

Viral Causes of Uveitis in Cats

Assos. Prof. Alexandra Trbolová, DVM, PhD.

Clinic of Small animals
University of veterinary medicine and pharmacy in Košice
Komenského 73
041 81 Košice
Slovenská republika

STRESZCZENIE:

Zapalenie błony naczyniowej przedniego odcinka oka u kotów może obejmować nie tylko tęczęwkę ale też przednią część ciała rzęskowego oraz naczyniówkę. Czasami stan zapalny dociera też do siatkówki. Nie wszystkie zapalenia związane są z patogennym zakażeniem. Często powodowane są urazem lub rozrostem nowotworowym, a część z nich ma tło nieznane (idiopatyczne). Objawy kliniczne "uveitis" to bolesność i zaczerwienienie oka, zwężona źrenica, nadwrażliwość na światło, nadmierne łzawienie, niskie ciśnienie płynu wewnątrzocznego. Czasami dochodzi do wylewu krwi do komory przedniej oka. Zawsze w komorze przedniej występuje efekt Tyndalla.

INTRODUCTION:

Anterior uveitis in cats may involve the iris, or both the iris and the anterior part of the ciliary body. Intermediate uveitis predominantly involves the posterior part of the ciliary body, posterior uveitis involve the choroid, but close association of the retina means that inflammation of both choroid and retina is the usual situation. Not all uveitis are caused by pathogens. Some results from trauma, some from cancer. Often no clear cause can be found and the occurrence is labeled "idiopathic" - we can't figure out what the cause is. Clinical signs include pain, photophobia, blefarospasm, lacrimation, inflammation hyperaemia of visible vessels, aqueous flare, hyphaema, miosis, low intraocular pressure and swollen iris with loss of iris detail.

Słowa kluczowe : Uveitis, Zapalenie błony naczyniowej, Efekt Tyndalla, Zwężenie źrenicy, Aqueous flare, Nadmierne łzawienie, Niskie ciśnienie oczne, FIV, FIP, FeLV, FHV-1.

Key words: Uveitis, Tyndall effects, Aqueous flare, Miosis, Epifora, Low IOP, Hyperemia of visible vessels, FIP, FIV, FeLV, FHV-1.

Feline immunodeficiency virus (FIV)

A significant proportion of cats with uveitis are infected with FIV, usually in the absence of infection with any other agent commonly associated with uveitis. There is no consensus as to how precisely FIV infection might lead to uveitis. It is possible that viral replication in cells of the uvea or vascular tissue may have a direct pathogenic impact. This role could involve hypersensitivity responses to deposition of antigen-antibody complexes such as is known to happen with glomerular nephritis in FIV+ cats and has also been

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implicated in FIP-induced uveitis. Other possible causes involve autoimmune responses sparked by cross-reactivity between viral and uveal proteins, or exposure of uveal proteins to immune attack because of virally induced disruptions of the blood-ocular barrier, or virally induced alterations in normal suppressor-cell function and self-tolerance - recognition of one's own tissue, known actions of FIV. Abnormal levels of antibody activity in the eyes of cats with uveitis have frequently been noted. (Chang i Carter) (English, Davidson i Nasisse)

There are no features of primary FIV-associated uveitis that absolutely distinguish it from uveitis caused by other pathogens, it does have some characteristic tendencies. Anterior uveitis, for instance, is universally acknowledged to be most common. The incidence of anterior uveitis in cats with FIV is noteworthy because posterior involvement with inflammation of the retinal vasculature is the most common ophthalmological finding in patients with HIV. It is generally acknowledged that primary FIV-associated uveitis is mild to moderate in severity, but more usually chronic than acute in nature. The disease is usually seen in cats older than 5 years with symptoms often unnoted by the owner prior to veterinary examination. (Fontenelle i Powell) (Gionfriddo) (Ishida, Shibana i Tanaka)

FIV occurs most often in adult, free – roaming, nonpedigree cats and is more common in males than females. Clinical problems associated with FIV infection rarely occur in isolation and other signs, together with haematological changes, are often found.

There is no single feature of primary FIV-associated uveitis that will be found in 100% of instances, but there are findings that are perhaps more likely than not to be seen, particularly because of its tendency to be chronic. Clinical symptoms are usually nonspecific and include:

- 1. Tearing and blepharospasm.** Blepharospasm and reflex tearing are usual symptoms of anterior uveitis.
- 2. Aqueous flare.** Aqueous flare is the characteristic mark of anterior uveitis and indicates a breakdown of the blood-aqueous barrier that keeps the aqueous fluid clear by preventing passage of protein into the anterior chamber, and increased permeability of the ocular vasculature, leading to presence of inflammatory cells within the aqueous [Townsend]. Normally, the path of a beam of light directed by an examiner into the anterior chamber is invisible or nearly so. With anterior uveitis the beam is well outlined, as dust motes will make light entering a window visible (the "Tyndall effect"). The flare is graded +4 to +1, depending on the level of light scattering produced by the opacity of the fluid.
- 3. Snowbanking.** Intermediate uveitis (pars planitis) is usually marked by white coalescing infiltrates in the anterior vitreous that appear as puffy "snowbanks" visible peripherally along the ora serrata (the area below the end of the choroid and behind the ciliary body) and frequently extending over the pars plana. The incidence of pars planitis in FIV+ cats is unusual enough that some authorities associate it particularly with FIV infection.
- 4. Periperal iridal hypemia.** The iris becomes swollen and engorged with blood along it periphery
- 5. Dyscoria.** The pupil assumes an abnormal shape.

