Cloudy Eye in a Labrador Retriever

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THE CASE

A 7-year-old spayed Labrador retriever crossbreed is presented for a 5-day history of an intermittently red, cloudy left eye. The owner states that the patient had previously been diagnosed with allergic conjunctivitis and has had intermittent flare-ups. The patient has reportedly been coughing for 3 days and, although still eating and drinking, her appetite is decreased. Her BCS is 7/9, which is consistent with previous visits.

On general physical examination, mild mandibular lymphadenopathy, moderate dental tartar, rectal temperature of 103.8ºF (39.9ºC), and a tense abdomen on palpation were noted. An initial ophthalmologic examination of the left eye reveals blepharospasm; absent menace response; questionable dazzle reflex; a fixed, mid-range pupil with subtle dyscoria and no apparent direct pupillary light reflex or consensual pupillary light reflex from the left to the right eye; pronounced episcleral injection and conjunctival hyperemia; mild edema, and suspected moderate aqueous flare (***Figure 1***, next page). Although a tapetal reflex is visible, the fundus in the left eye cannot be visualized by indirect or direct ophthalmoscopy. The right eye appears normal.

What are your next steps?

*Byline reflects affiliation on original publication. On publication in January 2020, the author's current affiliation is Mississippi State University.

IOP = intraocular pressure
STT = Schirmer tear test

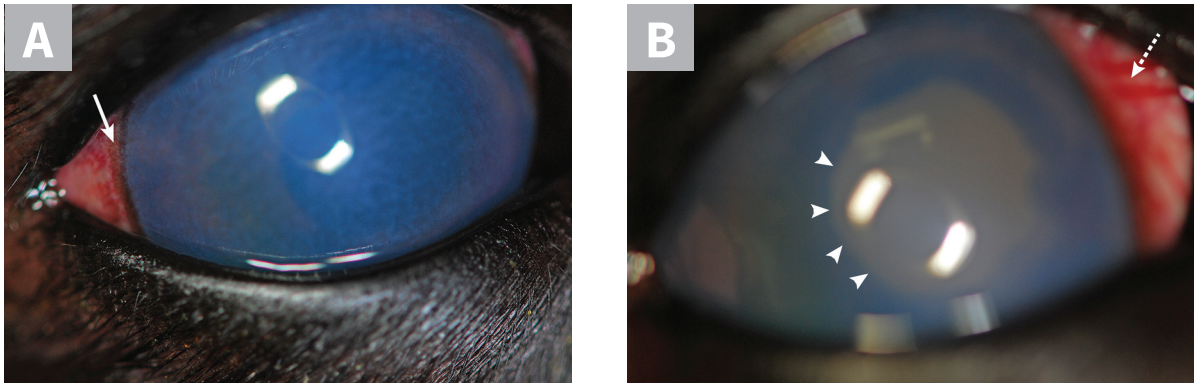
THE CHOICE IS YOURS ...

CASE ROUTE 1

To recommend a more in-depth ophthalmologic examination, including detailed examination of both eyes, Schirmer tear test (STT), fluorescein staining, tonometry, and gonioscopy, based on suspicion of primary glaucoma, and refer the case to an ophthalmologist, go to page 18.

CASE ROUTE 2

To recommend measuring intraocular pressure (IOP) and a systemic diagnostic investigation, including CBC, serum chemistry profile, and chest radiography, based on suspicion of uveitis and secondary glaucoma, go to page 21.



▲ **FIGURE 1** The affected eye showing (***A***) pronounced conjunctival hyperemia (***arrow***) and moderate-to-severe corneal edema, as well as (***B***) episcleral injection (***dashed arrow***) and a mid-sized pupil with slight dyscoria (***arrowheads***)

CASE ROUTE 1

You recommend a more in-depth ophthalmologic examination, including detailed examination of both eyes, STT, fluorescein staining, tonometry, and gonioscopy, based on suspicion of primary glaucoma, and refer the case to an ophthalmologist.

