Title
Diseases of the vitreous, retina, and choroid

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Publication Date
1980

Peer reviewed

DISEASES OF THE VITREOUS, RETINA, AND CHOROID

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Because of the close association of the vitreous, retina, and choroid, conditions affecting one often involve the others as well. Generally, it is unusual to have severe vitreal disease without concurrent or associated retinal disease (although the reverse is often true).

In order to appreciate the complexities of retinal, choroidal, and vitreal disease, the reader must have a basic understanding of the normal embryology, anatomy, and physiology of these structures.

VITREAL DISEASE

Persistence of Hyaloid Vasculature. Varying degrees of persistence of the hyaloid vascular system may occur. Because vision is rarely affected, this condition does not require treatment. The most common and benign persistent hyaloid remnant is termed "Mittendorf's dot," which is a small posterior polar opacity of the lens capsule. It may also appear as a small gray circle and is the site at which the hyaloid artery attaches to the anterior condensation of vitreous adjacent to the lens. Often, a tiny remnant of artery remains behind the lens and hangs (loosely coiled) in a canal (Cloquet's) in the vitreous.

A more extensive persistent artery may terminate on the posterior lens capsule with a branched appearance. Depending on the amount of tissue remaining, vision may be disturbed, especially in conditions in which the pupil is constricted. Some of these vessels are patent and contain blood so that retrolental hemorrhage may occur.

Rarely, there may be extensive proliferation of fibrovascular tissue, often with invasion of the posterior lens, in which case the condition is termed "anterior persistent hyperplastic primary vitreous." Other ocular anomalies such as a variable degree of microphthalmia, elongated ciliary processes, and retinal dysplasia may be present. Affected eyes are usually blind owing to cataract. Lens extraction and vitrectomy may be performed, but the prognosis is guarded. If vision is affected by central opacities, chronic mydriatic therapy (1 percent atropine weekly is best) may be utilized to improve vision.

Vitreous Floaters. White or grey opacities of various sizes may commonly be seen in the vitreous of otherwise normal eyes randomly and in certain breeds and families of dogs. These are usually in the form of strands that move with ocular movements and may increase in quantity as the animal ages. The cause and substance of these are uncertain. Their main importance is in their differentiation from inflammatory exudates (hyalitis), which represent retinal and/or posterior uveal inflammation. Inflammatory exudates are often darker and hazier than benign floaters. The presence of inflammatory exudates necessitates a search for the primary process.

Asteroid Hyalosis. This is a degenerative disease of older animals and is usually unilateral. The vitreous remains in its gel state and contains numerous, tiny, round, opaque bodies that reflect light and vibrate with ocular movement. They are calcium-lipid complexes and do not appear to interfere with sight, nor are they necessarily involved with other ocular disease. Treatment is neither feasible nor necessary.

Hyalitis. Inflammation of the vitreous (hyalitis) is usually secondary to uveitis and retinitis. Inflammatory cells, exudate, and blood enter the vitreous, giving it a diffuse, hazy appearance; the fundus cannot be seen clearly. Successful treatment of the underlying disease process is followed by restoration of vitreous clarity. However, if hemorrhage and/or fibrin form clots, traction bands can form, which may result in retinal separation and severe distortion of the globe with blindness.

RETINAL AND CHOROIDAL DISEASE

Absence or Underdevelopment of Tapetum. The tapetum is a specialized part of the choroid. Its function and significance are not clear. When it is absent or underdeveloped,

clinical signs are not apparent. Frequently, albino or color-dilute animals will not have tapeta, but absence or hypoplasia can occur in pigmented animals as well. At this time it would seem that the presence or absence of a tapetum is not clinically significant.

Peripheral Cystoid Retinal Degeneration. From middle age onward, the peripheral sensory retina (adjacent to the ora ciliaris retinae) begins to show structural changes of splitting with the formation of cysts. They are best visualized with indirect ophthalmoscopy and mydriasis. The condition is considered a normal aging phenomenon, and vision appears not to be affected.

