Feline Uveitis: Diagnosis and Treatment

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Uveitis is the inflammation of any or all parts of the vascular tunic of the eye; the vascular tunic includes the iris, the ciliary body, and choroid. A good knowledge base, up-to-date reference materials, and good instruments will improve the diagnosis of uveitis. Feline uveitis can be caused by numerous infectious agents in addition to neoplasia and less likely trauma. The infectious causes most commonly associated with feline uveitis include feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis, systemic fungal infections, toxoplasmosis, and bartonellosis. Neoplastic causes of uveitis can be primary or secondary. Iris melanoma is the most common primary uveal neoplasia and trauma-associated sarcoma is the second most common primary uveal neoplasia. Treatment for the clinical signs of anterior uveitis include topical steroidal or non-steroidal anti-inflammatory agents, parasympatholytic agents for ciliary spasm, to keep the pupil dilated, and to prevent posterior synechia. Posterior uveitis should be treated with systemic medications that will address the underlying cause. Enucleation of blind, painful eyes not responsive to medications is a means to alleviate the animal's discomfort and to further diagnose the underlying cause.
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The uvea is the middle or vascular tunic of the eye that is covered externally by the fibrous tunic that includes the sclera and cornea.[1] The uvea provides the majority of the blood supply to the inner nervous tunic or neural retina and is comprised of three components: the iris, the ciliary body, and the choroid. The iris is the anterior most portion of the uvea that forms an incomplete diaphragm between the anterior and posterior chambers and it functions to regulate the amount of light entering the posterior segment of the eye. Two muscles that regulate the iris' position are the sphincter (or constrictor) muscle and the dilator muscle. The sphincter muscle is a flat band of circular bundles of unstriated muscle fibers that functions to determine the shape of the pupil and is primarily under parasympathetic control. The dilator muscle is composed of a single layer of unstriated muscle fibers that is under sympathetic control. The ciliary body is located posterior to, but continuous with, the iris and is considered part of the anterior uvea. The anterior aspect of the ciliary body is the pars plicata and it produces aqueous humor. The posterior aspect of the ciliary body is the pars plana and it produces some vitreous humor. The tight junctions between the two epithelial layers of the ciliary body are the site of the blood-aqueous-barrier, which limits access to the

eye by large molecules and cells. The choroid is the posterior portion of the uvea that is continuous anteriorly with the ciliary body and extends posteriorly to encircle the optic nerve. The choroid is composed of blood vessels and pigmented connective tissue or stroma; it is located external to the retina and supplies nutrition to the outer retina. The choroid has four layers, from innermost (adjacent to Bruch's membrane and the retinal pigment epithelium) to outermost (adjacent to the sclera), they include the choriocapillaris, the medium-vessel layer and tapetum, the large-vessel layer, and the suprachoroidea. The tapetum is in the dorsal portion of the fundus and lies within the medium-vessel layer of the choroid and serves to amplify incoming light to enhance vision. Because the blood vessels of the choroid are permeable to low molecular weight compounds and proteins, the tight junctions between the retinal pigment epithelial cells create a barrier between the choroidal tissue fluid and the retinal tissue fluid.[2]

Diagnostics

In addition to a good knowledge base and up-to-date reference materials, good quality diagnostic instruments are essential for complete assessment of the eye. A good light source such as a Finoff ocular transilluminator (a diffuse light source) and a small hand held slit lamp (a focal light source) are excellent instruments for the evaluation of anterior segment clinical signs. The hand held slit lamps are affordable and available from medical supply distributors that sell ophthalmic instruments. Applanation tonometry is important for determining the intraocular pressure (IOP) and the most

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commonly used instrument is the Tono-Pen® VET. A fundus examination is performed by direct or indirect ophthalmoscopy. Direct ophthalmoscopy requires either a direct ophthalmoscope or a newer instrument, the PanOptic (Welch Allyn), which allows a larger field-of-view (5×) than the traditional direct ophthalmoscope. The method most widely used by veterinary ophthalmologists is indirect ophthalmoscopy and requires a bright light source such as a transilluminator and an indirect lens. The most commonly used indirect lenses are the 20 or 30 diopter (D) lenses. In general, a lens with a larger dioptric strength (eg, 30D) is easier to use with a miotic pupil while most indirect lenses can be used in a dilated pupil (eg, 20 or 30D). A lens with lower dioptric strength will allow a smaller field-of-view but better magnification and a lens with higher dioptric strength will allow a larger field-of-view but magnification is diminished.

