Enferm Infecc Microbiol Clin. 2021;39(9):451–453

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Original article

Neuroretinitis caused by *Bartonella henselae* in Gipuzkoa, 2014–2019☆

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ARTICLE INFO

Article history:
Received 17 June 2020
Accepted 13 July 2020
Available online 24 August 2021

Keywords:
Bartonella henselae
Neuroretinitis
Cat scratch disease

ABSTRACT

Introduction: *Bartonella henselae* causes cat scratch disease (CSD), spread by a cat scratch or bite. Cats are its main reservoir. This sometimes results in optic neuritis or neuroretinitis.
Objective: To review these conditions in Gipuzkoa (Spain), 2014–2019.
Methods: A retrospective review of serology registries and clinical registries, selecting those with consistent clinical signs, contact with cats and positive serology for *B. henselae* (IgG-IFA ≥1/256).
Results: Sixty-four patients had CSD. Of these, one had optic neuritis and 3 had neuroretinitis (4/64; 6.3%). In 3 patients, flu-like symptoms preceded eye symptoms. Two suffered from loss of visual acuity at discharge, despite prolonged treatment with antibiotics and corticosteroids.
Conclusion: Optic neuritis and neuroretinitis caused by *B. henselae* are severe complications with a non-negligible incidence among patients with CSD in Gipuzkoa. We recommend ruling out CSD in patients with symptoms of optic neuritis or neuroretinitis (sudden vision loss, etc.) and contact with cats.

Neurorretinitis por *Bartonella henselae* en Gipuzkoa, 2014–2019

Palabras clave:
Bartonella henselae
Neurorretinitis
Enfermedad por arañazo de gato

RESUMEN

Introducción: *Bartonella henselae* causa la enfermedad por arañazo de gato (EAG), transmitida por arañazo o mordedura de gato, su principal reservorio. En ocasiones produce neuritis óptica o neurorretinitis.
Objetivo: Revisar estas patologías en Gipuzkoa (España), 2014–2019.
Métodos: Revisión retrospectiva de registros serológicos y clínicos, seleccionando aquellos con manifestaciones clínicas compatibles, contacto con gatos y serología positiva para *B. henselae* (IFI-IgG ≥1/256).
Resultados: Sesenta y cuatro pacientes presentaron EAG; entre estos, uno tenía neuritis óptica y 3, neurorretinitis (4/64, 6,3%). En 3 casos un cuadro pseudogripal precedió a los síntomas oculares; 2 presentaron pérdida de agudeza visual al alta, a pesar del tratamiento prolongado con antibióticos y corticoides.
Conclusión: La neuritis óptica y la neurorretinitis por *B. henselae* son complicaciones graves que presentan una incidencia no despreciable entre los pacientes con EAG de Gipuzkoa. Recomendamos descartar la EAG en pacientes con síntomas de neuritis óptica o neurorretinitis (pérdida brusca de visión, etc.) y contacto con gatos.

DOI of original article: https://doi.org/10.1016/j.eimc.2020.07.007
☆ Please cite this article as: Salicio-Bermejo Y, Cilla-Eguiluz G, Blanco-Esteban A, Martin-Peñaranda T, Grandioso-Vas D, Echeverría-Irigoyen MJ. Neurorretinitis por *Bartonella henselae* en Gipuzkoa, 2014–2019. Enferm Infecc Microbiol Clin. 2021;39:451–453.
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Introduction

Bartonella henselae is the aetiological agent of cat-scratch disease (CSD), a usually-benign and self-limiting infection characterised by regional lymphadenopathy associated with influenza-like symptoms[1,2], transmitted through the scratches or bites of cats, its main reservoir[2–4]. Less frequently, extranodal manifestations can present[1,4], with the eye being the organ most often affected[5].

Parinaud oculoglandular syndrome is the most typical ocular manifestation.[2,3,5] Other reported ocular manifestations are uveitis[4], neuroretinitis[1–4], inflammatory optic nerve oedema and retinal vessel occlusion[1,4,5]. Neuroretinitis is the most common complication of the infection and, in turn, *B. henselae* is the most common infectious cause of neuroretinitis[3].

