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Causes of Feline Uveitis: a Retrospective Study of 96 Cases at the Faculty of Veterinary Medicine Bucharest, 2012-2015

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Abstract

Uveitis is a common cause of blindness in feline patients as incorrectly treated or its chronicization can lead to formation of pre-iridal fibrovascular membranes, pupillary block and secondary glaucoma. The objective of this study was to investigate the causes of uveitis in cats diagnosed at the Faculty of Veterinary Medicine, Bucharest between 2012 and 2015. Medical records were reviewed and cats were considered if complete diagnostic work-up, clinical examination and imaging studies were performed. All the feline cases were serologically tested for at least two of the common infectious causes: feline leukemia virus, feline immunodeficiency virus, feline coronavirus, Toxoplasma gondii, and Bartonella spp. Ninety-six cats with a mean age of 5.42 years, ranging from 1 month to 17 years old, with a male to female ratio of 1.33/1 were diagnosed with uveitis. The European domestic cat was overrepresented at 76% followed by Birman cat (6.3%), Persian cat (4.2%), Russian blue (4.2%), Norwegian cat (2%), British Short Hair (1%), Sphynx (1%) and Cornish Rex (1%). Infectious diseases were the cause of uveitis in 31 cases (32.3%), neoplasia was diagnosed in 22 cases (22.9%), uveitis secondary to septic keratitis in 8 cases (8.3%) and uveitis secondary to direct ocular trauma in 6 cases (6.3%). Twenty-nine cats (30.2%) with a mean age of 4.33 years old were diagnosed with idiopathic or immune-mediated uveitis, less than previously reported. Aqueous flare occurred in 91 cats and keratic precipitates were noted in 39 cats. The most common infectious cause of uveitis in this study was *Toxoplasma gondii* (n=18). Infectious diseases remain the most common cause of feline uveitis, therefore systemic evaluation and serological investigations should be performed in all cats with uveitis, cataract and glaucoma.

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Keywords: feline, keratic precipitates, idiopathic, Toxoplasma, uveitis.

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1. Introduction

Uveitis is one of the most frequent and significant ophthalmic disorder in feline patients often associated with important systemic diseases. The uveal tract is the vascular supply to the intraocular structures and the site of the blood-ocular barriers (Townsend, 2008). Early diagnosis of uveitis is essential due to the intimate connection of the uvea with the lens, retina and optic nerve.

Different classification schemes for uveitis are available. Causes of feline uveitis may be grouped in exogenous causes which include direct ocular trauma, corneal ulceration (Ion et al., 2015, 2016) and lens induced uveitis or endogenous causes divided into infectious (viral, bacterial, mycotic, protozoal, parasitic), neoplasia (Boydell and Enache, 2012; Ionascu et al., 2012) and immune-mediated or idiopathic.

Endogenous agents are reported to be the most common cause of uveitis in cats (Bäckström et al., 1984; Jinks et al., 2015). Infectious agents frequently associated with feline endogenous uveitis include: feline leukemia virus (FeLV) (Willis, 2000; Colitz, 2005), feline immunodeficiency virus (FIV) (English et al., 1990), feline coronavirus (FeCoV) (Jinks et al., 2015), feline infectious peritonitis (FIP) (Colitz, 2005; Horhogea et al., 2011; Jinks et al., 2015), *Bartonella* spp. (Fontenelle et al., 2008; Lappin et al., 2000; Stiles, 2011), *Toxoplasma gondii* and fungi (Nasisse et al., 1985).

Clinical signs of uveitis include decreased vision, blepharospasm, photophobia, conjunctival hyperaemia, third eyelid protrusion, ciliary flush, miosis, dyscoria (D-shaped pupil), decreased intraocular pressure, aqueous flare, keratic precipitates, corneal oedema, hyphaema, hypopyon, changes in iridal color, anterior synechia (Chavkin et al., 1992; Colitz, 2005; Davidson et al., 1991; Jinks et al., 2015), pars planitis, vitreous exudates, optic neuritis (Townsend, 2008; Colitz, 2005). Posterior synechia, cataract, lens luxation, secondary glaucoma and rubeosis iridis can occur in chronic cases (McLellan and Miller, 2011).

