Case Control study into the association of B. henselae infection with Feline Uveitis.

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Abstract

This study is awesome.

1 Introduction

Uveitis is a delibitating disease that can leave cats blind. Clinical signs of Uveitis are the same regardless of cause and can include aqueous flare, iritis, keratic precipitates, hyphema, and hypopyon [1]. The most common causes of endogenous feline uveitis include *Bartonella sp.* , toxoplasmosis, feline immunodeficiency virus (FIV), lymphosarcoma (LSA) with or without feline leukemia virus (FeLV), feline infectious peritonitis (FIP), cryptococcosis, and idiopathic causes [2]. Identifying the cause of uveitis can be difficult due to the non specific clincal signs, and the lack of adequote diagnostic test [3]. Diagnostic tests include Serology via Immunofluorescent assay, Enzyme Linked Immunosorbant assay,or Western Blot, and identifying the organism by culture or PCR. PCR and culture can be performed on both blood and Aqueus humor, in an attempt to establish causation by locating *Bartonella sp.* at the site of inflammation. Unfortunately *Bartonella sp.* levels in blood and Aqueus humor fluctuate during infection and infected cats may still show a negative test, and hence multiple test are indicated[4]. Likewise amplyfying DNA from the eye does not nececarily imply causation, and can indicate contamination during sample collection [1].

Bartonella sp. is a common transient infection ni cats, with most not showing any clinical signs. transmitted by fleas On average 20 percent of cats are seropositive to *Bartonella sp.*, although this varies widely with geographic location[5]. Areas with warm, humid environments have higher seroprevalence, and these areas are good environments for fleas, indicating the importance of fleas as a vector. The association of *Bartonella sp.* and uveitis was first reported by Lappin et al[6], and subsequent studies have found conflicting results, with Ketring reporting increased serum antibodies to *Bartonella sp.* in cats with uveitis[7], however Fontanelle found cats without uveitis more likely to have *Bartonella sp.* antibodies than cats with uveitis.

Bartonella sp. has also been implicated in cases of chronic stomatits, anemia, CNS disorders[8]. *Bartonella sp.* is an important pathogen from a human health perspective as well, being responsible for Cat Scratch Disease, *Bartonella sp.* also causes ocular complications in 5 to 10 percent of people that become infected

through Cat Scratch Disease [9]. The reference population for this study is privately owned domesticated cats in the United States, and study findings will be generalisable to the 85 million cats in the United States [10].

1.1 Objectives and Study Hypothesis

The Objective of this study are as follows:

- To determine the prevalence of *Bartonella sp.* exposure in cats presenting to commercial and university veterinary hospitals for annual checkup.
- To study the relationship between infection with *Bartonella sp.* and feline uveitis.

The Study Hypothesis is there is a higher incidence of feline uveitis amoung cats that have been exposed to *Bartonella sp.*.

2 Methods

Utilising a commercial database (Banfield corporation, Mars inc Cases will be taken from Banfields inhouse opthalmology service records, and the Veterinary Medical Database [11].

Exposure will be measured with a comercially available Western immunoblot test [12]. This test is widely used and correlates more closely with the ability to isolate *Bartonella sp.* from cats than does the Immunofluorescent assay or Enzyme Linked Immunosorbant assay [13]. Western Blot results of 3+ and 4+ will be considered positive for the purposes of this study. The use of an objective exposure method effectively masks Practitioners when collecting samples from controls, and limits recall/reporting bias.

Case definition will be uveitis positive as diagnosed by tono.. with a cutoff of . No evidence of trauma, cataract, intraocular neoplasia, or corneal ulceration (as detected by flureocin stain) after eliminating all other causes of uveitis and positive Western Blot test results Cases will have blood taken and tested for FIV/FeLV as these diseases can also cause uveitis.

Blood will be taken from these cats (with the written consent of the owner) and sumitted to UC Davis Laboratory for Serology and BLood culture. All sample collection in cases will take place before any therapy is instituted.

Sample size was requirements were calculated using the prevalence figure observed in part one of this study..

Controls will be taken from cats visiting banfield hospitals for annual checkups. As a part of their checkup, cats are routinely tested for FIV and FeLV , and Toxoplasmosis according to company policy. This removes the potential confounder of FIV/FeLV which is another cause of uveitis in cats. These cats represent a broud sample of the reference population, that could themselves develop uveitis as a result of *Bartonella sp.* exposure.

Data quality was good, with the use of a large database allowing any incomplete records to be eliminated without suffering. Collection of histories by DVM's and Registered Veterinary Technicians ensures quality and consistency, and case definitons by qualified opthalmologists ensures good case definitions.

