Pathology of the Vitreous

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General Considerations

• Vitreous is difficult to evaluate histologically
• Liquefied vitreous may not or only partially survive processing
Asteroid Hyalosis

- Dogs +/- other species
- One form of vitreal degeneration
- Lipid-calcium complex
- Age related and secondary to disease
- Often seen with neoplasms (iridociliary neoplasms, melanocytic neoplasms)
- The exact composition of asteroid bodies varies between studies (Wang et al, Mol Vis 2006; Kador et al, Eye, 2008; Labruyere et al, Vet Radiol Ultrasound 2008)
Asteroid Hyalosis

Courtesy of COPLOW
Asteroid Hyalosis
Asteroid Hyalosis
Asteroid Hyalosis
Vitreal Hemorrhage

- Normal vessels (trauma, uveitis)
- Immature vessels (fibrovascular membranes, neoplasia)
- Abnormal vessels (systemic hypertension, PHPV/PTVL)
- Blood disorders (coagulopathies)
Vitreal Hemorrhage

- Rapid fibrin clot and slow fibrinolysis
- Hemolysis of red blood cells
- Limited cell infiltration
- Low turnover of macrophages, few hemosiderophages

- The purpose of this measured response may be to maintain ocular immune privilege and ocular function by avoiding a marked response leading to granulation tissue formation.
Vitreal Hemorrhage
Vitreal Hemorrhage
Vitreal Hemorrhage
Canine Ocular Gliovascular Syndrome

- Intraocular hemorrhage
- Retinal detachment
- Fibrovascular proliferation
- Glaucoma

- Aggregates of glial (GFAP positive) cells in the vitreous
- Neovascular proliferation extending into the vitreous from the retina or optic nerve head
- Hyalin collagen surrounds the neovascular proliferation.

Canine Ocular Gliovascular Syndrome
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Courtesy of COPLOW
Canine Ocular Gliovascular Syndrome
Shih Tzu Vitreoretinopathy

- Shih Tzus
- Retinal detachment
- Retinal tears
- Fibrovascular proliferation
- Glaucoma

- Cell poor collagen deposition in the vitreous
- Cells in the vitreous are myofibroblasts

- Papaioannou et al, J Comp Path 2013
Shih Tzu Vitreoretinopathy

Papaioannou et al, J Comp Path 2013

Courtesy of COPLOW
Shih Tzu Vitreoretinopathy

Courtesy of COPL OW
Pathology of the Retina and Optic Nerve

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Retina
General Considerations

- Glaucoma related changes discussed elsewhere
- Minimal healing capacity
Retinal Detachment

• Potential causes
  • Trauma
  • Inflammation
  • Neoplasia
  • Vasculopathies
  • Traction
  • Congenital lesions
  • Retinal degeneration
  • Glaucoma/buphthalmos
Retinal Detachment

- Actual causes Canine (PL database, 100 cases)
- Neoplasia 21%
- Inflammation/trauma 34%
- Vasculopathies/systemic hypertension 9%
- Undetermined 36%

- Inflammation/trauma: 4 VKH, 3 granulomatous scleritis and 2 diabetic cataract/granulomatous endophthalmitis. 13 cases are endophthalmitis from penetrating trauma, fungal, asymmetric uveitis. 12 cases had findings/ history of trauma w/o endophtalmitis.
- 23/36 undetermined cases had severe intraocular hemorrhage and fibrovascular proliferation with the retinal detachment (“idiopathic retinal detachment”). In the other 13 cases, the significance of the retinal detachment was unclear.
Retinal Detachment

- Actual causes Feline (PL database 50 cases)
- Neoplasia 50%
- Inflammation/trauma 32%
- Vasculopathies/systemic hypertension 6%
- Undetermined 12%

- Inflammation/trauma: 18% with findings/history of trauma where inflammation was not a significant component and 14% with severe inflammation (penetrating trauma, fungal, etc).
Retinal Detachment