6. Lymphoplasmacytic nodules. Nodules formed by aggregates of lymphocytes and plasma cells and the proliferation of small vessels upon the surface of the iris (“neovascularization”) often accompany chronic uveitis like that associated with FIV. Conversely, the granulomatous (neutrophilic) lesions often observed in uveitis caused by FeLV and FIP are generally absent with FIV. There is also a general paucity of retinal lesions by comparison to cats with uveitis from other causes .

7. Posterior synechia. Adhesion of the iris to the envelope covering the lens, a feature of chronic anterior uveitis.

8. Globe hypotomy and secondary glaucoma. Anterior and intermediate uveitis are accompanied by abnormally low pressure (hypotomy) in the aqueous fluid. Because of the generally more chronic nature with FIV-involvement, the inflammation-induced changes in the normal outflow pathway of fluid often lead to glaucoma (elevated pressure in the vitreous fluid).

9. Anterior subcapsular cataracts. Clouding of the lens, particularly the forward-facing portion, another consequence of chronicity. (Chang i Carter) (English, Davidson i Nasisse)

Feline infectious peritonitis (FIP)

Feline infectious peritonitis is one of the most common causes of uveitis in cats. FIP is found more frequently in younger cats than older cats and is more common in pedigree cats kept in multicat household. Nonophthalmic signs of this immunemediated disease are very variable but usually include nonspecific signs of illness such as lethargy, pyrexia, inappetence and weight loss. Neurological signs are common, and progressive, although they may also affect the posterior uvea. Both eye are often involved, although the lesion are not bilaterally symmetrical. The pathogenesis is associated with perivascular pyogranulomatous inflammation and subsequent breakdown of the blood aqueous barrier. Inflammatory cells and plasma proteins such as fibrin leak into the aqueous or vitreous, giving rise to aqueous flare, keratic precipitates, and hypopyon in the anterior chamber or vitritis when the vitreous is involved. Inflammation of the iris vessels, and sometimes frank hyphema. If it is possible to examine fundus a range abnormalities may be observed. Serum hyperproteinaemia is associated with characteristic hyperviscosity if total protein levels are high enough. Intense vasculitis and perivascular exudates; focal or diffuse chorioretinitis, choroidal exudation, retinal oedema and/or haemorrhage may be observed. Retinal detachments can occur in some cases. Optic neuritis may be present.

Feline leukemia virus (FeLV)

FeLV is an immunosuppressive retrovirus like FIV. Two disease courses occur in cats infected with FeLV: persistent viremia with progressive infection or and self-limiting, regressive infection. It is well established that cats infected with FeLV who are also infected with FIV have a greater likelihood of developing progressive infection and that co-infected cats have a greater liability to secondary diseases than those with either infection alone. Ocular diseases generally have only a small association with FeLV, and uveitis in cats with

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FeLV infection is probably not a direct result of the virus but rather related to secondary invasion of infectious agents caused by immunosuppression or FeLV-related cancer. Lymphosarcoma, is the most common cancer in cats with FeLV and is even more common in those coinfecting with FIV. Lymphoma is a significant cause of uveitis in cats generally and in particular in FeLV positive cats, in whom the lymphoma is induced directly by the virus rather than indirectly, as in the case of FIV. Important information is, that FeLV positive cats with lymphosarcoma of the eye and uveitis had a reduced survival rate compared to cats without concurrent uveitis. These cats were more likely to have advanced disease; hence both uveitis and FIV may darken the prognosis for ocular lymphosarcoma. Common findings on the initial presentation is usually a mild, with anterior uveitis, which may progress to inflammation of all intraocular tissue (panuveitis) or frank tumor formation. Other findings may include corneal masses, blood in the anterior chamber between cornea and lens, retinal degeneration, and hemorrhage. FeLV-induced lymphosarcoma often presents as thickening of the iris with associated flesh-colored lesions. These lesions are most often bumpy but may be diffuse in a way difficult to distinguish from uveitis from other causes. (Willis)

Feline herpesvirus (FHV-1)

FHV - 1 herpes is a common feline upper respiratory virus that produces an infection that is chronic in most cats and can be reactivated periodically, often after periods of stress. Some studies suggest that cats infected with FIV may be prone to herpesvirus infection and may experience more severe symptoms. Involvement of the eye is a characteristic feature of infection. The most common clinical ocular manifestations of FHV-1 are conjunctivitis and keratitis, but anterior uveitis may be another manifestation of the infection. The virus does not seem to be directly pathogenic intraocularly, but there is a growing suspicion among researchers that much of what is currently classed “idiopathic uveitis” is caused by secondary immune responses to its presence. Herpes DNA has been found in the aqueous fluid of 14% of cats with diagnosed with “idiopathic” uveitis, with 50% registering local production of antibody against it. Herpes has an affinity for nerve tissue, and it has been proposed that FHV-1 gains entry to the interior of the eye via nerve fibers. Common findings in herpes-induced uveitis is anterior in character and lacks distinguishing features from idiopathic anterior uveitis: nonspecific signs of ocular discomfort, miosis, corneal precipitates, blood or proteinaceous material in the anterior chamber. (Maggs, Lappin i Nasisse) (Pedretti, Passeri i Amadori) (Poland, Vennema i Foley) (Willis).