Diagnosis is often challenging and requires complete physical and ophthalmic examination, imaging studies and additional laboratory investigations including complete blood count, serum biochemistry and serology for infectious diseases. Aqueous humor aspiration and cytological evaluation may reveal inflammatory cells especially in lymphocytic plasmacytic uveitis or in FIP but is unlikely to establish a definitive diagnosis (Wiggans et al., 2014). A comparison of aqueous humor antibody levels to serum antibody levels has been suggested as beneficial in diagnosis of *Toxoplasma* (Chavkin et al., 1994) and *Bartonella* associated uveitis (Fontenelle et al., 2008; Lappin, 2000).

According to previous reports, between 38% and 70% of cats with uveitis had an associated systemic disease (Chavkin et al., 1992). In other feline uveitis studies, approximately 30% to 62% of affected cats had no identifiable concurrent systemic disease (Gemensky et al., 1996).

A recent retrospective study (Jinks et al., 2015) investigating causes of feline uveitis revealed no underlying etiology in 40.8% of 120 cats taken into study. Neoplasia represented 5% of the cases and the rest was diagnosed with infectious diseases. FeCoV was found as the causative agent in 34.7% of the cases, *Toxoplasma gondii* in 23.7%, *Bartonella* spp. in 43.2%, and FIP in 15.8% of the infectious causes.

The aim of this study was to investigate causes of uveitis in Romanian cats and their association with sex, age and clinical signs.

2. Materials and Methods

Records of cats presented to the Small Animal Teaching Hospital of Faculty of Veterinary Medicine Bucharest, between 2012 and 2015, diagnosed with uveitis were reviewed. Cats were included only if complete ophthalmic and physical examinations were performed and if serological tests for at least two of the common infectious diseases were conducted. Additionally, serum chemistry analysis, complete blood cell count, imaging and histopathological studies were recorded.

Ophthalmic examination included the use of head-mounted magnifiers under diffuse and focal light sources, Schirmer tear tests, fluorescein stain, IRIS Vet (Eickenmeyer), direct ophthalmoscopy (PanOptic, Welch Allyn) and rebound tonometry (Tonovet). Uveitis was diagnosed when at least two or more of the following ocular signs were noted: miosis, aqueous flare, corneal oedema, decreased intraocular pressure, iridal hyperhaemia, iridal nodules, iris colour change, rubeosis iridis, keratic precipitates, hyphema, hypopion and also the presence of synechia, increased intraocular pressure with secondary glaucoma in chronic cases (Håkanson and Forrester, 1990; Jinks et al., 2015).

Cats with general clinical signs such as: pyrexia, lethargy, anaemia, ascites, pleuresia, breathing difficulties and/or neurological signs were considered to have ocular manifestation of systemic diseases.

The presence of miosis, the intraocular pressures, the degree of aqueous flare and the presence of synechia were recorded. The degree of aqueous flare and cell numbers within the anterior chamber were graded on a scale from 1= trace to 4+ = severe flare, clotted aqueous, fibrin, and over 50 cells (Jabs et al., 2005; Wiggans et al., 2014).

Cats' diagnoses were divided into idiopathic uveitis, infectious uveitis, neoplastic uveitis and uveitis secondary to corneal ulceration and direct ocular trauma. The idiopathic category included cases in which no causative agent was detected through laboratory investigations.

Commercial kits (SNAP FIV/FeLV Combo Test, Idexx Laboratories) were used for diagnosis of FIV and FeLV-associated uveitis. An immunofluorescent antibody assay was performed to detect FeCoV antibodies. Serum was tested for IgM and IgG *Toxoplasma gondii* antibodies through the Small Animal Hospital Laboratory of the Faculty of Veterinary Medicine Bucharest. Cats were tested for *Bartonella* spp. following blood cytology and immunofluorescent serology. No cat was tested for mycotic diseases.