- Material in the subretinal space (hemorrhage, inflammation, proteinaceous, vitreous)
- Hypertrophy +/- hyperplasia of the retinal pigment epithelium (not required)
- Outer retinal atrophy
- Retinal tears

- Retinal tears can be identified by the presence of interrupted retinal segments with rounded edges with gliosis

- In rare cases, retinal detachment prior to the development of glaucoma can have a sparing effect on the inner retina (ie clinical glaucoma without inner retinal atrophy)
Retinal Detachment

- Not possible to accurately determine the age of the RD
- Proliferative and hypertrophic changes to the RPE can be detected 24h after RD (1-3 days)
- Photoreceptor atrophy/degeneration after 1-3 days
- Early changes to the ONL are present within a few days

- Anderson IOVS 1981; Anderson IOVS 1983
Retinal Detachment

• More severe atrophy implies chronicity (few days-1 week or more)

• RPE hypertrophy may decrease with chronic RD

• The severity, cause, nature of subretinal material, etc. all likely affect the development of retinal changes
Retinal Detachment
Retinal Detachment
Retinal Detachment
Retinal Detachment
Retinal Detachment
Retinal tears
Retinal Tears
Progressive Retinal Atrophy

• Dogs +/- cats
• Inherited/presumed inherited
• Clinical evaluation required for the diagnosis
• Lesions in globes removed for other diseases
• Histologic evaluation has limited value
• The molecular work in various breeds does not translate to specific histologic findings.
Progressive Retinal Atrophy

- Outer retinal atrophy
- May be focal-multifocal initially
- Ganglion cells may “drop” in the blended nuclear layers
- Progresses to full-thickness atrophy
- Complications may include retinal detachment and cataract
- Ddx include SARDS, Retinal detachment, toxic/nutritional retinal injury.
Progressive Retinal Atrophy

- PRA can be suggested as a dx when there is outer retinal atrophy, especially if early and multifocal
- Once there is full thickness atrophy, there are no specific features to suggest PRA vs ddx
- Cases with retinal detachment will not have features that allow a histologic dx of preceding PRA
Progressive Retinal Atrophy

Ganglion cell
Progressive Retinal Atrophy
Sudden Acquired Retinal Degeneration Syndrome

• Dogs, clinical evaluation required for the diagnosis
• Lesions in globes removed for other diseases
• Histologic evaluation has limited value
• Ddx include, PRA, Retinal detachment, toxic/nutritional retinal injury
• Previous clinical diagnosis of SARDS in most cases
Sudden Acquired Retinal Degeneration Syndrome

- Outer retinal atrophy, diffuse in early stages
- Progresses to full-thickness atrophy
- +/- minimal lymphoplasmacytic inflammation
- With full thickness atrophy, there are no specific features to suggest SARDs vs ddx
- Histologic evaluation offers no insight on the possible association with systemic/hormonal disease

- Keller et al. VO 2006; Carter et al. JAAHA 2009; Stuckey et al JAVMA 2013; Komaromy AM et al, VO 2015 [Epub ahead of print]; Heller AR et al, VO 2016 [Epub ahead of print].
Sudden Acquired Retinal Degeneration Syndrome
Sudden Acquired Retinal Degeneration Syndrome
Fluoroquinolone-Induced Retinal Toxicity

- Cats
- Acute
- Rare/unlikely to be examined histologically
- The lesions do not occur at recommended doses in normal cats
- Photoreceptor loss

- Gelatt KN et al, VO 2001; Weibe V et al, JAVMA 2002
- Ramirez Pharmacogenet Genomics 2011.
- Rampal S et al Hum Exp Toxicol 2008 (ofloxacin rabbits)
Fluoroquinolone-Induced Retinal Toxicity

