

IS THE CAT'S EYE BLIND, PAINFUL, OR CHANGING COLORS? Kerry L. Ketring, DVM, DAVCO

OPHTHALMOLOGY

Anterior uveitis or iridocyclitis is inflammation of the iris and ciliary body. This is the second most common ocular disease in cats, with feline herpesvirus type 1 (FHV-1)-related disease being number one. Many systemic diseases will first manifest as an anterior uveitis and the prognosis for not only the eyes, but for the life of the animal may depend on identifying the systemic disease. Since few cats die as adults from complications of FHV-1 or become irreversibly blind from the disease, you could view anterior uveitis as the most serious ocular disease in cats. Lymphoplasmacytic anterior uveitis is the most common cause of secondary glaucoma. Many etiologies of anterior uveitis also have zoonotic potential. These last two facts make it imperative that early diagnosis, etiology, and treatment protocol be obtained.

Signs

Pain

Ocular pain manifested by blepharospasms, squinting, prolapse of the third eyelid, and photophobia are common in anterior uveitis. This pain is caused by spasms of the ciliary body and therefore is reduced only by cycloplegics. Topical anesthetics will not reduce the signs quickly as they do in the case of corneal ulcers. Therefore, the application of a topical anesthetic is a good diagnostic test as to the cause of pain.

Decreased Intraocular Pressure

Active production of aqueous is reduced significantly in anterior uveitis. Consequently, the intraocular pressure (IOP) is reduced. This can frequently be determined by digital tonometry, but if measured with the Tono-Pen XL, an IOP of less than 10mmHg is often found. This may be the most sensitive sign of early disease and is the best test to monitor for improvement or for the most severe complication, secondary glaucoma.

Swollen Iris and Rubeosis Irides

The iris will be swollen or "puffy" in appearance. The normal small crypts in the iris will not be visualized. Not infrequently, small circular dilations termed ectropion uveae will be seen at the pupil margins. These are dilations in the two epithelial layers of the posterior iris caused by inflammation. Rubeosis iridis is neovascularization of the iris. This may give the entire iris or only a section, a reddish color. Multiple gray or pink nodules (Busacca nodules) are occasionally found scattered throughout the anterior surface of the iris stroma. These have been seen in cats with toxoplasmosis.

Miosis

In cases of anterior uveitis, the pupil will become miotic. This may result in a noticeable anisocoria. The affected or miotic pupil may further constrict with a focal beam of light. The consensual response to the non-affected eye should be normal. The affected pupil will not dark-adapt or dilate in dim light. Also, tropicamide 1% (Tropicacyl 1%, Alcon, Inc.) should completely dilate a pupil in 15 minutes. Unequal dilation of the pupils after application of tropicamide could indicate anterior uveitis in the small pupil. This has proven to be a very reliable and objective sign of anterior uveitis.

Corneal Edema

Anterior uveitis is frequently associated with damage or inflammation of the corneal endothelial cells termed endotheliitis. This will result in diffuse corneal edema. If severe, the corneal edema will prevent visualization of the anterior chamber and iris.

Deep Limbal Injection

Blood vessels may be prominent on the scleral side of the corneal-scleral junction. This is termed a ciliary flush. Also, straight vessels may extend out 1–4mm onto the cornea entirely around the corneal circumference. This brush border of ciliary vessels, frequently referred to as ciliary injection, can indicate deep corneal disease, but is most frequently associated with anterior uveitis. Unlike the superficial branching vessels, associated with corneal and scleral diseases, that take weeks to extend out onto the cornea, these vessels may appear in 24 hours.

Flare and Cells in the Anterior Chamber

A flare is the increased cloudiness of the aqueous. This is due to an increased protein content of the aqueous as it leaks from the damaged blood vessels in the iris and ciliary body. A flare is arbitrarily graded 1 to 4 depending on

the severity. A bright focal beam is directed into the eye and the path of the beam is viewed from an angle to determine the presence and degree of flare. A darkened room and bright focal beam are a must. Cells may be present in the anterior chamber. White blood cells, termed hypopyon, or red blood cells, termed hyphema, may settle in the inferior anterior chamber. In this case, cells can be visualized floating in the anterior chamber.

In cases of anterior uveitis and concomitant hyperlipidemia, the anterior chamber will fill with fat. This gives the anterior chamber a milky appearance and frequently prevents visualization of the iris and lens.