Case Progression

The case was referred to a board-certified ophthalmologist. On further ophthalmologic examination, the right eye appears normal with an intact menace response, dazzle reflex, and a normal-sized pupil with positive direct pupillary light reflex but absent consensual pupillary light reflex from right to left. Indirect ophthalmoscopy of the right eye reveals a small, well-demarcated, circular, hyper-reflective lesion in the peripheral tapetum, most consistent with an inactive chorioretinal scar.

STT readings are >15 mm/min and fluorescein staining is negative in both eyes. Tonometry reveals an IOP of 18 mm Hg in the right eye and 57 mm Hg in the left eye (normal, 10-25 mm Hg with <20% difference in IOP between eyes). Evaluation of the iridocorneal angle (via gonioscopy) of the unaffected eye is performed by gently touching an indirect ophthalmoscopic lens on the axial cornea after applying a topical anesthetic and looking through the lens at the point of contact. Evaluation reveals a narrow iridocorneal angle, which indicates pectinate ligament dysplasia. Based on these findings, one drop of a topical prostaglandin analog (latanoprost 0.005% ophthalmic solution) is administered in the left eye, and the patient is admitted to the clinic for a few hours to monitor for a drop in IOP.

Clinical Considerations

Based on signalment and clinical findings, including evidence of pectinate ligament dysplasia in the unaffected eye, primary angle closure glaucoma is an important differential diagnosis in this case. Other important differentials to consider for a red, cloudy, painful eye include keratoconjunctivitis sicca, corneal ulceration, and uveitis, the latter potentially with secondary glaucoma. Keratoconjunctivitis sicca and corneal ulceration as underlying causes were ruled out, and because the aqueous flare is mild, the uveitis and IOP are likely attributable to primary glaucoma rather than a systemic cause.

Glaucoma is a leading cause of blindness in dogs, with goniodysgenesis-related primary angle closure glaucoma (PACG) being the most common of the primary glaucomas.[1-4] Goniodysgenesis refers to abnormal architecture of the iridocorneal angle that contributes to obstruction of outflow of aqueous humor. This abnormality is believed to have an underlying genetic component[1-3] and is seen with relatively high prevalence in purebred dogs, including American Cocker spaniels, basset hounds, Siberian huskies, chow chows, and Boston terriers, among others.[1]

PACG typically manifests as an acutely painful eye with increased IOP and blindness. Some breeds (eg, basset hounds) also have significant anterior uveitis and corneal edema associated with an acute attack, which can be clinically confusing and may complicate treatment.[5] Although canine glaucoma is generally associated with elevated IOP (≥50 mm Hg), IOP may fluctuate widely in glaucoma and may in fact be within or lower than the normal range at the time of presentation. This may especially be true of chronic disease involving pressure damage to the ciliary body's production of aqueous humor or in patients with significant intraocular inflammation, which also can have a negative impact on aqueous humor production.

Prognosis for vision and globe retention is dependent on quick recognition of clinical signs and prompt treatment to decrease IOP, as just a few hours of pronounced IOP elevation can result in blindness. In general practice settings, medical management is the safest and most accessible way to decrease IOP. Prostaglandin analog (eg, latanoprost) therapy, typically coadministered with topical carbonic anhydrase inhibitors (eg, dorzolamide), is the most effective medical therapy for PACG in dogs.[6] β-blockers (eg, timolol) also reduce IOP but, when administered alone, their IOP-lowering effect is insufficient[7]; thus, they should be reserved for prophylactic or adjunctive therapies. Systemic hyperosmotics (eg, intravenous mannitol, oral glycerol) may also be used for marked IOP reduction[6,8] but should be used with caution and only after routine blood work (eg, renal values, electrolytes), especially in older or debilitated animals or animals with cardiovascular disease (see ***Table***). Surgical interventions in acute cases are typically reserved for patients with a fair-to-good prognosis for vision. These procedures should be performed by a board-certified veterinary ophthalmologist and may include gonioimplants, cyclophotocoagulation (transcleral laser or endolaser), and/or aqueocentesis.

