



Case report

Not cat-scratch disease: *Bartonella henselae* neuroretinitis associated with non-feline pet mammals[☆]



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ABSTRACT

To describe the occurrence of *Bartonella*-associated neuroretinitis secondary to non-feline pet exposure, we retrospectively reviewed medical records and imaging from patients with a clinical and serologic diagnosis of *Bartonella henselae* (BH). Retinal imaging included color fundus photography, optical coherence tomography (OCT) and fluorescein angiography (FA). Four eyes of two patients with cat-scratch disease were included in this study, with a mean age of 35 years. The mean follow-up was 13 months, after presentation of infectious neuroretinitis. Both patients suffered from bilateral neuroretinitis after direct contact with family pets (ferret and guinea pig). All patients were treated with a long-term systemic antimicrobial therapy. Visual acuity in all improved to 20/30 or better at six months. In conclusion, humans may develop cat-scratch disease when they are exposed to *Bartonella henselae* (BH) in the saliva of infected cats or BH-containing flea feces reaching the systemic circulation through scratches or mucous membranes. As the cat flea (*Ctenocephalides felis*) may reside on non-feline mammals, *Bartonella*-associated neuroretinitis may result from contact with other furred family pets.

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Introduction

The majority of pathogenic species causing infectious disease in humans are zoonotic [1]. The reported prevalence of human infections due to *Bartonella* species has increased due to both changes in human civilization and improved diagnostic testing. There are over 20 different *Bartonella* spp known to cause infections in humans, with *Bartonella henselae* (BH) being the most common [2]. BH is a gram-negative rod that infects erythrocytes and endothelial cells usually presenting in people as cat-scratch disease (CSD), with felines serving as the main reservoir for BH [3]. While over 90 % of affected patients report a history of cat contact

[4], CSD has been increasingly reported in patients without a history of cat exposure [5].

Cat-scratch disease comprises a constellation of systemic findings that includes fever, malaise and regional lymphadenopathy begin no more than 1–2 weeks following contact with a BH-reservoir [2,3]. The annual incidence of systemic bartonellosis in the United States is reported to be 12,500 cases [6], with ocular manifestations occurring in approximately 4.4 % of patients [7]. Ocular findings of CSD may include both anterior segment inflammation and posterior segment manifestations. Neuroretinitis (NR) is one of the most common posterior segment complication of CSD occurring in 1–2 % of total patients with BH infection [8].

Herein, we describe 2 patients with *Bartonella*-associated NR related to non-feline pet exposure. This report aims to raise awareness regarding the potential for vision-threatening zoonoses acquired from household pets.

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Case reports

Case 1

A 51-year-old woman presented with a central scotoma and decreased vision in her right eye (RE) for several days during the early fall. Her past medical history included seasonal allergies treated with occasional use of oral antihistamines (desloratadine, hydroxyzine) and an inhaled corticosteroid (mometasone furoate). She reported the onset of headache, malaise and inguinal lymphadenopathy around one week after being scratched on her face and bitten on her lip by her pet ferret (*Mustela putorius furo*). At presentation, best-corrected visual acuity (BCVA) was 20/40 in the RE and 20/25 in the left eye (LE). The anterior segment examination was normal in both eyes. Posterior segment findings revealed bilateral disc edema and a macular star in the RE. Central subretinal fluid was seen with optical coherence tomography (OCT) B-scans. Focal retinitis with overlying vitreous cells was present along the retinal vascular arcades in both eyes (Fig. 1).

Blood analysis of full blood count and biochemistry were within normal limits. Results of serologic studies excluded the presence of *Toxoplasma gondii*, *Borrelia burgdorferi* and *Treponema pallidum*. However, serology was positive for anti-BH antibodies (IgM titers 1:10, IgG titers 1:512). Following 6-weeks of oral azithromycin 500 mg/daily and ketorolac ophthalmic solution 0.5 % four times a day for two weeks in the RE, visual acuity improved to 20/20 in both eyes (Fig. 2).