Keratic Precipitates

Keratic precipitates (KPs) are conglomerates of white blood cells, fibrin, and/or red blood cells, which adhere to the inferior endothelium. They may be pinhead-size masses or much larger masses called mutton fat precipitates. Their presence indicates a granulomatous type or chronic anterior uveitis.

Blindness

Total blindness is not a common sign of anterior uveitis. If the animal appears clinically or functionally blind and a tapetal reflex can still be demonstrated, additional causes of blindness should be evaluated. This usually indicates optic nerve or retinal disease. Lack of a positive dazzle reflex, regardless of the degree of aqueous flare, indicates posterior segment disease.

Causes of Anterior Uveitis

Various schemes have been used to classify the etiologies of feline anterior uveitis. No single categorizing scheme covers all cases. Even with a thorough history, a complete ocular and physical examination, and a laboratory profile including serology, as many as 50%–70% of the cases are still diagnosed as idiopathic by many investigators. I do not believe that a primary immune-mediated uveitis is a common entity in the cat. Even lymphoplasmacytic uveitis is most likely precipitated by an exogenous cause. As our knowledge and diagnostic capabilities increase, the percentage of idiopathic and presumed immune-mediated cases will decrease.

Trauma

Animals hit by cars or large blunt objects, such as baseballs, frequently develop an acute anterior uveitis. Physical examination following such trauma should always include a thorough ocular exam. Corneal lacerations always have anterior uveitis that must be treated after the laceration is surgically repaired.

Corneal ulcers, superficial and deep, frequently have an associated anterior uveitis. It is important to evaluate the anterior segment in every case of corneal ulceration.

Phacolytic

The lens protein is a foreign protein to the eye and the animal since it is normally contained and isolated early in utero within the lens capsule. In young animals with rapidly developing cataracts, anterior uveitis is common. The lens material liquefies and passes through the lens capsule to cause an immune reaction and severe anterior uveitis. In addition to the previous signs of anterior uveitis, the anterior chamber may be deeper and the cataractic lens will have a flat anterior surface and a wrinkled capsule; all of these are signs of a loss of lens material. In chronic cases, keratic precipitates are commonly found. If properly treated and controlled, vision may improve as the lens protein leaks through the lens capsule, thus reducing the size and density of the lens. If severe or not controlled, the inflammation will extend posteriorly resulting in posterior uveitis and retinal detachment. Phacolytic uveitis is not as common in the cat as it is in the dog where it is always associated diabetic cataracts.

Phacoclastic

Phacoclastic is considered a more severe form of inflammation resulting from trauma to the lens which results in rupture of the lens capsule. Trauma to the lens in the cat may lead to a lens-induced sarcoma.

Metastatic Ocular Tumors

Metastatic ocular tumors which cause anterior uveitis are rare in the cat compared to the dog.

Primary Ocular Tumors

Malignant melanomas of the iris, ciliary body, and, rarely, choroid are the cause of anterior uveitis only late in the course of the condition. Ciliary body adenocarcinomas also have the potential of causing anterior uveitis.

Medulloepitheliomas are rare in the cat. Initially, primary ocular tumors cause little inflammatory response. Feline lymphosarcoma complex is the most common neoplasia resulting in anterior uveitis in the cat.

Table 1. Etiology of Feline Anterior Uveitis - Infectious, Parasitic, and Neoplastic

Bacteria:

Bartonella sp.

Mycobacterium sp.

Septic lens implantation

Viruses:

Feline Leukemia Virus (FeLV)

Feline Infectious Peritonitis Virus (FIPV)

Feline Herpes Virus (FHV-1)

Feline Immunodeficiency Virus (FIV)

Mycotic:

All systemic mycotic infections

Parasitic:

Toxoplasma gondii

Cuterebra larva

Dirofilaria immitis

Encephalitozoon cuniculi

Onchocerca lupi

Leishmania sp.

Neoplasia:

Feline lymphosarcoma complex (LSA)

Metastatic neoplasia from a variety of primary sites

Primary intraocular neoplasia (FDIM, iridociliary adenoma)

Uveitis Masquerade Syndrome

Vector Borne Diseases

The incidence of tick-borne and vector disease has increased in the last five years, but still varies significantly depending on your geographic area. The incidence of chronic asymptomatic cases and polymicrobial infection makes it difficult to correlate ocular disease and systemic disease in all areas. Diagnoses based on serology, including polymerase chain reaction (PCR) procedures, may have resulted in increased awareness of prior existing diseases. Vector-borne diseases reported to date in cats include *Anaplasma phagocytophilum* (feline anaplasmosis), *Cytauxzoon felis*, *Bartonella* sp., *Leishmania* sp., and *Ehrlichia* sp. *Bartonellosis* is the only disease that has been frequently associated with anterior uveitis in the cat. Leishmaniasis is a very rare finding in the United States in cats that have never been out of the country