Outcome

Approximately an hour after administering latanoprost, the patient's IOP has decreased to 28 mm Hg and the pupil is miotic. The patient appears more comfortable, and corneal edema is subjectively reduced but vision is still questionable. The patient is discharged on latanoprost (1 drop in the left eye q12h), prednisolone acetate 1% (1 drop in the left eye q12h), and dorzolamide (1 drop in the left eye q8h).

TABLE

To view a table showing commonly used glaucoma drugs, go to **cliniciansbrief.com/article/top-5-glaucoma-drugs** or scan the QR code.

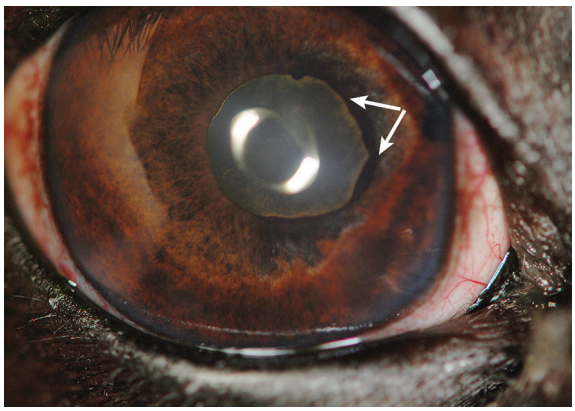
Using QR codes from your mobile device is easy and quick!

Simply focus your phone's camera on the QR code as if taking a picture (but don't click!). A notification banner will pop up at the top of your screen; tap the banner to view the linked content.

IOP = intraocular pressure
PACG = primary angle closure glaucoma
STT = Schirmer tear test

On recheck examination in one week, the patient's blepharospasm, anterior uveitis, corneal edema, and episcleral injection have significantly improved in the left eye (***Figure 2***); however, dyscoria and pigment dispersion are present, along with an inconsistent menace response and posterior synechiae. On tonometry, IOP is 13 mm Hg OS and 11 mm Hg OD, but the optic nerve head looks dark in the left eye on indirect ophthalmoscopy, likely indicating loss of myelin due to damage from the elevated IOP.

The patient is discharged with instructions to continue latanoprost twice daily in the left eye, start timolol twice daily in the right eye for prophylaxis, and taper prednisolone acetate over 1 week in the left eye. In addition to recommending IOP checks every few months, you recommend ongoing evaluation by a veterinary ophthalmologist to monitor primary glaucoma and assess risk to the other eye, through specialized tests and expertise (eg, confirmation of gonioscopic findings, high-resolution ultrasonography).[4]



▲ **FIGURE 2** Corneal edema and episcleral injection have improved. Dyscoria and posterior synechiae are still present (***arrows***).

Your Choice's Implications

Immediate medical intervention for PACG was implemented to control IOP; the eye was comfortable and vision was restored, although menace response was inconsistent. Although medical therapy may be initially effective at lowering IOP, most cases stop responding to medications because the outflow eventually becomes impaired,[9] so most PACG patients ultimately require some form of surgical management, including possible enucleation for irreversibly blind, painful eyes.

Of importance, serious systemic illnesses, including infectious disease and neoplasia, were not considered despite the history of inappetence and lethargy, coughing, and presence of chorioretinal scarring in the right eye. If the patient had secondary glaucoma from uveitis instead of PACG, she could have had a treatable but serious underlying illness that could progress over the week until recheck. In addition, without treatment of the underlying cause of uveitis, the uveitis and secondary changes in the eye could have worsened and affected the other eye, greatly affecting the prognosis for vision, globe retention, and life.

Most primary angle closure glaucoma patients ultimately require some form of surgical management, including possible enucleation for irreversibly blind, painful eyes.

CASE ROUTE 2

You recommend measuring intraocular pressure (IOP) and a systemic diagnostic investigation, including CBC, serum chemistry profile, and chest radiography, based on suspicion of uveitis and secondary glaucoma from the apparent dyscoria, aqueous flare, episcleral injection, and systemic clinical signs.