Case 2

A 19-year-old otherwise healthy man reported 3 weeks of decreased vision and central scotoma in his LE. Fever and

preauricular lymphadenopathy were noted in the early fall, 5 days before vision loss. He denied any contact with cats. However, a pet guinea pig (*Cavia porcellus*) had licked and bitten his face before the onset of systemic findings. At presentation, BCVA in the RE was 20/20 and 20/200 in the affected LE. The anterior segment examination was unremarkable in both eyes. Ophthalmoscopic examination of the RE showed a focal area of retinitis along the distal inferotemporal retinal arcade and subtle hyperemia at the nasal margin of the optic disc. Fundal examination of the LE highlighted hyperemia of the whole optic disc and radiate foveal edema resembling a hemi-macular star. Late disc leakage in the LE was identified on fluorescein angiography (FA) (Fig. 3).

Full blood count, rheumatoid factor, antinuclear antibodies and complement studies were normal. *Bartonella henselae*, *Toxoplasma gondii* and *Treponema pallidum* serologies were also requested. The only positive finding was BH serology which confirmed high-titer anti-BH antibodies (IgG titers 1:1024). Partial resolution of disease was noted after 8-weeks of oral doxycycline 200 mg/daily plus rifampin 600 mg/daily and nepafenac ophthalmic suspension 0.1 % three-times a day for two weeks in the LE. At 3-month follow-up visit, his BCVA in the LE was 20/30, and continued improving to 20/25 at 6 months after starting treatment. One year after presentation, BCVA in the left eye was 20/20.

Discussion

Herein we describe two cases of serologically confirmed *Bartonella*-associated NR believed to be related to non-feline family pet exposure. Classically, CSD is diagnosed when three of the following four clinical criteria are met: (1) History of traumatic cat exposure; (2) a positive skin test in response to CSD antigen; (3) characteristic lymphadenopathy; and (4) lymphadenopathy not

