

CASE SERIES

Case Series of Neuroretinitis in Cat Scratch Disease

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ABSTRACT

Introduction: Neuroretinitis is a typical ocular presentation of cat scratch disease (CSD). It is characterised by optic disc swelling with macular star formation. *Bartonella henselae* is the commonest cause of neuroretinitis. **Case series:** This article provides a retrospective review of the variations in three patients' clinical presentations and responses to the two of the treatment options available for the disease. We report a retrospective case series of neuroretinitis in CSD with three patients who presented to the ophthalmology clinic at Selayang Hospital from June 2016 to August 2019. All patients had a history of contact with cats with two of them had a history of fever before developing ocular symptoms. All patients presented with optic disc swelling and macular star. In addition, Case 2 presented with mild vitritis and Case 3 with multiple foci of choroiditis. A serology analysis of *Bartonella henselae* was positive for both immunoglobulin (Ig) M and IgG in all three patients. Two of the patients were treated with oral doxycycline, while Case 3 was treated with oral sulfamethoxazole and trimethoprim. All patients had a poor vision at their initial presentation, but none of them warranted oral prednisolone and had good visual outcomes. **Conclusion:** Neuroretinitis is a typical ocular presentation of CSD. Diagnosis is confirmed via positive serologic testing for *Bartonella henselae*. Although neuroretinitis is self-limiting, various treatment options can hasten disease recovery with good visual outcomes.

Keywords: Neuroretinitis, Cat scratch disease, Bartonellosis

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INTRODUCTION

Cat scratch disease (CSD) is a systemic infectious disease caused by *Bartonella henselae* (1). Fever, lymphadenopathy and skin lesions following a cat scratch or bite are seen in CSD patients (2). Cat fleas are the natural vector of *Bartonella henselae*. By scratching and biting at the fleas, the infected fleas are collected under cats' nails and between their teeth. The *Bartonella* bacteria can then be transmitted to humans via cat scratches or bites (2).

About 5–10% of patients with CSD have been estimated to have ocular involvement, with neuroretinitis occurring in 1–2% of patients (2). Neuroretinitis is an inflammatory optic neuropathy characterised by optic disc swelling and macular star formation (1). Macular star formation occurs due to the depositing of lipid exudates in the retinal layer, which creates the typical star pattern.

The aim of this case series is to describe the clinical features of neuroretinitis due to CSD and their response to antibiotic treatments.

CASE SERIES

This is a retrospective case series of three patients who presented at the ophthalmology clinic of Selayang Hospital, Malaysia from June 2016 to August 2019. All patients had a history of contact with cats, as manifested through neuroretinitis, with positive serology for *Bartonella henselae*. Two of them presented with fever before presenting with ocular symptoms. Table I shows a summary of the three cases.

Case 1

A 44-year-old woman presented with a painless progressive blurring of vision in the left eye for two days. She had a history of high-grade fever for a few days before developing ocular symptoms. She was diagnosed with hypertension and no other medical illness. She had four vaccinated cats at home with no history of cat bites.

General examination revealed that she was afebrile with stable vital signs. Her left eye examination showed visual acuity was 6/24 and not improved with pinhole. The relative afferent pupillary defect (RAPD) was negative. The anterior segment examination was normal with normal intraocular pressure (IOP). Fundus examination showed features of neuroretinitis characterised by inferior optic disc swelling accompanied by hard exudates arranged in a partial star shape around the

Table 1: Summary of neuroretinitis cases in cat scratch disease.