Retinal Separation (Detachment). A distinction is made here between true retinal detachment and separation. The site of discontinuity in clinically termed retinal "detachment" is almost always between the retinal epithelium (retinal pigment epithelium) and the sensory retina (neural retina). These two layers are part of the same tissue, so that the term "separation" would be more accurate and will be used throughout this section. If the retinal epithelium were to lose continuity with the choriocapillaris (an unusual occurrence), this would be a true detachment.

Retinal separation is usually secondary to intraocular inflammatory disease, especially choroidal disease. It can also be associated with renal disease and systemic hypertension, or it can occur alone (idiopathic). If the area of separation is small and flat, it is called a flat separation. If a bulla is formed, the term "bullous separation" is used. When there is complete separation so that only the attachments at the optic disk and ora ciliaris retinae are intact, this may be called funnel-shaped or morning glory separation. Dialysis refers to a tearing of the peripheral or peripapillary attachments. Rhegmatogenous separations refer to those associated with breaks, tears, or holes in the retina. Indirect ophthalmoscopy through a dilated pupil is the easiest method of diagnosis of retinal separation. If the separation is complete, the folded sensory retina is often grossly visible just behind the lens without the use of any diagnostic instruments.

Once the diagnosis of retinal separation is made, a search for the cause is imperative for successful treatment. When it is associated with ocular maldevelopment (such as the collie eye anomaly or retinal dysplasia), treatment is not feasible. If associated with choroidal, vascular, or renal disease, these entities must be treated simultaneously.

Generally, the prognosis for retinal separation is poor. If there is sufficient distance between the retinal epithelium and the sensory retina so that proper nutrition of the photoreceptor cells is lacking, there may be irreversible degenerative changes in these cells after ten days. If these two layers are reunited prior to this time, return of function may occur. For simple effusive separations, symptomatic treatment includes the use of systemic corticosteroids and diuretics in addition to definitive treatment of any primary disease. Corticosteroids should be used at anti-inflammatory levels for an extended period, sometimes as long as six weeks, before being considered ineffective. Prednisolone and dexamethasone are commonly used. Prednisolone should be used orally at 1.0 mg/kg or higher daily, tapering to the usually recommended 0.5 to 1.0 mg/kg range after 10 to 14 days. Dexamethasone can be given orally at the rate of 0.25 to 2.0 mg (depending on weight of patient) daily.

Furosemide is commonly used at 2 to 4 mg/kg orally once or twice daily. If the patient is hypertensive, oral methyldopa at approximately 5 mg/kg twice daily may be helpful, in addition to a tranquilizer such as promazine (orally at approximately 2 mg/kg twice daily).

Therapy is empirical, particularly with respect to the diuretics. However, the use of this regimen in purely idiopathic effusive cases is often helpful. These cases generally have a better prognosis simply because there are no (obvious) contributing pathologic processes. Rhegmatogenous separations or those in which there is dialysis usually do not respond to any type of therapy.

Surgical therapy is widely used in humans but is difficult to apply to animals mainly because surgical exposure is not adequate. Also, many veterinary patients are presented late in the process, so that correction would not result in vision. These animals often have rhegmatogenous separations or are dialyzed.

Retinitis and Choroiditis. Although there are some specific diseases in which there is primary retinitis or choroiditis, secondary changes usually occur in the initially uninvolved tissue. Unless this type of disease is suspected, and ophthalmoscopy is performed, most lesions will be missed in their early stages. It is not until there is diffuse bilateral involvement, anterior progression, optic nerve involvement, or secondary changes such as retinal separation that clinical signs are manifested. If the chorioretinitis is secondary to systemic disease (which it usually is), the animal may be manifesting other signs that may suggest ophthalmic examination. For example, a young dog with signs of encephalitis or gastroenteritis may have distemper, and ophthalmic examination may pro-

vide additional supportive evidence of the same.