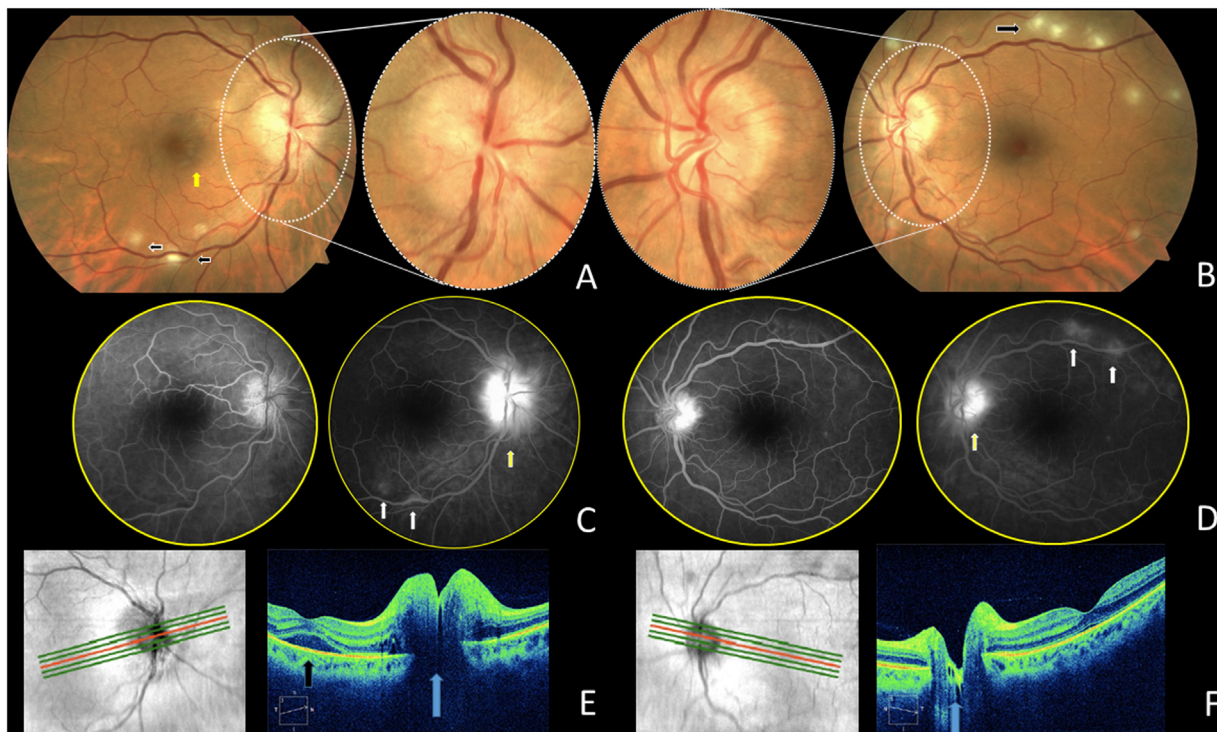


Fig. 1. *Bartonella henselae* neuroretinitis in a 51-year-old woman (case 1). Color fundus photography (A) in the right eye (RE) and (B) in the left eye (LE) at presentation. Black arrows show focal retinal whitening corresponding to retinitis in both eyes. Yellow arrow highlights macular fluid & lipid constituting a macular star. Magnified insets display optic disc edema, more in the RE than in the LE. Fluorescein angiography of the RE (C) and LE (D) depicts late hyperfluorescence from focal retinitis (white arrows) in both eyes. Yellow arrows also show late hyperfluorescence which extends beyond optic disc boundaries. Spectral-domain optical coherence tomography (SD-OCT) B-scans over the macula and optic disc in the RE (E) and LE (F) confirmed central subretinal fluid (black arrow in E) and bilateral optic disc edema (blue arrows in E and F). The green and red lines indicate the location and direction of the SD-OCT B scans.