A complete history and vaccination status, if available, are imperative pieces of information to collect when evaluating cats with uveitis. In addition, a good general physical examination with a complete blood count, serum biochemistry panel, and urinalysis should be part of the initial work-up because many causes of uveitis in cats are secondary to systemic diseases. In addition, other diagnostic tests including serum titers, polymerase chain reaction (PCR), cytology, and biopsy may be necessary to specifically diagnose the etiological cause of uveitis.

Uveitis

Uveitis refers to inflammation of the vascular tunic or uvea. Anterior uveitis or iridocyclitis refers to inflammation of the iris and ciliary body and posterior uveitis refers to inflammation of the choroid. Panuveitis refers to inflammation of both the anterior and posterior uvea. There are numerous causes of feline uveitis.

Clinical Signs

General clinical signs of anterior uveitis are numerous and often nonspecific for the etiology. They include aqueous flare (turbidity of the aqueous humor because of accumulation of plasma proteins within the anterior chamber resulting from breakdown of the blood-aqueous-barrier), ciliary flush (hyperemia of the deep anterior ciliary vessels), conjunctival hyperemia (evident as dilated, tortuous and mobile vessels within the conjunctiva), corneal edema, decreased intraocular pressure (decreased production of aqueous humor and increased uveoscleral outflow), decreased vision, hyphema (blood within the anterior chamber), hypopyon (inflammatory cells within the anterior chamber), iris thickening, keratic precipitates (accumulation and attachment of inflammatory cells, fibrin, and pigment to the corneal endothelium), miosis (pupil constriction), pain (blepharospasm and epiphora), iris color change, and with chronicity, there can be posterior synechia (iris margin adhered to anterior lens capsule), cataract, lens subluxation/luxation, rubeosis iridis (neovascularization over the surface of the iris), and secondary glaucoma.

Specific Causes

Common specific causes of feline uveitis include feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), *Toxoplasma gondii*, *Bar-*

tonella henselae, fungal infections (often region-dependent), neoplasia, and trauma.

Feline Leukemia Virus

Feline leukemia virus (FeLV) is a vertically and horizontally contagious immunosuppressive retrovirus with oncogenic potential.[3] FeLV has direct effects on lymphoid tissue or bone marrow that result in ocular and systemic clinical disease.[4] Ophthalmic disease is often the initial presenting clinical manifestation of FeLV, similar to dogs and humans.[3] Uveitis due to FeLV can manifest as iridocyclitis, hypopyon, mutton fat keratic precipitates, secondary glaucoma, chorioretinitis, retinal detachment, or chorioretinal masses. In addition to uveitis, other ocular signs can include keratitis, orbital masses, eyelid masses, subconjunctival and nictitating membrane masses, and anterior chamber and anterior uveal tumors, eg, iridal nodules, and white-pink masses in the anterior chamber or adhered to the anterior iris. Diagnosis of FeLV is by peripheral blood ELISA, then confirmed with either an immunofluorescent antibody test or an ELISA antigen test 3 to 4 months after initial diagnosis. If the FeLV infection regresses and the viremia is terminated, then the repeated ELISA will be negative.[3] Treatment for the uveitis is discussed below. Systemic therapy is supportive care.

Feline Immunodeficiency Virus

Feline immunodeficiency virus (FIV) is an immunosuppressive retrovirus with oncogenic potential[5] and the primary mode of transmission is through biting.[6,7] Ocular disease in cats with FIV occurs either from direct viral damage or from opportunistic infections.[8] Typical ocular presentation can include mild to moderate chronic anterior uveitis characterized by lymphocytic plasmacytic inflammation.[3,9] Other ocular clinical signs can include secondary glaucoma, pars planitis (cellular infiltrate in the anterior vitreous),[8] and less commonly, choroidal involvement.[3] Coinfection of cats with other ocular pathogens, including *Chlamydia psittaci* and *T. gondii*, augments the ophthalmic manifestations of the other pathogens.[3] Diagnosis of FIV is by an ELISA for circulating antibodies against FIV, though more sensitive assays can be used and include polymerase chain reaction (PCR) for viral nucleic acids or viral culture.[3] Treatment for the uveitis is discussed below. Systemic therapy is supportive care.

Feline Infectious Peritonitis

Feline infectious peritonitis (FIP) is a coronavirus that causes chronic and progressive anorexia, weight loss, depression, fluctuating fever, weakness, and peritoneal and thoracic involvement. All cats are susceptible to FIP infection but it most commonly affects those between 3 months and 3 years of age.[10] It is estimated that 5 to 12% of seropositive cats will develop clinical signs typical of FIP.[11] Ocular involvement occurs more commonly in the noneffusive ("dry") form than with the effusive ("wet") form.[12] FIP breaks down the blood-ocular-barrier causing pyogranulomatous uveitis and fibrinous exudation into the anterior chamber. Posterior segment involvement results in pyogranulomatous chorioretinitis and retinal vasculitis manifested as perivascular cuffing, exudative retinal detachment, and optic neuritis. Diagnosis of FIP cannot be definitively made ante mortem except for histopathologic examination of biopsied tissues. Typical histopathologic findings of ocular tissues include lymphocytes, plasma cells, neutrophils, and macrophages, ie, pyogranulo-

matous inflammation.[13] Treatment for the uveitis is discussed below. Systemic therapy is supportive care.