Determination of whether a particular lesion is active or static is important, since chorioretinal scars are commonly seen throughout dog and cat populations and do not require treatment. Active lesions appear as grey or white areas with indistinct borders. These may extend into the vitreous so that visualization of other structures is obscured. These areas may be surrounded by edema, hemorrhage, or elevations of the sensory retina. Granulomatous inflammation is often more discrete than is nongranulomatous inflammation; the granulomas may appear fluffy or cotton-like and have more substance.

In the tapetal area, inactive lesions may be hyperreflective owing to retinal thinning, or there may be aberrant pigmentation. Inactive lesions in the non-tapetal area may be depigmented, hypopigmented, or hyperpigmented.

Once a lesion is determined to be active, treatment can be prescribed. One must carefully evaluate the patient to diagnose and treat the primary process. When a systemic diagnosis is not possible or if the ocular lesion is primary, symptomatic treatment should be instituted. This includes the use of systemic corticosteroids at high levels for several weeks. This is important because changes secondary to the inflammatory process itself may lead to irreversible damage, particularly to the retina. Contraction of fibrovascular tissue within the retina or vitreous may lead to further distortion of the intraocular contents. Broad spectrum antibiotics should be used simultaneously.

The prognosis must remain guarded, but ultimately it depends on the etiology. An important fact to keep in mind is that regardless of the cause of retinal and/or choroidal inflammation, the ophthalmoscopic signs are similar; one cannot determine the etiology simply on the basis of ocular fundus changes. If a lesion appears granulomatous, the possibilities are limited but there is still no specificity owing to appearance. Any time active retinitis and/or choroiditis is diagnosed, a complete physical examination must be performed. Non-granulomatous inflammation may be produced by many bacteria, viruses, and toxins. Granulomatous reactions are attributable to mycotic (such as blastomycosis, protothecosis, toxoplasmosis, coccidioidomycosis, cryptococcosis, and geotrichosis), protozoan, and helminthic (such as toxocariasis) infections.

Progressive Retinal Atrophy. Progressive retinal atrophy (PRA) comprises a group of diseases characterized by loss of outer retinal function. PRA describes only the endstage retinal disease and not the pathogenesis, although most are considered hereditary. Three canine breeds have been fairly well studied and represent a spectrum of changes with respect to the early disease. The Irish setter has been shown to have a rod-cone dysplasia in which neither photoreceptor cell matures structurally or functionally. The Norwegian elkhound has rod dysplasia with secondary cone atrophy. In the miniature and toy poodle, true rod and cone atrophy occur after apparently normal structural and functional maturation. PRA has been diagnosed in the cat, but the pathogenesis has not been determined for any particular breed.

Although there are different pathologic processes, PRA characteristically produces night blindness (nyctalopia) initially, which eventually progresses to include day blindness (hemeralopia), at which time the animal is totally blind. Ophthalmoscopic changes include early retinal vascular attenuation and tapetal granularity (owing to disturbance of the optical characteristics of the retina by degenerating photoreceptor cells). As the disease progresses, there is an increase in tapetal reflectivity (owing to a thinning retina), further vascular attenuation, and mottling of the non-tapetal area because of retinal epithelial disturbance (hyperplasia, hypertrophy, and hypopigmentation). In the late stages, the tapetum may be brilliantly hyperreflective, the optic disk may be atrophic, and the retinal vessels will be "ghost-like."

PRA occurs in virtually every breed of dog including mongrels. As mentioned before, the pathogenesis may be considerably different from breed to breed. The following is a list of a few breeds with the approximate age at which an ophthalmoscopic diagnosis can be made:

Breed	*Age*
Irish setter	6 months
Cardigan Welsh corgi	6 months
Cairn terrier	Under 1 year
Miniature long-haired dachshund	Under 1 year
Collie	Under 1 year
Doberman pinscher	1 to 2 years
Norwegian elkhound	2 to 3 years
Samoyed	3 years
English cocker spaniel	3 to 5 years
Miniature and toy poodles	3 to 5 years
Miniature schnauzer	4 to 6 years

Since all PRA cases seem to begin with night blindness and since vitamin A is widely known to be necessary for night vision, many people mistakenly advise using vitamin A as treatment. Regardless of this or any other type of therapy, the disease will continue to progress at its own variable rate.