The objective of this work was to describe cases of involvement of the posterior segment of the eye associated with *B. henselae* infection detected between 2014 and 2019 at the Hospital Universitario Donostia [Donostia University Hospital], which covers the majority of the population of Gipuzkoa (600,000 inhabitants).

Methods

Patients with positive serology for *B. henselae* were obtained from the laboratory's records. Those patients with specific IgG ≥1/256 (Bartonella IFA, Focus Diagnostics) were considered positive. The corresponding medical records were reviewed and those patients with clinical manifestations compatible with involvement of the posterior segment of the eye, a history of contact with cats and serology results negative for cytomegalovirus, *Toxoplasma*, HIV, syphilis and *Borrelia burgdorferi* were selected. The study was approved by the Gipuzkoa Clinical Research Ethics Committee.

Results

Seventy-four patients presented with CSD, four of which had involvement of the posterior segment of the eye (6.3%), one with infectious/inflammatory optic neuritis and three with neuroretinitis. Their demographic, clinical and serological characteristics, treatment and evolution can be seen in Table 1. Below is a brief description of each case.

Case 1

A 38-year-old man who, after three days of general malaise, myalgia and cough, presented sudden loss of vision in the lower field of his right eye (OD), reporting a clear horizontal level in half his field of vision. He worked in a rural setting with frequent contact with cats. At the time he presented IgG against *B. henselae* of 1/1,024 and negative IgM, with the IgG titre dropping to 1/128 five months later. He was diagnosed with infectious/inflammatory optic neuritis and treated with corticosteroids and doxycycline for six weeks. At discharge, nine months later, his visual acuity of OD remained reduced (0.6).

Case 2

A 31-year-old man who attended the Emergency Department after one week of fever, frontal and temporal headache with dysesthesia in that area, and blurred vision and pain in his left eye (OS). He owned a cat, which had scratched him multiple times. He presented IgG and IgM against *B. henselae* at a titre of 1/512. Diagnosed with neuroretinitis, he was treated with corticosteroids in combination with doxycycline and rifampicin for six weeks. At discharge, nine months later, his acuity of OS was 1.0.

Case 3

A 14-year-old boy who attended the Emergency Department after one week of fever, headache, odynophagia and loss of visual acuity in OS, which he described as "the presence of black spots". He owned several cats, including kittens. He presented specific IgG ≥1/2,048 and IgM 1/256, with the titres reducing two weeks later to 1/512 and <1/64, respectively. The patient was diagnosed with neuroretinitis and treated with corticosteroids in combination with ciprofloxacin and rifampicin for six weeks. At discharge, two months later, his visual acuity of OS was 0.9.

Case 4

A 19-year-old woman with visual disturbances over several days, such as dispersed scotomas and object deformities in OS, accompanied by an oppressive holocranial headache that was predominantly retro-ocular in OS. The loss of vision was worsening and became bilateral. She had frequent contact with a cat, which had scratched her multiple times. She presented IgG against *B. henselae* ≥1/1,024 and negative IgM; 12 weeks later, IgG was 1/256. Diagnosed with neuroretinitis, she was treated with corticosteroids in combination with ciprofloxacin and rifampicin for six weeks. At discharge, one year later, she presented visual acuity of 0.9 in OD and 0.05 in OS and optic atrophy in the temporal side of OS.

Discussion

In the literature, ocular involvement has been described in 5–10% of patients with CSD, mostly in the form of Parinaud oculoglandular syndrome, and in a lower proportion in the form of other atypical manifestations, including neuroretinitis[1,5]. In this review, four patients (6.3%) presented involvement of the posterior segment of the eye with a history of contact with cats, three in the form of neuroretinitis and one as infectious/inflammatory optic neuritis.

Neuroretinitis in patients with CSD was first described by Sweeny and Drance in 1970[6] and is considered the most common complication of *B. henselae* infection involving the posterior segment of the eye[5,7]. It is a syndrome of loss of visual acuity due to optic nerve oedema associated with macular exudates, typically in a star-shaped pattern[2,8], which was observed in two of the patients with neuroretinitis in this study (cases 2 and 3, Table 1).