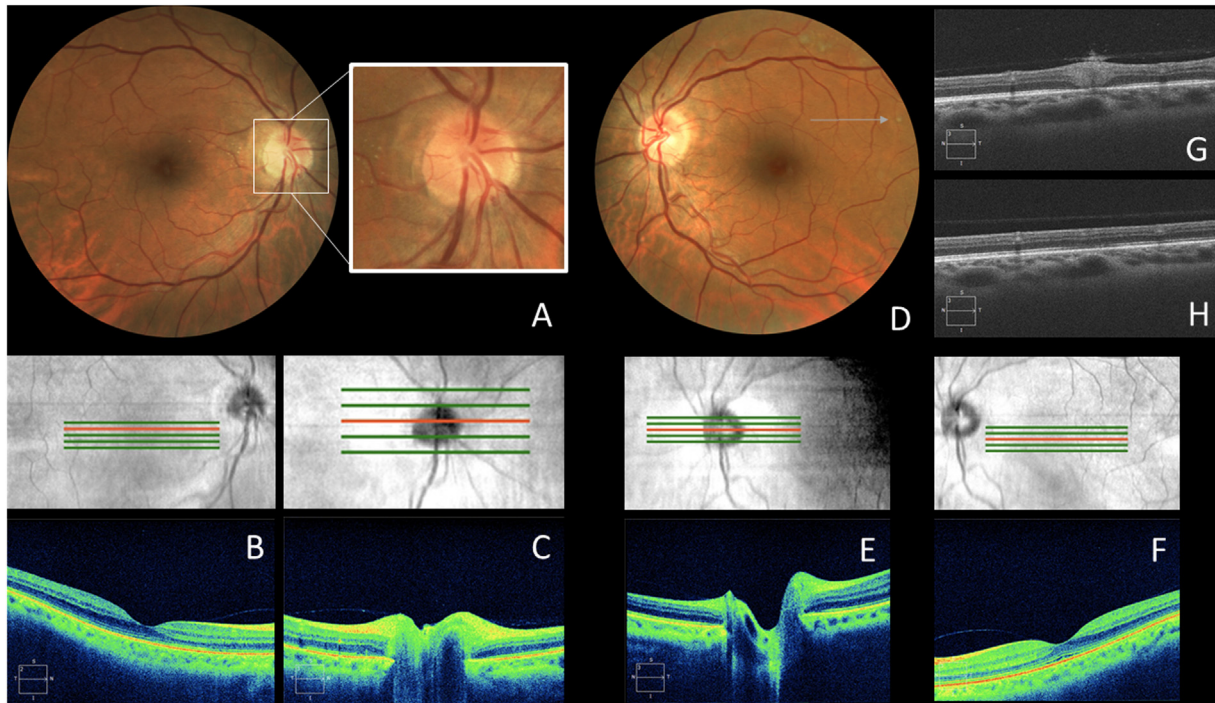


Fig. 2. Three-month follow-up imaging of case 1 as seen on (A) color fundus photography in the RE. Magnified inset shows retinal exudates temporal to optic disc, which still presents residual edema. Color fundus photograph (D) in the LE shows a subtle flame hemorrhage near superior pole of the optic disc. The green and red lines in B, C, E and F indicate the location and direction of the SD-OCT B scans below. The B-scans in (B) confirm absence of macular edema and much less swelling of the optic disc in (C). The B scans in (E) and (F) demonstrate no neuroretinitis. The gray arrow in (D) indicates the location and direction of an SD-OCT B-scan at presentation (G) through focal retinitis and after 6-weeks treatment in (H), with resolution of the retinitis and residual ellipsoid zone damage. A subtle chorioretinal scar in (D) indicates healing.

caused by other bacteria. Although cat exposure is a common element, it is not a prerequisite to CSD diagnosis [3,8].

Bartonella henselae is among the most common causes of infectious NR. However, other infectious entities should be considered in the differential diagnosis including toxoplasmosis, syphilis, tuberculosis and Lyme disease [2,8]. Currently, a laboratory diagnosis of CSD can be made based on serologic testing by indirect fluorescence assay (IFA). The IFA has been reported to have a sensitivity and specificity of 90 % in immunocompetent patients. Typically, if IgM is positive with values equal or greater than 1:10, then an acute infection with BH is thought to be present, but this elevation can be short-lived. IgG titers equal or exceeding 1:256 confirm CSD. Titers equal to 1:128 suggest possible CSD, and the serology should be performed again 2–3 weeks later. IgG of 1:64 or less is considered negative because BH IgG detection has low specificity due to its high seroprevalence in the normal population [9].

CSD is generally self-limiting in immunocompetent patients. Varying degrees of visual loss in patients with CSD have been reported and most of the eyes tend to improve. Nevertheless, NR due to ocular bartonellosis may be complicated by various posterior segment manifestations causing permanent visual loss such as retinal vascular occlusion or ischemic optic neuropathy [10]. Thus, better visual acuity outcomes were associated with patients who were treated [2,11].

Neuroretinitis is primarily a clinical diagnosis with characteristic findings of optic disc edema and a macular star of retinal exudation. However, the appearance of the macular star usually occurs later in the course of the disease. Hence, other pathological entities may mimic neuroretinitis and should be considered in the differential diagnosis of optic disc edema. Within this subset of patients, malignant hypertension, branch retinal vein occlusion, idiopathic intracranial hypertension, diabetic papillopathy and

anterior ischemic optic neuropathy would be important masqueraders for neuroretinitis [2,8].

Multimodal imaging is useful for diagnosing and monitoring infectious NR. Characteristic optical coherence tomography (OCT) findings include subretinal fluid and retinal edema not obvious on clinical examination. OCT also allows observation of epipapillary and epiretinal infiltrates thought to be collections of inflammatory cells in the vitreous abutting the optic disc and focal retinitis respectively [12]. *Bartonella spp* ability to infect vascular endothelial cells can cause leakage on retinal FA, noted as progressive hyperfluorescence from optic disc and/or focal retinochoroiditis, as seen on both our cases, because of increased vessel permeability caused by endotheliitis [13].