With the modern level of sophistication in producing foods for domestic animals, primary nutritional deficiencies would be rare unless dietary management is not appropriate for the species in question (see taurine deficiency). Most of the patients with PRA seen by this author have been apparently healthy. It is conceivable that there *is* a nutritional deficit but on a biochemical level. Thus, although there is sufficient nutritional intake, a defective or absent enzyme, for example, would still render the animal deficient. Research into this and other facets is ongoing and intensive.

In the meantime, the only adequate method of controlling this group of diseases is selective breeding. Affected animals should not be used, and timely neutering is recommended. Unfortunately, PRA is recessive in many (if not all) breeds, so that this leaves a large number of carrier animals that are undetectable by present diagnostic methods. Conscientious breeders may want to undertake a test-breeding program to identify phenotypically normal heterozygotes in their colonies. This combined with either early histologic (for those that are dysplasias) or electroretinographic examination will be a positive step toward eliminating this devastating disease.

Central Progressive Retinal Atrophy. Unlike PRA, central progressive retinal atrophy (CPRA) is a specific retinal epithelial dystrophy. It begins in the central (posterior) retina and proceeds peripherally. The retinal epithelial cells accumulate a light brown pigment and become hypertrophied to form individual giant cells or multicellular clumps of pigmented cells. The sensory retina is normal early in the disease, but soon the photoreceptor outer segments overlying the abnormal epithelial cells degenerate, followed by further degeneration of all outer retinal layers.

The process begins in the tapetal area temporal to and above the optic disk. At this time, altered vision is not clinically detectable. As the degenerative process intensifies and spreads, central vision is compromised but peripheral vision (particularly for moving objects) is normal. Late in the disease, the ocular fundus appears similar to that of late stage PRA but with the additional presence of pigment clumps.

The pigment in the epithelial cells is a normal lipopigment, which is increased in amounts. This may signify a primary metabolic defect of the retinal epithelial cells or perhaps a deficient or abnormal enzyme in the photoreceptor-epithelial cell environment. Although this is encouraging in terms of potential treatment or prevention, there is currently no beneficial therapeutic regimen. The disease is hereditary in many breeds of dogs, possibly dominant with variable penetrance, so that selective breeding is a plausible means of control.

Taurine Deficient Retinopathy and Feline Central Retinal Degeneration. Feline central retinal degeneration (FCRD) was originally thought to be a specific disease of unknown etiology that was only moderately progressive or non-progressive. Affected animals show no visual deficits but have ophthalmoscopic and electroretinographic abnormalities. Ophthalmoscopically, the lesion can vary from a small, circular area of retinal degeneration in the area centralis, to a larger, elliptical lesion with prominent nasal extensions or satellites. These lesions appear variably hyperreflective to dark, depending on the angle of incident light. The electroretinogram of these animals demonstrates a generalized cone abnormality.

It has been shown that cats fed a diet consisting only of dog food, or having casein as the only protein, develop similar disease (ophthalmoscopically) to that seen in FCRD cats. However, in these animals, continuation of the abnormal diet results in progression of the central lesion to complete retinal atrophy. Research has revealed that taurine, an aminosulfonic acid, is deficient in these diets. Taurine is necessary for proper retinal function, at least in the cat.

A question that might be asked now is whether FCRD cats were actually nutritionally deficient at one time but recovered before retinal damage had progressed too far, or whether FCRD and nutritionally induced retinal degeneration in the cat are separate diseases. Nevertheless, three points should be considered: (1) FCRD has not yet been shown to be hereditary, (2) improper nutrition in the cat is a significant cause of retinal degeneration, and (3) cats should not be fed an all dog food diet.

Taurine is almost absent in vegetables but is rich in meat, milk, or seafood. Cats apparently cannot synthesize adequate amounts of taurine and thus require an exogenous source. Although the progression of retinal degeneration in a deficient cat can be stopped by reversion to a normal diet, degeneration that has already taken place is permanent.

SUPPLEMENTAL READING

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