T. gondii

T. gondii is one of the most common intracellular protozoal parasites affecting animals and humans. The eye is a target organ and the domestic cat is the definitive host.[14,15] In addition to anterior uveitis, other ocular clinical signs can include granulomatous chorioretinitis and retinal vasculitis. The typical posterior segment lesions are multifocal, dark gray, hyporeflective lesions in the tapetal fundus and fluffy white lesions in the nontapetal fundus.[15] The definitive method of diagnosing toxoplasmosis is by histopathologic identification of the organism in a biopsied or postmortem sample. Other methods available for diagnosis are ELISA and immunofluorescent antibody tests. Serologic results consistent with active toxoplasmosis include an IgM titer (acute disease-phase antibodies), a high IgG titer (antibodies that can remain high for 2 years or longer), or, a rising IgG titer when paired serum samples are evaluated. Other available assays include PCR, which when combined with traditional serology, may enhance the sensitivity and specificity of the diagnosis. Additional diagnostic testing performed by veterinary ophthalmologists may include aqueocentesis to compare toxoplasmosis-specific antibodies in the aqueous humor and serum concurrently.[15] The most commonly used systemic treatment of toxoplasmosis is clindamycin hydrochloride at a dose of 12.5 mg/kg orally twice daily for 14 to 21 days. New antitoxoplasmic drugs are under investigation for use in humans and may be useful in cats. Treatment for the uveitis is discussed below.

Bartonella henselae

B. henselae is a fastidious, hemotropic, Gram-negative organism associated with cat scratch disease in humans. Cats are the main reservoir of this organism with worldwide distribution. Depending on the geographic location, prevalence of seropositive pet cats varies widely; 67% in Florida, 62% in California, 28% in Washington, DC, 12% in Chicago, 32% in Jordan, and 43.5% in Italy.[16-18] Major risk factors identified with prevalence of infection included flea infestation, living outdoors, or being adopted from a shelter or as a stray. Anterior uveitis has been reported as a clinical manifestation of bartonellosis in cats after natural exposure and experimental inoculation.[19] Diagnosis of bartonella uveitis may be difficult because of the high seropositivity in the feline population. However, Western blot analysis and/or PCR may be used for diagnosis when concurrent clinical signs suggest this as a likely underlying cause. Systemic treatment for bartonellosis is azithromycin at a dose of 10 mg/kg once daily for 21 days. All cats in the household should be simultaneously treated. Topical therapy for uveitis is described below.

Fungal Infections

Fungal infections are important causes of uveitis in all animals, including cats. In general, preexisting immunosuppressive disease does not significantly predispose cats to systemic fungal diseases.[20] Systemic antifungal treatment for all of the described fungal organisms includes fluconazole or itraconazole. The preferred treatment for ocular fungal infections is fluconazole, a triazole drug, with few side effects, that penetrates the eye and brain well.[20]

Cryptococcus neoformans is the most commonly diagnosed

feline disseminated fungal disease.[21] *C. neoformans* is a yeast-like basidiomycete fungus that is commonly found in soil and pigeon droppings. Two varieties, *C. neoformans* var. *neoformans* and *C. neoformans* var. *gatti*, cause disease in cats.[22] The primary mode of infection in cats is via inhalation into the rostral or caudal nasal cavity. If cryptococcal organisms are inhaled into the caudal nasal cavity, clinical signs of rhinitis may be absent allowing the infection to spread through the cribriform plate and into the olfactory bulbs and tracts, causing meningitis and, in some cases, optic neuritis.[23] Hematogenous spread from the nasal cavity can result in chorioretinitis.[23] Clinical signs of anterior uveitis, including keratic precipitates and fibrin in the anterior chamber, are seen more commonly in cases with chorioretinitis and clinical signs can be mild to severe. Optic neuritis is the second most common manifestation of cryptococcosis. Other less common ophthalmic signs that have been reported include retrobulbar abscess,[24] severely thickened and protruding nictitans,[25] and Horner's syndrome because of an aural mass.[26]

Histoplasma capsulatum is a saprophytic dimorphic fungus found in areas of temperate climates between Texas and the Ohio, Missouri, and Mississippi river valleys, and it grows well in nitrogen rich soils containing bat and bird droppings. Cats are equally likely to develop histoplasmosis as are dogs but ocular signs may occur more often in cats with disseminated histoplasmosis than with other fungal infections.[21] The most common clinical ophthalmic sign is granulomatous chorioretinitis; other clinical signs can include conjunctivitis and chemosis, anterior uveitis, retinal detachment, and optic neuritis.