Case Progression

Tonometry reveals IOP of 18 mm Hg in the right eye and 57 mm Hg in the left eye (normal, 10-25 mm Hg with <20% difference in IOP between eyes). CBC reveals a stress leukogram and mildly elevated hematocrit but is otherwise unremarkable. Serum chemistry profile reveals mildly elevated total protein and mild hypokalemia but is otherwise within normal limits. Thoracic radiographs reveal a mildly diffuse generalized bronchial lung pattern indicative of bronchitis. A SNAP 4Dx Plus test (idexx.com) is negative for *Dirofilaria immitis*, *Anaplasma* spp, *Borrelia burgdorferi*, and *Ehrlichia* spp. Based on geographic location, fungal disease testing may be appropriate. Urine antigen testing for blastomycosis is elected.

Although the diagnostic investigation did not identify an underlying cause for the uveitis, an IOP of 57 mm Hg confirms the suspicion of glaucoma, and the patient is sent home on a topical carbonic anhydrase inhibitor (ie, dorzolamide q8h in the left eye), prednisolone acetate 1% (q6h in the left eye), and oral carprofen (2.2 mg/kg PO q12h). Although the SNAP 4Dx test results are negative, prescribed doxycycline (5 mg/kg PO q12h for 4 weeks) was prescribed empirically for other potential tick-borne diseases.

Clinical Considerations

Based on findings from physical and ophthalmologic examination (ie, lethargy, coughing, inappetence, significant aqueous flare with corneal edema), uveitis with secondary glaucoma is an important differential diagnosis, along with keratoconjunctivitis sicca, corneal ulceration, and uveitis (potentially with secondary glaucoma).

Although there are many causes of secondary glaucoma in dogs, the most common are lens-induced uveitis in dogs with cataract, primary lens luxation, infectious or immune-mediated uveitis, and neoplastic disease.[10] Ocular signs associated with systemic infectious (particularly tick-borne disease) or neoplastic diseases may be unilateral or bilateral and are sometimes present with no other clinical signs. Thus, treatment with doxycycline in this case was a reasonable and safe choice in the event a tick-borne illness was contributing to uveitis. Infectious causes of uveitis may be regional (eg, tick-borne or fungal disease). Signalment may also be important when determining risk for certain immune-mediated diseases.

Prognosis for vision and globe retention with secondary glaucoma is greatly dependent on prompt lowering of IOP and aggressive treatment of uveitis, including identification and treatment of possible underlying infectious or neoplastic causes. It is important to recognize the mechanism responsible for IOP elevation in all cases of secondary glaucoma. Certain medications (eg, latanoprost) that intensify miosis could actually worsen IOP

Infectious causes of uveitis may be regional (eg, tick-borne or fungal disease).

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OD = right eye
OS = left eye

elevation in conditions such as primary lens luxation (common in terrier breeds[11]), in which the primary mechanism of IOP elevation is a pupil block. Because uveitic glaucoma can be caused by cell infiltrates and debris obstructing the iridocorneal drainage angle and/or pupillary block from synechiae, adequate control of intraocular inflammation is imperative. This can typically be achieved by high-dosing frequency of topical corticosteroids (up to q4-6h) if the patient's cornea is fluorescein-stain negative with no ulceration and/or NSAIDs (up to q6h). If a thorough diagnostic investigation, including blood work to evaluate kidney values, has been performed, oral NSAIDs may be beneficial, particularly if there is posterior segment involvement. Oral corticosteroids may also be used in some cases but may not be recommended if all potential infectious and neoplastic causes have not been investigated and excluded. Topical carbonic anhydrase inhibitors (eg, dorzolamide) decrease aqueous humor production and are the treatment of choice for adequate control of IOP in these cases. Surgical treatments such as cyclophotocoagulation and gonioimplants may be performed by a veterinary ophthalmologist but tend to have poorer outcomes than in primary glaucoma patients because of underlying inflammation.