Like other BH-neuroretinitis cases, our patients symptoms occurred during the late summer and early fall. There is a marked seasonality in the prevalence of infection with *Bartonella* and CSD coincides with the peak of flea infestation in mammals [14].

Transmission of BH from cats onto non-feline pets can occur through the cat flea (*Ctenocephalides felis*). The bacteria can reproduce in the digestive system of the cat flea and survive for several days in the flea feces. The main origin for infections in humans seems to be the inoculation through a skin trauma or a lick with saliva contaminated with flea feces. The flea feces, which contain BH, can also be transferred by other vectors such as ticks or blood-eating arthropods [15,16].

Mucous membranes, such as conjunctiva or nasal mucosa, may be the avenue of the transmission of the disease without scratch or wound history. Eye rubbing may lead to direct inoculation of this pathogen to allow BH a primary niche to spread into systemic circulation [13,17].

Ferrets have become common family pets in the United States, and their curious and friendly nature makes them suitable pets for many. Nevertheless, they can sometimes carry microorganisms

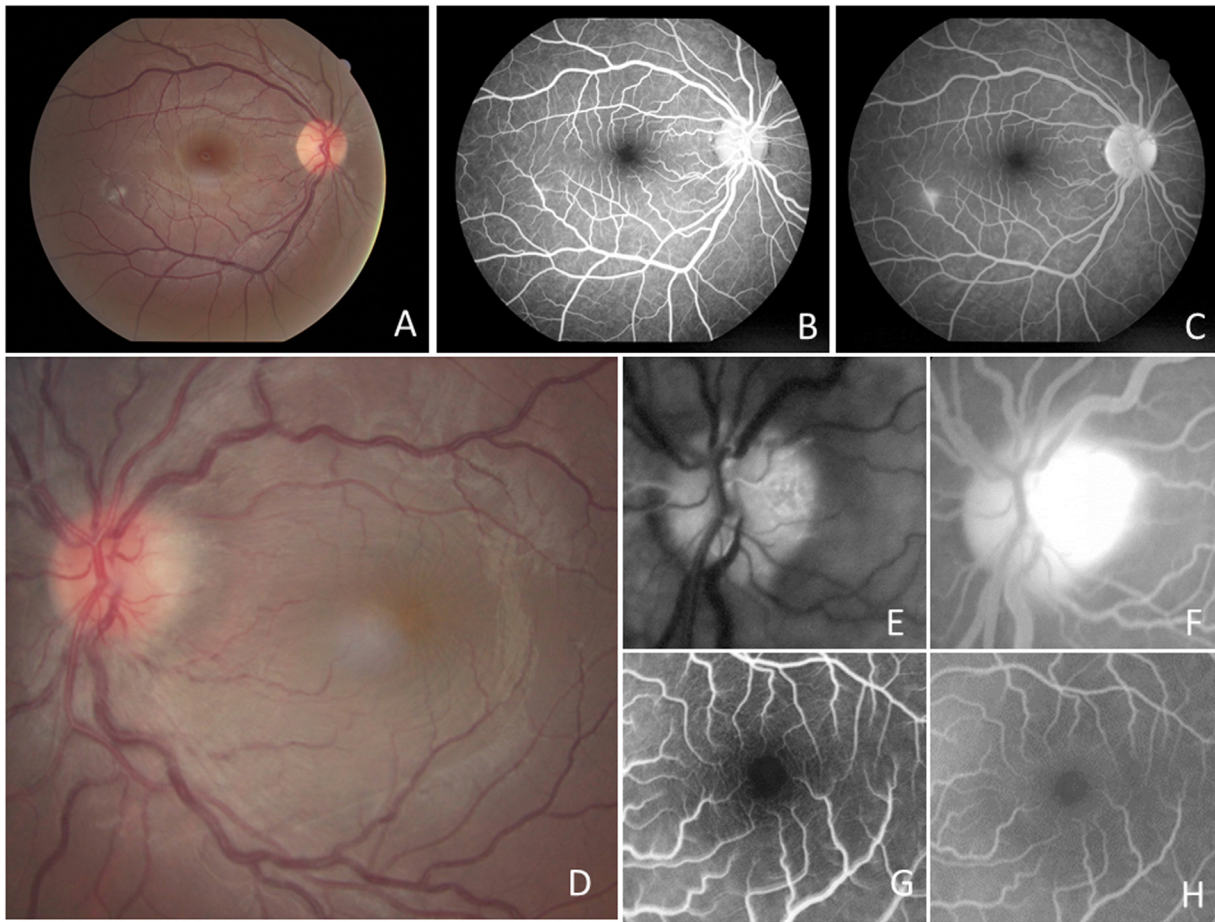


Fig. 3. *Bartonella henselae* neuroretinitis in a 19-year-old man (case 2). Color fundus photograph (A) of the right eye (RE) shows a focal area of retinitis in the temporal macula along the inferotemporal vascular retinal arcade. Fluorescein angiography (FA) of the RE (B, C) displays leakage from this retinal area. Optic disc shows subtle hyperemia and mild FA staining at the nasal margin of the disc. Magnified color fundus photography of the LE in (D) highlights optic disc edema and a subtle radial lines due to macular edema and/or subretinal fluid, partially blocked by an imaging artifact. Magnified FA imaging depicts temporal disc edema in (E) and late hyperfluorescence in (F) due to leakage. Macula images in (G) and (H) also show a subtle central ring of hyperfluorescent staining.

that can make people sick. For instance, ferrets can be infested with fleas more in warmer months as occurred in Case 1. *Ctenocephalides spp.* have been reported in these mammals, transmitting *Bartonella spp.* directly between animals and humans. BH could also spread from ferret bites and scratches contaminated with flea feces [18].

