

Glaucoma and Uveitis in small animals

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Glaucoma

- Glaucoma Definition – evolving
 - Progressive neurodegeneration associated with increased intraocular pressure
 - Human definitions include progressive death of retinal ganglion cells & their axons with/without elevation in IOP
 - Undocumented pressure spikes?
 - Ischemic or excitotoxic damage to RGC?
 - General Definition: "...the final common pathway of a group of diseases with increased IOP, decreased RGC sensitivity and function, RGC death, optic nerve axonal loss and concurrent ONH cup enlargement, incremental reduction in visual fields, and blindness." (Gelatt, 2006)
- Glaucoma Classifications
 - Primary
 - Abnormal development of the iridocorneal angle
 - Secondary
 - Uveitis
 - Anterior lens luxation
 - Neoplasia
 - Hyphema
 - Acute vs. chronic
- Diagnosis of Acute Glaucoma
 - Elevated intraocular pressure
 - Corneal edema
 - Non-responsive mydriatic pupil
 - Often absent menace in affected eye
 - Absent consensual PLR from affected to unaffected eye
 - *Absent consensual PLR from affected to unaffected eye*
 - Episcleral injection
 - Signs of ocular discomfort: blepharospasm, elevated nictitans, discharge, rubbing
 - Loss of appetite
 - Depression, lethargy
- Chronic Glaucoma (>24–48hr)
 - Buphthalmos
 - Deep corneal vascularization
 - Aphakic crescent
 - Dark, cupped optic nerve head

- Generalized retinal degeneration (late)
- Feline Primary Glaucoma?
 - RARE reports of goniodysgenesis
 - European Short Hair
 - Burmese
 - In the vast majority of cases – 2° to uveitis
 - Aqueous humor misdirection – slow, insidious onset
- Therapeutic Options – Medical
 - Increase aqueous outflow
 - Decrease aqueous production
 - Decrease volume of vitreous body
 - 99% water
 - Neuroprotection
- Increase aqueous outflow
 - Parasympathomimetics (DMBR, pilocarpine)
 - Mechanism:
 - Induce miosis and decrease resistance to corneoscleral outflow
 - Avoid in 2° glaucoma – risk posterior synechia
 - Likely most beneficial early in disease
 - CAUTION: Systemic toxicity may develop with cholinesterase inhibitors!
 - Hypersalivation
 - Vomiting
 - Diarrhea
 - Prostaglandin Analogues – latanoprost/Xalatan, travaprost/Travatan, bimatoprost/Lumigan
 - Exact MOA unknown
 - Increase uveoscleral outflow
 - First line therapy in emergency setting
 - Administer q12 hours
 - Caution in secondary glaucoma
 - Potentiation of inflammation
 - Pupillary block
 - Not effective in cats
- Decrease aqueous production
 - Carbonic Anhydrase Inhibitors – brinzolamide/Azopt, dorzolamide/Trusopt
 - Well tolerated
 - primary or secondary glaucoma
 - TID administration
 - Can be given q30 minutes in ER setting initially
 - Beta-Blockers (timolol)
 - TID administration
 - Can be used in primary or secondary glaucoma
 - Caution in asthmatic cats

- Decrease volume of the vitreous – generally reserved for acute cases, potentially visual eyes
 - Mannitol 20% (5ml/lb IV over 20minutes)
 - DO NOT USE WITH CARDIAC/RENAL DISEASE
 - Do not offer water for 4 hours after administration
 - Requires intact blood–aqueous barrier – not as useful in secondary glaucoma
 - Glycerin ((1–1.5g/kg PO)
 - DO NOT USE IN DIABETIC PATIENTS
 - Likely to cause vomiting/nausea
 - Do not offer water for 4 hours after administration
 - Can be sent home with clients for emergency administration at home
 - General In–Hospital Acute Glaucoma Treatment
- General In–hospital Acute Glaucoma Treatment
 - Give Trusopt then Xalatan (refrigerated)
 - Recheck IOP in 30 minutes
 - if <30mmHg no further immediate treatment
 - If >30mmHg give Trusopt, hospitalize, place catheter
 - Mannitol 20% over 20 minutes, withhold water
 - Take outside to urinate after administration, recheck pressure
 - If pressure >40, give another drop of Xalatan
 - Continue Trusopt q30minutes for 2 hours until pressure <30mmHg
 - If pressure remains >30mmHg, another dose of 20% Mannitol may be given IV
- Acute Glaucoma Follow–up
 - Gonioscopy of unaffected eye and prophylactic treatment if abnormal
 - Vision may be permanently lost during initial pressure spike
 - Often focus is on maintaining vision in unaffected eye for as long as possible and keeping the affected eye comfortable
 - Target pressure in a visual glaucomatous eye is lower than normal <15mmHg
 - Frequency of monitoring pressure varies – maximum q3 months
 - Pressures >30–40 mmHg ARE PAINFUL – recommend surgery
- Surgical options for visual eyes
 - Consider when
 - Little or no uveitis is present
 - Pressure remains mildly to moderately elevated despite anti–glaucoma meds
 - Acute glaucoma that doesn't respond to emergency therapy in a potentially visual eye (affected <24–48hr)
 - Transcleral Cyclocryotherapy
 - Repeated freeze/thaw cycles to destroy ciliary body
 - Poor long term control