Because the underlying causes and secondary ocular effects of uveitis may be difficult to treat, the prognosis for vison and globe retention in uveitic glaucoma is guarded, particularly in chronic cases. Consultation with a veterinary ophthalmologist is strongly recommended.

Outcome

At the one-week recheck, the patient is slightly improved clinically, with subjective improvement in comfort, and is eating again. In the left eye, there is no menace, dazzle, or consensual PLR from left to right eye, and the pupil is fixed and midrange in size. She has trace corneal edema, the episcleral injection is approximately the same, and the owner reports that the eye appears to be "bulging" more. IOP is 47 mm Hg despite treatment with dorzolamide. Results of testing for blastomycosis are negative. Suspicious of primary glaucoma with the resolution of aqueous flare but increased IOP, you recommend referral to a veterinary ophthalmologist. However, the owner declines your recommendation due to financial concerns. In an effort to decrease IOP, a drop of latanoprost is administered in the left eye and the patient is admitted for the day to recheck IOP. Thirty minutes later, IOP is still elevated at 50 mm Hg, and another drop of latanoprost is given. IOP is still elevated at 48 mm Hg 1.5 hours after the initial dose.

Due to the poor prognosis for vision and globe retention, enucleation with histopathology of the affected eye is elected by the owner. By the time of suture removal 2 weeks later, histopathology confirms a diagnosis of goniodysgenesis with severe optic nerve head cupping and ganglion cell loss, consistent with primary angle closure glaucoma (PACG). You start the patient on timolol in the remaining eye (1 drop q12h) and the client is referred for further diagnostics. Treatment with a topical β-blocker in the remaining eye was instituted based on a randomized, prospective study showing that prophylactic treatment of at-risk fellow eyes in dogs diagnosed with PACG with either topical β-blocker or demecarium bromide delayed onset of glaucoma relative to the control group.[7] Recheck of IOP in the remaining eye every 1 to 3 months indefinitely is recommended, and the owner is warned to be vigilant for any signs of redness, cloudiness, squinting, or decreased vision in that eye, as PACG is a bilateral disease and the fellow eye is high risk for developing glaucoma.

Your Choice's Implications

Secondary glaucoma was suspected due to the presence of uveitis, elevated IOP, and other clinical signs on physical examination that suggested possible systemic disease. A thorough uveitis diagnostic investigation was appropriate based on aqueous flare, episcleral injection, systemic clinical signs, and dyscoria, as many of the possible differentials for systemic disease are serious and may warrant immediate intervention. When results were rela-

tively unremarkable, treatment for clinical signs of secondary glaucoma and uveitis was implemented. Ultimately, the patient had PACG, and persistent IOP elevation resulted in loss of the eye. Because IOP fluctuates throughout the day and from day to day,[12,13] one measurement does not provide a complete picture. Thus, rechecking IOP sooner (ie, in 2 to 3 days versus 1 week) may have been helpful in this case by prompting additional therapy; however, given the 5-day duration of clinical signs prior to initial presentation, it may not have significantly impacted eventual outcome.

Many serious systemic illnesses were ruled out in this case by performing a thorough diagnostic investigation. Most importantly, the eye was submitted for histopathologic evaluation to confirm diagnosis of PACG. Histopathologic evaluation of the globe is of utmost importance in glaucoma cases in which owners elect enucleation, as it provides important prognostic information including likelihood of undiagnosed infectious or neoplastic disease, as well as the risk for disease similarly affecting the other eye, thus informing rational treatment planning.

IOP = intraocular pressure
PACG = primary angle closure glaucoma

Conclusion

This case highlights the challenge of determining whether glaucoma is primary or secondary, especially if owners are financially constrained or unable to accept referral. In addition, many cases of PACG exhibit a degree of inflammation and pigment dispersion, which can further complicate the clinical picture. This case illustrates the importance of recognizing that primary glaucoma may be encountered in any breed, including crossbreed dogs.

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