Many households also have pets such as guinea pigs. These small mammals could fit into a pocket and also bite, causing infections such as CSD. Some *Bartonella spp.* are hosted by guinea pigs and could be transmitted to humans by exposure to an infected animal and/or its ectoparasites [19].

We believe that, in our cases, the pet ferret and pet guinea pig were hosts of BH and there was asymptomatic transmission to humans by cat fleas on them. We considered to test the ferret or guinea pig for BH. Unfortunately, serologies could not be done to ascertain whether the animal has had exposure.

The optimum treatment strategy for neuroretinitis due to *Bartonella henselae* is not clear since it depends on age, immune status, and systemic manifestations [20]. In patients with vision loss and/or moderate to severe systemic symptoms, a 4- to 6-week regimen of doxycycline with rifampin or macrolide antimicrobials may provide some benefit. The routine use of systemic corticosteroids in infectious neuroretinitis is not recommended [2,7].

We recognize that our study is limited and not necessarily representative of the entire CSD population. However, in reporting

the possibility of *Bartonella*-associated NR from contact with other household pets, this study highlights the importance of emerging zoonoses from these non-felines mammals. Due to the rarity of *Bartonella* NR, there are few large studies in the literature; therefore, in our opinion, reports of these atypical cases are valuable [7].

In summary, pet owners are at risk of non-feline scratch disease and *Bartonella*-associated NR when they are exposed to BH in the saliva or cat flea feces of infested pets. We hope that this small descriptive case series will raise awareness of the possibility of other non-feline domestic mammals as carriers of BH.

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Ethical approval

This study was approved by the Institutional Review Board Committee at Fundación Oftalmológica Los Andes. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Jorge Orellana-Rios: Conceptualization, Methodology, Resources, Writing - original draft, Writing - review & editing. **Juan I. Verdaguier-Diaz:** Conceptualization, Methodology, Resources, Writing - original draft. **Gabriela Opazo:** Resources, Writing - review & editing. **Belinda C.S. Leong:** Conceptualization, Writing - review & editing. **Claudio Zett:** Resources. **R. Theodore Smith:** Visualization, Supervision, Writing - review & editing. **K. Bailey Freund:** Conceptualization, Methodology, Supervision, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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