store below 25°C (77°F). Multi-use tube. Discard within 30 days of first use.

HOW SUPPLIED: Mirataz™ is supplied in a 5 gram aluminum tube.

MANUFACTURED FOR:
Kindred Biosciences, Inc.
1555 Bayshore Highway, suite 200
Burlingame, CA 94010

NADA 141-481, Approved by FDA

Made in USA.

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