Clinically, neuroretinitis manifests as a sudden loss of visual acuity, generally unilaterally[1,2,4], often preceded by influenza-like symptoms[1]. All four patients in this study reported previous non-specific symptoms (fever, headache, general malaise and/or myalgia), with the ocular involvement being unilateral in three of them. However, bilateral involvement is not uncommon, as is reported in the review by Ksiaa et al. (54.1%)[8]. Regional lymphadenopathy, a typical characteristic of CSD, is less common in involvement of the posterior segment of the eye: Habot-Wilner et al. described it in 20% of their patients[4]. In this series, the presence of retroauricular lymphadenopathy was observed in one patient.

The diagnosis of ocular CSD is based on characteristic clinical findings, history of contact with cats and serology indicative of recent infection with *B. henselae* (positive IgM and/or IgG ≥1/256)[8]. The four cases presented here had positive serology results (all IgG ≥1/512 and two IgM ≥1/256). It is common in the context of CSD for IgM not to be detected because the disease is subacute (patients may be treated late in its course) and because IgM in *B. henselae* infections is short-lived[2].

Doxycycline, rifampicin, macrolides or fluoroquinolones, usually in combinations of two antibiotics, are generally recommended for the treatment of neuroretinitis[1]. In the latest revision of

Table 1
Patients' demographic and clinical characteristics, treatment and clinical course.

Characteristics	Case 1	Case 2	Case 3	Case 4
Year	2016	2017	2017	2018
Sex	M	M	M	F
Age, years	38	31	14	19
Fundus	OD: optic nerve oedema	OD: no alterations	OD: no alterations	OD: temporal face of optic nerve effaced
	Splinter haemorrhages	OS: initially, optic nerve oedema, flat retina and macula free of alterations. Two weeks later, optic nerve oedema	OS: oedema with macular star	Optic nerve oedema
	Papillomacular bundle oedema	with macular star	Left temporal optic nerve effaced with hyperaemia and capillary ingurgitation	Multiple exudative detachments
	OS: no alterations			OS: optic nerve oedema Papillomacular bundle oedema Multiple exudative detachments
Systemic symptoms	Yes	Yes	Yes	Yes
Lymphadenopathy	No	No	Retroauricular	No
Initial VA	0.6	0.3	0.4	OD: 0.8 OS: 0.1
Treatment	Corticosteroids + doxycycline	Corticosteroids + doxycycline + rifampicin	Corticosteroids + ciprofloxacin + rifampicin	Corticosteroids + ciprofloxacin + rifampicin
Final VA	0.6	1	0.9	OD: 0.9 OI: 0.05
Bartonella henselae IgG	1/1,024	1/512	≥1/2,048	≥1/2,048
Bartonella henselae IgM	Negative	1/512	1/256	Negative
Diagnosis	Infectious/inflammatory optic neuritis	Neuroretinitis	Neuroretinitis	Neuroretinitis

M: male; F: female; OD: right eye; OS: left eye; VA: visual acuity.

UpToDate[9], combined antibiotic treatment associated with corticosteroids is recommended for all patients with neuroretinitis secondary to CSD, doxycycline and rifampicin in patients over eight years of age, and azithromycin or trimethoprim–sulfamethoxazole plus rifampicin in those younger than eight. There is no consensus on the optimal duration of treatment, but it has been recommended to maintain it for at least six weeks[9].

While ocular involvement due to CSD can resolve spontaneously with a favourable visual prognosis in immunocompetent patients[1,8], it is not uncommon for vision loss to persist, as has been observed in 6–13.5% of cases in some reviews[4,7]. Close ophthalmological follow-up is therefore important in these patients. Two of the patients in this study presented a unilateral loss of visual acuity at discharge despite the prolonged antibiotic treatment: the patient with infectious/inflammatory optic neuritis presented a visual acuity of 0.6 in OD and one of the patients with neuroretinitis 0.05 in OS.

In conclusion, involvement of the posterior segment of the eye is a complication of CSD that can sometimes have serious sequelae such as loss of visual acuity. This is of particular significance as CSD often affects young subjects (more potential years of cumulative disability). It is necessary to consider the possibility of *B. henselae* infection in any inflammatory involvement of the posterior segment of the eye so that specific treatment can be started as early as possible.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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