Blastomyces dermatitidis is a dimorphic fungus found in moist, rich, acidic soil. Blastomycosis generally presents as a unilateral or bilateral anterior or posterior pyogranulomatous uveitis. Clinical signs can include severe aqueous flare, keratic precipitates, rubeosis iridis, retinal detachments, and intraretinal and subretinal pyogranulomas.[27]

Coccidioides immitis is a dimorphic fungus found in the soil not commonly diagnosed in cats.[20] There are few reports of ocular coccidioidomycosis in the literature. Clinical presentation is associated with pyogranulomatous uveitis.

Other fungal infections reported in cats include infection with *Aspergillus sp.* and *Candida albicans*.

Noninfectious Causes of Uveitis

Primary and secondary uveal neoplasia can result in uveitis. Iris melanoma or melanocytoma is the most common primary uveal neoplasia in cats[28] and can begin as a benign flat freckle-like lesion. Some of these freckles never progress, but others can become raised and develop multiple lesions on the iris. Clinical signs can include dyscoria or misshapen pupil, iridal thickening, anterior uveitis, and secondary glaucoma. The metastatic rate of feline iris melanoma is estimated to be 63%. Eyes with iris melanoma or melanocytoma that progress quickly and result in active uveitis or secondary glaucoma should be enucleated for therapeutic and diagnostic purposes and because of the high metastatic rate. Histopathologic evaluation by a veterinary ophthalmic pathologist is recommended.

Trauma-associated sarcomas are the second most common primary ocular tumor in cats. These are highly malignant neoplasms that are incited by previous trauma to the eye. Often the traumatic event is an average of 5 years before

diagnosis. Clinical signs include chronic uveitis, secondary glaucoma, intraocular hemorrhage, and single to multiple white-pink masses. Early enucleation is important because the tumor will course up the optic nerve and metastasize to regional lymph nodes.[28]

Other ocular neoplasms include primary ciliary body adenomas or adenocarcinomas, lymphosarcoma associated with FeLV, and metastatic uveal neoplasms.

Treatment

Specific systemic antimicrobial agents for infectious causes of uveitis are noted under each specific section. However, anterior uveitis is also managed topically and the goal is to quickly decrease inflammation, which will minimize damage to intraocular structures.

Medical management of anterior uveitis should be started immediately to prevent the development of secondary glaucoma. Topical therapy will not compromise the immune system of the patient. Topical 1% prednisolone acetate or 0.1% dexamethasone ophthalmic suspensions are potent steroidal anti-inflammatory medications that enter the eye at therapeutic concentrations but will not affect the posterior segment. Therefore, if posterior uveitis is present, appropriate systemic therapy is imperative. Topical steroidal medications should be used initially every 4 to 6 hours in cases of significant uveitis then tapered slowly as clinical signs resolve. Alternatively, topical nonsteroidal anti-inflammatory medications, eg, flurbiprofen, suprofen, or diclofenac, may be used if the dosing of steroids is detrimental to the patient (presence of Herpesvirus keratitis or conjunctivitis) at a dose of one drop every 8 to 12 hours. Cycloplegic parasympatholytic drugs such as atropine or tropicamide are used to dilate the pupil, manage pain by paralyzing the ciliary body muscles, and prevent posterior synechia. Atropine ointment is preferred in cats because of its bitter taste and is used once to twice daily. An alternative cycloplegic medication, if a risk of secondary glaucoma exists, is tropicamide. Tropicamide is a short acting parasympatholytic that typically lasts 4 to 6 hours and can be discontinued if the intraocular pressure becomes elevated.

Secondary glaucoma should be managed concurrently with uveitis, if present. If the IOP is elevated (compared with the contralateral unaffected or lesser affected eye, or greater than 18 mmHg), then discontinue atropine or tropicamide and begin topical antiglaucoma therapy. Topical carbonic anhydrase inhibitors include dorzolamide and brinzolamide. These are used at a dose of one drop three times daily. A new family of antiglaucoma medications, the prostaglandin analogs including latanoprost and travaprost are contraindicated in cases of primary uveitis and secondary glaucoma because they may promote further inflammation.

Enucleation of blind painful eyes that do not respond to therapy is the best treatment for the patient. In addition to alleviating pain and discomfort, histopathologic evaluation will also be diagnostic.

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