Neoplasia was diagnosed following histopathological examination of enucleated eyes or post-mortem examination. Infectious cases were considered based on associated systemic clinical signs along with a high titre of antibody-based serological investigations, or cytological evaluation of a blood smear and identification of the organism.

Statistical analysis was performed to compare causes of uveitis by age, sex and breeds and ocular signs and means and probabilities were generated by IBM-SPSS, Version 22.

3. Results and Discussions

Ninety-six cats with uveitis were considered in this study. The mean age ± SD of all cats in this study was 5.24 ± 4.84 years (Fig. 1), ranging from 1 month to 17 years old, with a male to female ratio of 1.33/1 (55 males and 41 females) (Fig. 2). There were 30 intact and 25 castrated males, and 23 intact and 18 neutered females. Eight breeds were represented, with the European domestic cat overrepresented at 76% followed by Birman cat (6.3%), Persian cat (4.2%), Russian blue (4.2%), Norwegian cat (2%), British Short Hair (1%), Sphynx (1%), Cornish Rex (1%) (Fig. 3).

In a retrospective study of 53 cats with uveitis, English et al. reported that 69.8% of cases were idiopathic uveitis. In the present study no causative agent could be detected in twenty-nine cats (30.2%). These cats had an average age of 4.33 years old, 17 females and 12 males, and were diagnosed with idiopathic uveitis of a presumed immune-mediated cause (Fig. 4).

Infectious disease was the cause of uveitis in 31 cases (32.3%), neoplasia was diagnosed in 22 cases (22.9%), uveitis secondary to corneal ulceration in 8 cases (8.3%) and uveitis due to direct ocular trauma in 6 cases (6.3%). Of the 31 cases of infectious causes (32.3%), 18 were males (32.7%), (8 neutered, 10 intact) and 13 females (31.7%), (3 neutered, 10 intact) (Fig. 5).