- Non-specific treatment – significant inflammation
- Diode laser transcleral cyclophotocoagulation (TSCP)
 - preferentially destroys pigmented cells within ciliary body
 - More specific – significant inflammation can still be a problem
 - May be more useful when combined with glaucoma shunts
 - Shunts
 - low long-term success rates due to clogging
 - May be more useful when combined with TSCP
 - 41% visual, 76% good IOP control at 12 months (Sapienza, 2005) – loss to follow up
- Endolaser cyclophotocoagulation
 - Newest and most specific
 - Combined with phacoemulsification of the lens or lensectomy to allow access to the ciliary body
 - Canine
 - Primary glaucomas
 - Hospitalized 1 week following procedure – 30% chance of IOP spikes
 - IOP <20mmHg in >85% patients at 1 year
 - Vision: 70% visual at 1 year
 - Medications: 95% on fewer medications at 1 year
 - Feline:
 - Glaucoma secondary to cataracts/lens luxation
 - 17% chance of IOP spikes within 24 hours
 - IOP <25mmHg in >91% patients at 1 year
 - Vision: 92% visual at 1 year
 - Medications: 50% completely off glaucoma medications at 1 year
- Neuroprotection?
 - Progression of glaucomatous damage to the retina despite “normal” IOP
 - Glutamate released by damaged retinal ganglion cells (RGC’s) causes damage to surrounding RGC’s (controversial)
 - Glutamate receptor antagonism = NMDA receptor antagonist (Memantine)
 - Canine dose: 0.15–0.3mg/kg/day
 - Variable results in human studies
 - Alterations in retinal/ONH blood flow
 - Carbonic anhydrase inhibitors improve ONH blood flow in rabbit model
 - Ca²⁺ channel blockers
 - Amlodipine – decreases vascular resistance in ophthalmic and short posterior ciliary arteries

- Nifedipine – prevents endothelin-1 mediated vasoconstriction and ameliorates effects of glutamate in humans

Uveitis

- Symptoms of anterior uveitis
 - Decreased vision
 - Blepharospasm
 - Conjunctival hyperemia
 - Ciliary flush
 - NM protrusion
 - Corneal edema
 - Circumlimbal corneal neovascularization*
 - Aqueous flare
 - Fibrin
 - Hypopyon
 - Lens luxation/subluxn*
 - Secondary glaucoma*
 - Hyphema
 - Keratic precipitates
 - Iridal hyperemia
 - Iridal nodules
 - Iris color change*
 - Miosis
 - Decreased intraocular pressure
 - Anterior vitreal cell or flare
 - Cataract*
 - Anterior or posterior synechia*
 - Iris rubeosis*
- Major Classifications
 - Trauma
 - Blunt
 - Penetrating (including iatrogenic)
 - **Lens induced**
 - Phacoclastic
 - Phacolytic
 - **Metabolic**
 - Drug-induced
 - Scleritis
 - **Pigmentary**
 - Idiopathic
 - Neoplasia
 - **Infectious**
 - Fungal
 - Parasitic
 - Protozoal
 - Rickettsial (canine)
 - Algal
 - Bacterial
 - Viral
 - **Uveodermatologic Syndrome (canine)**
 - Ulcerative keratitis
 - Toxemia
 - Radiation Therapy
- General Considerations
 - History including vaccination status and travel
 - Complete physical exam
 - Baseline CBC, serum chemistry, UA