Bartonellosis in the cat as it relates to anterior uveitis has been, and still is, a debatable topic. Some individuals feel that there is no scientific proof that the disease is associated with anterior uveitis in the cat. My diagnosis of *Bartonella*-associated anterior uveitis has been based on a positive Western immunoblot test (FeBart™ National Veterinary Laboratory), serological testing in an attempt to rule out other etiologies, appropriate antibiotics, and rapid (less than seven days) improvement of all clinical signs. Most experts now recommend positive serology and a positive PCR or culture in order to make a definitive diagnosis of Bartonellosis. The newest test available is from Galaxy Diagnostics, Inc. (galaxydx.com). Their EnrichmentPCR™ test uses an enrichment growth medium prior to PCR testing and is reported to be the most sensitive test available. It is important to remember the test results would be negative if the cat was not bacteremic at the time of sampling. Since cats have been shown to develop a relapsing pattern of bacteremia, serology is also indicated to evaluate for prior exposure. Keep in mind that regardless of the test utilized, you are only identifying the organism or its prior presence. The testing does not prove that *Bartonella* is the cause of the disease, i.e., the anterior uveitis. It is at this point that controversy still abounds!

Miscellaneous

Bilateral anterior uveitis has been reported in cats with platelet dysfunctions and other bleeding disorders, renal disease, and hypertension. Systemic hypertension has to be considered the number one cause of anterior uveitis in the geriatric cat when there is blood in the anterior chamber or iris stroma. In any case of bilateral anterior uveitis, a complete physical and laboratory evaluation is indicated.

Diagnosis

The diagnosis of anterior uveitis is made based on the clinical signs observed. The etiology is based on serology, associated systemic signs, and possibly a paracentesis of aqueous. In severe cases, especially if the eye is irreversibly blind or if the animal's life is in jeopardy, enucleation and histopathology to obtain a definitive etiology is indicated. Enucleation and histopathology reports frequently list "lymphoplasmacytic anterior uveitis, etiology unknown." This is usually considered an immune-mediated condition. But toxoplasmosis and bartonellosis have also been shown to have the same finding.

Treatment

In all cases of anterior uveitis, the entire globe and animal should be thoroughly evaluated. This is especially true if the cat is blind and in cases of bilateral anterior uveitis with possible systemic disease. In many cases, treatment will consist of only topical medication. Topical corticosteroids, cycloplegics, and mydriatics are the minimal drugs that will be used to treat an uncomplicated anterior uveitis. Systemic diseases, such as mycosis, will have to also be treated specifically.

Mydriatics and Cycloplegics

Mydriatics are necessary to dilate the pupil and reduce the incidence of posterior synechia, secondary cataracts and glaucoma. Cycloplegics paralyze the ciliary body, which reduces pain. Atropine does both functions and should be used to effect, once daily. Atropine also improves vascular permeability and helps reduce aqueous flare. Keep in mind that 1-drop of 1% atropine delivers .5mg of atropine. Therefore, an animal can be systemically atropinized by topical applications. This could, in addition to other problems, cause a decrease in tear production.

Corticosteroids

Corticosteroids are needed for their anti-inflammatory effect, inhibition of fibroblastic proliferation, and they improve vascular permeability. Topical administration is preferred if only the anterior uvea is involved and if there are no corneal ulcers. Dexamethasone and prednisolone acetate are preferred because of their potency and bioavailability. In severe cases, application is every two to four hour initially. If corneal ulcerations are present, systemic corticosteroids may be used. Systemically, they do not interfere with epithelialization. The reported contraindications for the use of corticosteroids should be kept in mind. Personal preference is oral prednisolone initially at a dosage of 1mg/lb divided b.i.d.

Nonsteroidal Anti-inflammatory Drugs (NSAID)

Prostaglandins have been shown to play an important role in ocular inflammation. Anti-prostaglandins reduce capillary permeability, stabilize lysosomal membranes, and suppress leukocyte migration. The mechanism of action of anti-prostaglandins is different than corticosteroids and therefore the two are frequently used together. Currently available NSAIDs include flurbiprofen (Ocufer® , generic), suprofen (Profenal®), dichlofenac (Voltaren®, generic), and ketorolac (Acular®). Two newer products, brofenac (Xibrom®) and nepafenac (Nevanac®), boast twice daily efficacy. The topical anti-prostaglandin, .03% flurbiprofen sodium, is my drug of choice. Nevanac® is used by many ophthalmologists in severe cases and/or when frequent administration is not possible.