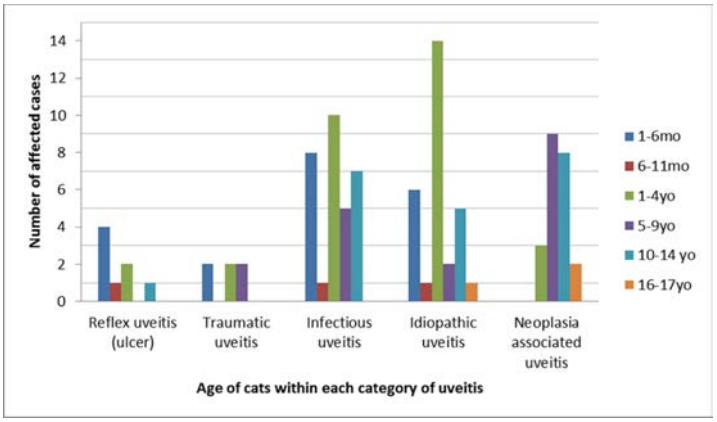

Fig. 1. Frequency of uveitis and association with age

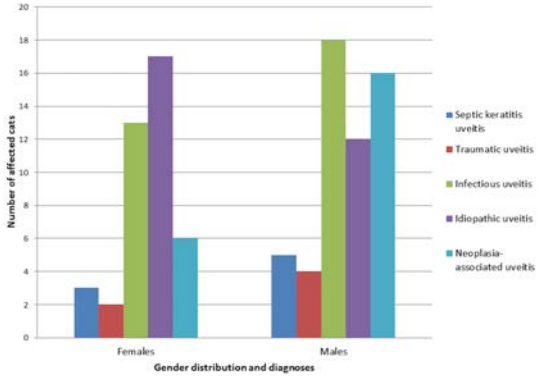

Fig. 2. Distribution of gender within each category

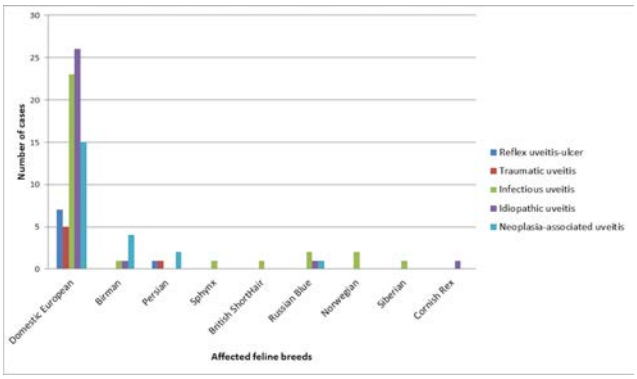

Fig. 3. Distribution of feline breeds presented with uveitis

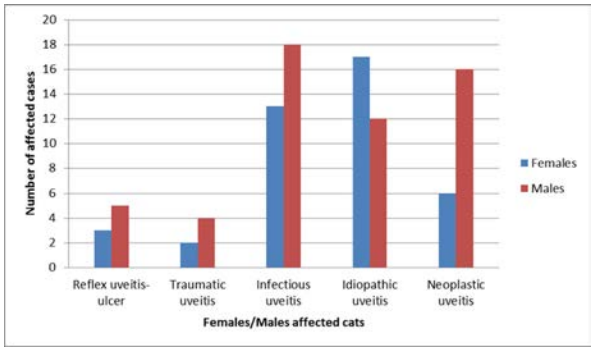

Fig. 4. Gender distribution and diagnosis

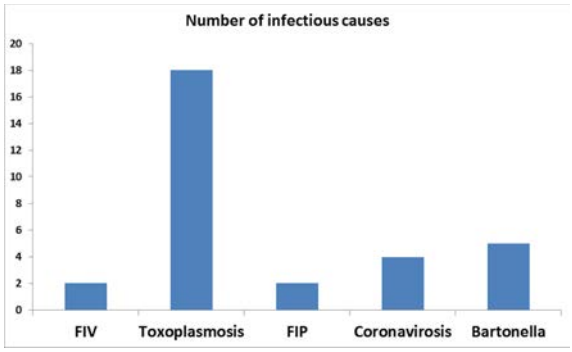

Fig. 5. Frequency of infectious causes of feline uveitis

Peiffer et al. (1991) reported that only 15% of 139 cases of feline uveitis were of infectious causes, 13% were neoplastic and 70% were of idiopathic causes (Peiffer and Wilcock, 1991). The most frequent infectious agent diagnosed in this study was *Toxoplasma gondii* (Fig. 6) in 18 cases (58% of total infectious causes), *Bartonella* spp. (Fig. 7) in 5 cases (16.1%), FeCoV in 4 cases (12.9%), FIP in 2 cases (6.4%) and FIV in 2 cases (6.4%) (Fig. 8). Bilateral uveitis was more frequent in *Bartonella* and FeCoV affected cats, whereas *Toxoplasma*-associated uveitis presented in a higher number unilaterally (Table 1).

Table 1. Unilateral and bilateral infectious uveitis

Infectious cause	**Unilateral/bilateral feline uveitis (%)**
Bartonella	OS 2 (2.1%)
	OD 0
	OU 3 (3.1%)
Feline Coronavirus	OS 1 (1%)
	OD 1 (1%)
	OU 2 (3.1%)
Toxoplasma	OS 9 (9.4%)
	OD 6 (6.3%)
	OU 3 (3.1%)
Feline infectious peritonitis	OU 1 (1%)
	OS 1 (1%)
Feline immunodeficiency virus	OS 1 (1%)
	OU 1 (1%)

Fig. 6. OD *Toxoplasma*-associated uveitis (D-shaped pupil)