Courtesy of COPLOW
Systemic Hypertension

- Usually bilateral, asymmetrical
- Vessels of the retina, choroid, rarely iris
- Arterioles have hyaline thickened walls and narrowed lumen ("fibrinoid necrosis")
- PAS staining can help visualize the vascular changes
- Retinal detachment, hemorrhage and necrosis
- Rarely optic nerve lesions
- Intraocular hemorrhage, fibrovascular proliferation, glaucoma
Systemic Hypertension
Systemic Hypertension
Systemic Hypertension
Diabetic Retinopathy

- Loss of pericytes
- Thickening of the basement membrane of vessels
- Retinal hemorrhages
- Glycemic control may protect against ganglion cell loss in dogs
- No significant proliferative component

Diabetic Retinopathy

 Courtesy of COPLOW
Diabetic Retinopathy

Raccoon, courtesy of Dr. Chris Reilly
Diabetic Retinopathy
Diabetic Retinopathy vs Systemic Hypertension
Retinal Inflammation

• Infectious retinitis (canine distemper, Toxocara canis, Haemophilus somnus, Bovine Viral Diarrhea, Toxoplasma gondii, West Nile Virus)
  – As part of systemic disease
• Extension of uveitis/endophthalmitis (trauma, bacterial, fungal, Prototheca, etc)
• Perivascular lymphoplasmacytic retinitis with lymphoplasmacytic uveitis (no specific significance)
Canine Distemper

Inclusion
Tapetal Sparing

- Dogs, horses, others
- Dorsal retina tends to be less affected by glaucomatous change
- Tapetum not necessary
- Increased susceptibility ventrally rather than dorsal/tapetal resistance

Tapetal Sparing
Retrograde atrophy

- Die-back atrophy
- Loss of ganglion cells secondary to optic nerve injury
- Most commonly seen with canine orbital meningiomas
- Must be differentiated from inner retinal atrophy/glaucoma
Retrograde atrophy
Peripheral Retinal Cysts

- Peripheral cystoid degeneration
- Dogs
- Aging change
- Pathologic examination of globes does not support the suggestion (G4) that these cysts may be clinically significant as part of retinal detachment
- Similar cystic degeneration is seen in cats and horses in the ciliary pars plana (not the retina)
Peripheral Retinal Cysts
Optic Nerve
General Considerations

- Glaucoma related changes discussed elsewhere
Trauma

- Proptosis
- Necrosis/malacia
- Hemorrhage
- Atrophy, gliosis and fibrosis with chronicity

- Horses
- Necrosis with Gitter cells
- Atrophy and fibrosis with chronicity
- Gitter cells may extend in the vitreous (exudative optic neuropathy).
Trauma
Trauma
Ischemic Optic Neuropathy

- Horses
- Acute hypovolemia
- Surgical occlusion of ext/int carotid arteries (guttural pouch mycosis)
- Edema and hemorrhage
- Atrophy and fibrosis with chronicity
- +/- periparillary retinal hemorrhage and degeneration
Ischemic Optic Neuropathy
Ischemic Optic Neuropathy
Optic Neuritis

- Canine distemper
- Granulomatous meningoencephalitis
- Tick-borne encephalitis virus
- Idiopathic optic neuritis

- Unlikely to be examined histologically pre-mortem, or at all in the case of idiopathic optic neuritis.
Optic Neuritis

Courtesy of Dr. Amber Labelle
Proliferative Optic Neuropathy

- Older horses
- Benign lesion
- Proliferation of macrophages and glial cells

- Saunders Vet path 1972
Proliferative Optic Neuropathy

From Saunders and Rubin 1975
Schnabel’s Atrophy

- Dogs
- Glaucoma
- Vitreous extends in the cavitated optic nerve
Schnabel’s Atrophy
Schnabel’s Atrophy
Schnabel’s Atrophy

Courtesy of COPLOW
“Optic neuroma”

• Dogs
• Nodular proliferation of peripheral nerve adjacent to the optic nerve
• Associated with glaucoma
• Not recognized clinically
• Significance?
“Optic neuroma”
“Optic neuroma”