2.1 Statistical Evaluation

Data was be collected into an SQL Database and queried. Statistical analysis was performed intially performed using Fischers exact test to compare prevelence rates between cases and con-

trol. Further modelling was undertaken utilising a conditional logistic regression model, both with and without age, housing status, date of sample collection, and geographical location included. Covariates were included in the analysis if the odds ratio for exposure changed by 10% or more after their addition. Both geographic location and age were included in the final analysis, although housing status and age were not deemd signifigant (this may indicate cats admitted to a veterinarian for regular checkups are more likely to have regular flea control treatment, regardless of housing status)

Age, geographic location, housing status, and *Bartonella sp.* status were entered into .. Cats were grouped into 4 groups (¡2, 2-5, 5-10, ¿10) as *Bartonella sp.* infection is more common in younger cats flea risk was catagorically assigned high or low, based on a combination of indoor/outdoor status and state of origin (Alaska, Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming all assigned low risk, all other states high, according to [5]) Cases and controls were matched for age and geographical location (Each University Veterinary Hospital and the Banfield hospitals in the same state). This matchign for location ensures comparable case and contrl populations, removing potential selection bias. Further control cats are selected from cats undergoing annual vaccination and checkup, showing a similar level of care and investment in their animals health by owner, and hence would probaby take their animal to investigate any incidence of uveitis.

Ethical permission was granted by UC Davis School of Veterinary Medicine. appropriate forms. can be found..

3 Results

4 Discussion

4.1 Strengths and Limitations

Using cats from the same reference population is better than previous studies that utilised cats from an animal shelter. Cats in a shelter are more likely to have been outdoors and exposed to fleas, and hence be seropositive, reducing any observed difference. Using indoor/outdoor status as proxy for flea exposure was chosen to reduce the . This design coul dbe imporved with actual flea exposure history from owners, although there is potential for misclassification based on owners not admitting to fleas. The vauge clinical signs associated with uveitis manke. the difficulty in coming u pwith a strict case defintion for uveitis is another issue with theis study. Relying on Board Certified Opthalmologists are certainly the most qualified to assess cases of uveitis, there is still the possibility of diagnostic criteria differing between clinicians. This is in comparison to other diseases of the eys such as glaucome (also a potential sequale to uveitis) where an objective test (measuring Intra ocular pressure with tonometry) and strict cutoff value can be utilised to form a consistsent case definition. further the chance of some controls having uveitis that was missed on the usual cursory examination at their annual vaccination consultatoin cannot be ruled out. This differential miscalassification would reduce any effect seen as more controls would actually be cases.

References

[1] Cynthia C Powell, Carey L McInnis, Jennifer P Fontenelle, and Michael R Lappin. Bartonella species, feline herpesvirus-1, and Toxoplasma gondii PCR assay results from blood and aqueous humor samples from 104 cats with naturally occurring endogenous uveitis. *Journal of feline medicine and surgery*, 12(12):923–8, December 2010.

[2] Cynthia C Powell. Diagnosis and Treatment of Feline Uvetitis. *Compendium Continuing Education, North American Edition.*, 23(3), 2001.

[3] Jennifer P Fontenelle, Cynthia C Powell, Ashley E Hill, Steven V Radecki, and Michael R Lappin. Prevalence of serum antibodies against Bartonella species in the serum of cats with or without uveitis. *Journal of feline medicine and surgery*, 10(1):41–6, March 2008.

[4] Lynn Guptill. Feline bartonellosis. *The Veterinary clinics of North America. Small animal practice*, 40(6):1073–90, December 2010.

[5] P Jameson, C Greene, R Regnery, M Dryden, a Marks, J Brown, J Cooper, B Glaus, and R Greene. Prevalence of Bartonella henselae antibodies in pet cats throughout regions of North America. *The Journal of infectious diseases*, 172(4):1145–9, October 1995.

[6] MR Lappin and JC Black. Bartonella spp infection as a possible cause of uveitis in a cat. *Journal of the American Veterinary Medical ...*, 1999.

[7] Kerry L KL Ketring, Evelyn E Zuckerman, and William D Hardy Jr. Bartonella: a new etiological agent of feline ocular disease. *Journal of the American ...*, 2004.

[8] L Nasir, Julie Rosenberger, Irish Setter, Golden Retriev, N-acetylcysteine Decreases Vascular Endothelial, Douglas H Thamm, Ann M Mitzey, and Ilene D Kurzman. 2005 ACVIM Abstracts. *Journal of Veterinary Internal Medicine*, 19(471), 2005.

[9] NK Wade, L Levi, and MR Jones. Optic disk edema associated with peripapillary serous retinal detachment: an early sign of systemic Bartonella henselae infection. *American journal of ...*, 2000.

[10] The Humane Society of the United States. U.S. Pet Ownership Statistics, 2011.

[11] University Veterinary Hospitals. Veterinary Medical Database.

[12] National Veterinary Laboratory Inc. FeBart Test.

[13] WD Hardy Jr, EE Zuckerman, and JWM Gold. Immunogenic proteins of Bartonella henselae defined by western immunoblots with naturally infected cat sera. *95th General Meeting, ...*, 1995.