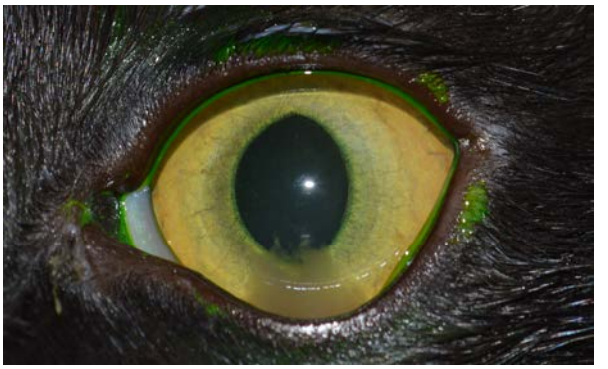

Fig. 7. OS *Bartonella*-associated uveitis

Fig. 8. OS FIV-associated uveitis

Neoplastic uveitis was diagnosed in 16 males (29.1%) (12 neutered, 4 intact) and 6 females (14.6%) (5 neutered, 1 intact) with a mean age of 8.77 ±4.23 years, ranging from 3 years to 17 years (Fig. 9). The most common reported neoplastic uveitis is feline diffuse iris melanoma (Grahn et al., 2006) followed by trauma-associated sarcoma (Dubielzig, 2009). Lymphoma is the most frequent metastatic intraocular tumor in the cat (Grahn et al., 2006). The most common neoplastic uveitis in the present retrospective study was feline diffuse iris melanoma followed by lymphoma, metastatic disease and trauma-related sarcoma (Fig.10).

Miosis and associated ciliary muscle spasm occurs in uveitis as a response to inflammatory mediators that act directly on the iris sphincter muscle (Townsend, 2008). Corneal ulceration can trigger anterior uveitis and miosis through a reflex pathway involving the ophthalmic branch of cranial nerve V (Colitz, 2005; Stiles, 2011). In this study, miosis occurred in 73 of total cases of feline uveitis (76%), in 31 cats with infectious uveitis (42.5%), 24 cats (32.9%) diagnosed with idiopathic uveitis, all cats with septic keratitis (11%), all cats with traumatic uveitis (8.2%) and 4 cats with neoplastic uveitis (5.5%) (Fig. 11).

Aqueous flare was absent in 5 cases (5.2%), 1+ to 2+ flare were seen in 50 cases (52%) and clotted aqueous humor (flare 3+ to 4+) was noted in 41 cats (42.8%), mostly in cases of infectious uveitis (15 cases).

The intraocular pressure decreases during inflammation due to a reduction of aqueous humor production and increase of outflow (Stiles, 2011; Townsend, 2008; Colitz, 2005). In chronic cases the intraocular pressure increases due to formation of pre-iridal fibrovascular membranes, secondary cataract and lens luxation (Van der Woerdt, 2000). The intraocular pressures in this study recorded a minimum of 2 mmHg in 1 case of idiopathic uveitis and a maximum of 60 mmHg in a case of chronic *Toxoplasma*- associated uveitis, with a mean of 17.92±13.39 mmHg. In cats with infectious uveitis the intraocular pressures ranged between 3 to 60 mmHg, with a mean of 14.6±12.8 mmHg. The lowest intraocular pressure recorded in neoplastic uveitis was 5 mmHg and the highest was 48 mmHg with a mean of 29.7±12.7.