Treatment of viral – caused uveitis

Therapy for uveitis is both specific and nonspecific. Nonspecific therapy addresses inflammation, pain, and such effects of chronic uveitis as synechia formation (adhesion of iris to lens). Specific therapy addresses the pathogenic cause of the uveitis, plus any modifications of nonspecific therapy that might be called for with individual pathogens. Another important factor is the location of the uveitis: the closer to the front of the eye the inflammation is, the more likely topical treatment is to be helpful; the more posterior the inflammation, the more likely that systemic medicating will be called for. Nonspecific therapies - these generally

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include two classes of drugs, anti-inflammatories and mydriatics to dilate the pupil; NSAIDs may assist dilation by blocking the prostaglandins that cause ciliary spasm.

Topical treatment

1. Glucocorticoids 2- 6x daily (depending on severity of symptoms)
 - Prednisolone acetate (1% suspension)
 - Dexamethasone (0.1% solution or 0.05% ointment)
2. NSAIDs (2-4x daily depending on severity of symptoms)
 - Flurbiprofen (0.3% solution)
 - Ketorolac (0.5% solution)
 - Diclofenac (0.1% solution)
3. Mydriatics
 - Atropine (0.5% and 1% solution and ointment) 2-4x daily for 3-4 days
 - Tropicamide (1% solution)

General treatment

1. Glucocorticoids
 - Prednisolone or prednisone (0.5-2.2 mg/kg) 1-2x daily
2. NSAIDs
 - Aspirin (10 mg/kg) every second day
 - Ketoprofen (2 mg/kg initially, then 1 mg/kg) 1x daily

Important informations:

Topical glucocorticoids may not be used when the cornea is ulcerated or otherwise not intact; use of systemic steroids requires ruling out of bacterial or fungal diseases.

Atropine drops are used reluctantly in cats, who will salivate profusely as they drain down the nasolacrimal duct; ointment may cause fewer symptoms. Additional caution needed with those with impaired tear production or at risk to develop glaucoma.

Antiviral Drugs. Azidothymidine (AZT) is the only HIV antiretroviral drug in general use as a clinical treatment for FIV in cats. Tenofovir, a drug superior to AZT for use in cats in almost every way, is a nucleoside closely related to cidofovir, which, as noted later, has been used successfully in topical treatment of feline herpetic conjunctivitis and keratitis. The combinations of tenofovir or abacavir with either lamivudine or emtricitabine (companion drugs never used alone) would have action suppressing FIV superior to either used alone. What beneficial impact on uveitis supplements with direct antiviral suppressive action would

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have alone, in combination with one another, or in combination with antiretroviral drugs is purely speculative.

Immune Modulators. A number of drugs have been tested for favorable activity in the immune systems of cats with FIV and/or FeLV, including acemannan, staphylococcus protein A (SPA), and (most recently) lymphocyte T cell immunomodulator (LTCI). None, however, has been assessed specifically as therapy for primary FIV-associated uveitis. One notable exception is interferons, which have both directly antiviral and immunomodulatory activity.

Feline Omega Interferon (Virbagen Omega). Although there have been no full scale studies of feline omega as therapy for uveitis, there is an intriguing one cat study. Treatment with a single five dose (1 MU/kg) course of subcutaneous feline omega interferon, plus oral dexamethasone at non-immunosuppressive dosage, resulted in a rapid improvement in the animal's general condition (which included arthritis and cystitis due to immunocomplexes) and resolution of his uveitis and retinitis. Whether the action of the feline interferon was directly antiviral, immunomodulatory, or some combination of the two is an open question, though concurrent administration of corticosteroids argues more strongly for direct antiviral action. (Lappin, Dow i Reif) (Legendre i Bartges) (Loesenbeck, Drommer i Heider, Findings in the eyes of serologically FIV (feline immunodeficiency virus) positive cats. [Article in German]) (Loesenbeck, Drommer i Egberink) (Whitaker).



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Fig. 1: A 4 month old Domestic shorthair male with bilateral anterior uveitis associated with feline infectious peritonitis. Presence of intensive chemosis, corneal vascularization, edema, and uveitis.



Fig.2: A 3 year old Domestic shorthaired neutered female with clinical symptoms of chronic uveitis caused by FIV infection. Typical secondary complications: cataract, and posterior synechia.

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