Antibiotics

Specific antibiotics/antifungals may be started if specific etiologies are suspected or proven, such as toxoplasmosis (clindamycin hydrochloride, i.e., Antirobe®, Upjohn; Ponazuril 20mg/kg q24h), tick-borne disease (doxycycline), and fungal disease (itraconazole, i.e., Sporanox®, Jansen). Azithromycin is no longer recommended in the treatment of bartonellosis. Its use has been associated with the development of resistant strains. Doxycycline at 10mg/kg q.d. to b.i.d. initially for seven days is now recommended. If the clinical response is favorable, it is continued two weeks past resolution of all signs or for a minimum of 28 days. If the clinical response is poor, the fluoroquinolone orbifloxacin at 2.5–7.5 mg/kg q.d. for two weeks is recommended in place of doxycycline. However, the use of any of these medications does not replace the specific treatment for the anterior uveitis. Topical antibiotics should not be routinely dispensed in cases of anterior uveitis. They have no clinical benefit, are an added burden for the owner and cat, and, in many cases, cause topical irritation to cats.

Sequela

Glaucoma

Remember that 97% of feline glaucoma cases are secondary to various etiologies of anterior uveitis. Dilating the pupil will reduce the incidence of secondary glaucoma due to posterior synechia. With posterior synechia, the iris will start to bulge forward due to the aqueous pressure in the posterior chamber. This bulging is called iris bombé and causes the anterior chamber to become shallow.

Broad peripheral synechia may also interfere with normal aqueous outflow. The IOP should be low in all cases of anterior uveitis and a normotensive eye in the presence of severe anterior uveitis should be considered a secondary glaucoma.

Frequently, the IOP will start to elevate as the anterior uveitis improves with treatment because of the production of aqueous increasing back to its normal level. If the IOP starts to rise above normal or near normal as the aqueous flare improves, the topical carbonic anhydrase inhibitor dorzolamide should be instituted t.i.d. in an attempt to reduce aqueous production and prevent glaucoma. Surgery is indicated in many cases of secondary glaucoma, especially if the inflammation has completely resolved and the pressure cannot be controlled medically. The surgery of choice would be some form of iridectomy. Irreversibly blind glaucomatous eyes in cats should be enucleated. Intravitreal injection and evisceration with intrascleral prosthesis are also seldom performed in the cat. This is due in part because of concern for the possible development of feline post-traumatic sarcomas.

Synechia

Anterior synechia would result in a full thickness corneal scar, termed an adherent leukoma. Posterior synechia would result in a capsular and cortical cataract that may or may not be progressive. Broad peripheral synechia is an adhesion of the base of the iris to the limbal endothelium of the cornea. Surgery is not indicated unless a complete synechia results in glaucoma.

Cataracts

Anterior capsular and subcapsular opacities are not uncommon following anterior uveitis. Pigment deposits are frequently present on the anterior lens surface. Cataracts are also caused by posterior synechia. If the damage to the lens is severe or prolonged, a mature cataract may develop.

Corneal Edema

If the damage to the endothelial cell layer is severe, corneal scars or edema may persist in part or the entire cornea. Corneal edema may necessitate treatment.

Iris Atrophy

Severe uveitis may result in iris atrophy. Uveal pigment should also be present on the anterior lens surface if the atrophy is caused by anterior uveitis.

Phthisis Bulbi

If the damage to the ciliary body and processes is severe, it will destroy the structure. The eye will become very soft and shrink in size. The eye is then blind, but comfortable. If the globe becomes too small, not only will the nictitans prolapse across the cornea, but the lids will become entropic. When this is severe and causes constant irritation and tearing, either the globe should be removed or the entropion surgically corrected.

Post-Traumatic Ocular Sarcoma (FPTOS)

This is reported to be the third most common intraocular tumor in cats. In many cases, there is no history of previous trauma or lens damage. There may be a long latency period of months to years between initial "trauma" and the severe neoplastic proliferation. Cases have been reported of growth outside of the globe into the orbit. FPTOS should be considered as the most severe sequelae to anterior uveitis and not a common cause of uveitis.