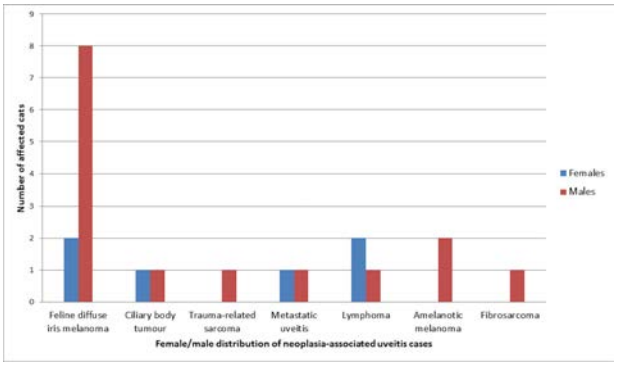

Fig. 9. Gender distribution of cats affected by neoplasia-associated uveitis

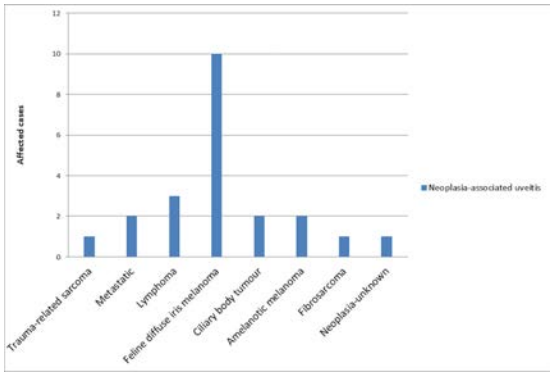

Fig. 10. Causes of neoplasia-associated uveitis

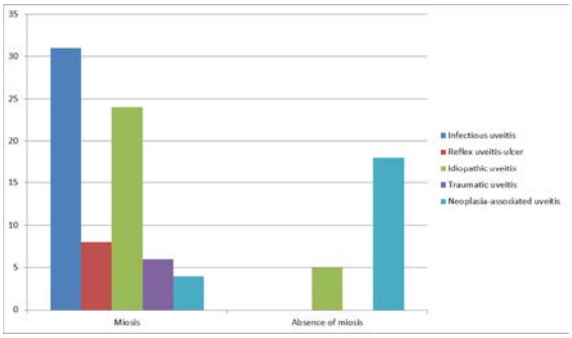

Fig. 11. Correlation between miosis and diagnosis

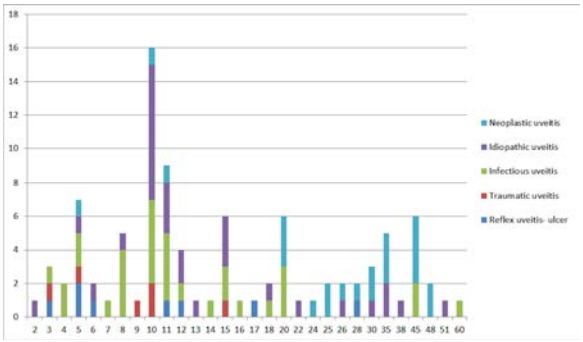

Fig. 12. Correlation between intraocular pressure and type of uveitis

Idiopathic cases had intraocular pressure values ranging from 2 to 51 mmHg with a mean of 16.2±11.4. The lowest intraocular pressure was recorded in traumatic uveitis ranging from 3 mmHg to 15 mmHg, with a mean of 8.6±4.2 and in septic keratitis from 3 mmHg to 30 mmHg, with a mean of 11.1±8.9 mmHg (Fig. 12).

Keratic precipitates were present at ophthalmological examination in 39 cats (40.6%), most commonly in infectious uveitis with 22 cases (56%), of which 4 were FeCoV affected cats (18.1%), 1 case of FIV (4.5%), 2 cases of FIP (9.09%), 15 cases of Toxoplasma-associated uveitis (68.18%), and in 15 idiopathic cases (38.5%).

Synechiae was present in 28 cats (29.2%), most frequently noted in infectious uveitis (35.7%), and followed by idiopathic and neoplastic cases (both with 32.1%). Pupillary seclusion was noted in 11 cases (11.5%) being more common in chronic idiopathic and neoplastic uveitis (both with 36.4%).

4. Conclusions

Uveitis is a significant cause of ocular disease in Romanian cats with a great potential of blindness and glaucoma in untreated cases. There were a significant number of feline uveitis cases with high intraocular pressure (maximum 60 mmHg) which suggested that many cases presented after a long period of time without treatment or their clinical signs had been missed at the initial ophthalmological examination.

The mean age of cats with uveitis is lower (5.24 years) than previously reported (7.62) years (Jinks et al., 2015).

Infectious uveitis is still the most common cause of feline uveitis but the occurrence was is less represented in this study (32.3%) than previously reported (54.2%) (Jinks et al., 2015). *Toxoplasma gondii* seems to play an important role in feline uveitis with 58% of cases considered in this study compared to 23.7% reported by Jinks et al. (2015). The frequency of idiopathic cases still remains high 30.2%, although lower than previously reported.

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