- Additional screening for infectious diseases
- Lens-Induced Uveitis
 - Phacolytic - inflammation due to lens proteins leaking through intact lens capsule
 - Typically low-grade inflammation
 - May be more severe in young or diabetic dogs with rapidly developing cataracts
 - Anti-inflammatories for late immature, mature, hypermature cataracts are a must
 - Topical NSAID (flurbiprofen) SID - BID
 - Topical corticosteroid SID-BID - caution with diabetes mellitus
 - Phacoclastic - inflammation following lens capsule rupture
 - Capsular rents difficult to detect - often have fibrin clot overlying
 - Wounds >2mm diameter have very poor prognosis without lens removal (phacoemulsification)
 - Wounds <2mm may be sealed over by fibrin/iris
- Metabolic
 - Hypertension
 - Retinal detachment
 - Retinal hemorrhages
 - Hyphema - later
 - Hyperlipidemia (lipid-laden aqueous)
 - Most common in hyperlipidemic dogs following cataract surgery
 - Occasionally seen in dogs without a history of ocular disease - postulated that hyperlipidemia could lead to uveitis
 - Treatment: resolves with resolution of hyperlipidemia
 - With hold food for 24 hours
 - low fat diet
 - consider Slentrol
- Pigmentary Uveitis
 - Golden Retrievers vastly overrepresented
 - Often becomes bilateral
 - Associated with uveal cyst formation
 - Look for excessive deposition of pigment on anterior lens capsule, posterior synechia, flare, pigment cells floating in anterior chamber
 - Uveal cysts may be blood-filled and blood clots may be present in anterior chamber
 - Sequelae: cataracts and glaucoma (mean 4.8 months after presentation)
 - Treatment: anti-inflammatories, anti-glaucoma medications

- Not well understood – 50% of globes have no histologic evidence of inflammation and remaining globes only have mild inflammation (Esson, 2009)
 - Disease progression despite treatment
 - Glaucoma related to pigment dispersion versus mechanical obstruction of angle by iridal cysts?
- Hyphema
 - Non-specific finding
 - Primary Differentials
 - Retinal detachment
 - Systemic hypertension
 - Intraocular neoplasia
 - Trauma
 - Uveitis
 - Coagulopathy
 - Recommended Initial Work-up
 - Blood work (CBC, Chemistry, UA)
 - Ocular ultrasound – assess for neoplasia, retinal detachment
 - Blood pressure (>180mmHg usually significant)
 - Tick titers/chest radiographs/abdominal ultrasound/coagulation profile depending on index of suspicion
 - Treatment
 - Treat underlying condition if present
 - Inflammation is present – topical corticosteroids TID-QID
 - Consider topical NSAID, but could potentiate rebleeding
 - Secondary glaucoma is a significant concern
 - Monitor pressures closely
 - Consider antiglaucoma medication such as dorzolamide/timolol if pressures in the mid-20's
 - Guarded prognosis for vision return
- Neoplastic: LSA
 - Most common metastatic tumor causing uveitis in dogs and cats
 - Aqueous humor cytology/iris FNA can be diagnostic
 - Uveitis may be severe
 - Often bilateral
 - Can look like anything in the eye or surrounding the eye
- Canine Uveitis of Unknown Etiology
 - 2002, North Carolina Study
 - 58% no underlying cause – idiopathic/immune-mediated
 - 25% neoplasia – lymphoma most common

- 17.6% infectious etiology – Ehrlichia and blastomycosis most common
- Initial Work-up
 - CBC, Chemistry, UA – minimum
 - Consider –
 - tick/fungal titers depending on region of country, travel history
 - Neoplasia screen – abdominal ultrasound, chest radiographs
 - Lymph node aspirate if lymphadenopathy present
- Ehrlichiosis
 - Ocular signs evident 3 weeks after fever onset
 - Ocular signs: conjunctivitis, conjunctival or iridal petechiations, corneal opacity, panuveitis with hyphema, retinitis, retinal detachment
 - Ocular signs may be present without any systemic disease
 - Diagnosis: serology
 - Treatment
 - 5–10mg/kg doxycycline PO SID–BID x 4 weeks
 - some treat with prednisone @ 1 mg/kg PO daily x 1–2 week
 - Topical prednisolone TID–QID
 - Atropine
 - Response (Kommenou, 2006, Greece)
 - 55% had complete resolution of ocular lesions
 - 25% had moderate response
 - 20% had poor response
 - Posterior segment involvement has poorer prognosis for response to treatment (Leiva, 2005, Spain)
- Blastomycosis
 - Distribution: Mississippi, Missouri, Ohio River Valley, mid–Atlantic states, Quebec, Manitoba, Ontario
 - Young, male, large–breed dogs most often affected
 - 30–40% of dogs have ocular disease
 - Anterior uveitis is most common ocular symptom
 - Present in 100% of cases in 1 study
 - Panuveitis, glaucoma, retinal detachment
 - Other sites of infection: lungs, skin, bones, LN, testes
 - Diagnosis
 - vitreal/drainage tract/LN aspirates
 - AGID serology
 - Urine antigen test
 - Treatment
 - itraconazole (best)

- amphotericin B (renal toxicity, poor ocular penetration)
 - prednisolone acetate
 - atropine
 - PX: Guarded
 - Positive response to treatment in 76% of dogs with posterior segment disease only
 - Positive response in 18% of dogs with anterior uveitis
 - Positive response in 13% of dogs with endophthalmitis/panuveitis
 - Eyes that will respond to treatment with itraconazole typically do within 4 weeks (Hendrix, 2004)
 - Eyes can be a reservoir of budding yeast (Hendrix, 2004)
- Feline causes of uveitis of unknown etiology
 - Infectious etiology – 38–70%
 - Bilateral most common
 - 80% male (MI & MC)
 - Mean age: 7.6 years (range: 3–15 years)
 - Idiopathic (lymphoplasmacytic on histo)
 - 48% bilateral
 - 72% male (MI & MC)
 - Mean age: 9.6 years (range: 3–15 years)
 - Work-up
 - CBC, chemistry, UA
 - Testing for specific infectious diseases
 - Most common infectious etiologies: FIP, FIV, FeLV, Toxoplasma, Bartonella, Cryptococcosis
 - Infectious: FIV
 - Mild to moderate anterior uveitis in ~35%
 - Keratic precipitates uncommon
 - Pars planitis (snow drifting)
 - Causes
 - Direct damage by virus
 - Secondary infections (esp. toxoplasma)
 - LSA associated with FIV
 - Treatment – symptomatic (topical corticosteroids and atropine)
 - Infectious: FIP
 - Uveitis can be only symptom
 - Uveitis more common in non-effusive form
 - “mutton fat” keratic precipitates
 - Posterior involvement possible

- Pyogranulomatous chorioretinitis
 - Retinal vasculitis with perivascular cuffing
 - Exudative retinal detachments
 - Optic neuritis
- Treatment – symptomatic (topical corticosteroids and atropine)
- Infectious: FeLV
 - Ocular symptoms usually 2° lymphoma
 - Causes
 - Direct action of virus on ocular tissues – uncommon
 - Secondary to LSA
 - Wide variety of presentations
 - Extraocular masses
 - Anterior chamber/uveal LSA tumors
- Feline Infectious: Toxoplasma
 - Eye is a target organ
 - Disease caused by active replication of organism
 - Posterior involvement most common
 - Granulomatous chorioretinitis
 - Retinal vasculitis
 - Optic neuritis
 - Diagnosis: serology
 - PCR of aqueous humor or peripheral blood not reliable test
 - Treatment
 - Symptomatic for uveitis
 - Clindamycin: 12.5mg/kg PO BID x 21–30d
- Feline Infectious: Cryptococcosis
 - Symptoms
 - Optic neuritis
 - Chorioretinitis
 - Retinal detachment
 - Diagnosis: serology, aspirates of affected tissue
 - Treatment
 - Itraconazole: 5mg/kg PO BID x 1 month past resolution and decrease in titer by 2 orders magnitude
 - Fluconazole: 50mg PO BID
 - Symptomatic for the uveitis
 - Infectious: Cryptococcosis
- Feline Infectious: Bartonella?
 - Has been detected (PCR) in aqueous humor of cats with uveitis

- High degree of seropositivity in general population
 - 12% in Chicago
 - 67% in Florida
 - Unclear what role it plays in feline uveitis
- Recommend test and treat if seropositive