Clinical profile	Case 1	Case 2	Case 3
Age	44	33	30
Gender	Female	Male	Female
Systemic comorbidity	Hypertension	Nil	Nil
Risk factor	Contact with cats but no history of cat bites	History of cat scratch	Contact with cats but no history of cat bites
Laterality	Left eye	Left eye	Right eye
Ocular symptom	Blurring of vision for 2 days	Blurring of vision for 2 weeks	Blurring of vision for 4 days
Ocular sign	<ul style="list-style-type: none"> Neuroretinitis 	<ul style="list-style-type: none"> Neuroretinitis Anterior chamber inflammation Mild vitritis 	<ul style="list-style-type: none"> Neuroretinitis Multiple choroiditis Single chorioretinal scar
OCT macula	<ul style="list-style-type: none"> Increased macular thickness Oedematous Henle's layer Presence of subretinal fluid 	<ul style="list-style-type: none"> Increased macular thickness Oedematous Henle's layer Presence of subretinal fluid 	<ul style="list-style-type: none"> Increased macular thickness Oedematous Henle's layer Presence of subretinal fluid
Systemic symptom	Fever	Nil	Fever
Systemic sign	Afebrile	Afebrile	Afebrile
<i>Bartonella henselae</i> serology	IgM 1:96 IgG 1:128	IgM 1:24 IgG 1:128	IgM 1:24 IgG 1:128
Vision at presentation	6/24	6/36	6/60
Vision at final visit post treatment	6/9	6/9	6/9
Treatment	<ul style="list-style-type: none"> Oral doxycycline 200 mg daily for 6 weeks 	<ul style="list-style-type: none"> Oral doxycycline 200 mg daily for 6 weeks Topical dexamethasone for 4 weeks 	<ul style="list-style-type: none"> Oral sulfamethoxazole and trimethoprim 960 mg twice per day for 6 weeks

Abbreviation: IgM: Immunoglobulin M, IgG: Immunoglobulin G

fovea manifested as partial macular star (Fig. 1A). Optical coherence tomography (OCT) of the left macula showed increased macular thickness with oedematous of Henle's layer and presence of subretinal fluid (SRF) (Fig. 1B). Right eye examination was normal. Systemically, there were no lymphadenopathy or skin lesions.

Given the history of fever, a provisional diagnosis of an infective cause of neuroretinitis was made. CSD was considered as one of the infective causes since the patient had a history of contact with cats. The patient's C-reactive protein level was 0.94 mg/L, and her Mantoux test was 18 mm with a negative QuantiFERON-TB test. *Bartonella henselae* serology was positive for both immunoglobulin (Ig) M (titre of 1:96) and IgG (titre of 1:128). Other infection screenings were negative.

Based on a positive *Bartonella henselae* serology test, a diagnosis of ocular CSD was made. This patient was

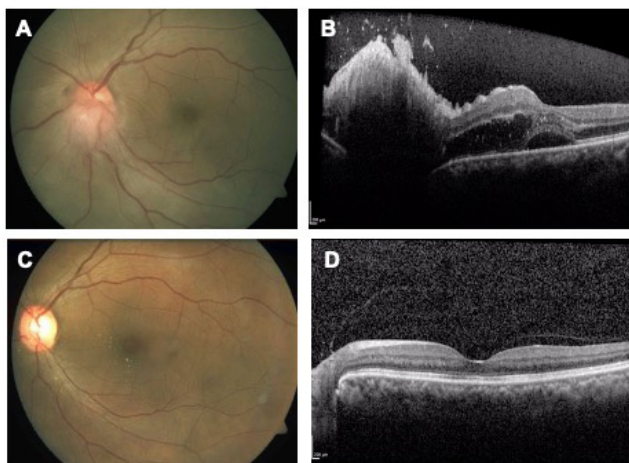


Figure 1: Fundus and optical coherence tomography (OCT) findings for left eye in Case 1. (A) Left fundus showed inferior optic disc swelling with early macular star at presentation. (B) Left eye OCT displayed presence of subretinal fluid (SRF) and oedematous of Henle's layer at presentation. (C) Left fundus showed resolving optic disc swelling and macular star six weeks post treatment. (D) Left eye OCT showed resolution of SRF and Henle's layer's oedema six weeks post-treatment.

treated with 200 mg oral doxycycline daily for six weeks. Her left eye vision improved to 6/9 with resolving optic disc swelling and macular star (Fig. 1C), and resolution of Henle's layer's oedema and SRF at six weeks follow-up (Fig. 1D).

Case 2

A 33-year-old man presented with a painless progressive blurring of vision in the left eye for two weeks. He had a history of cat scratch from his own cats. He had not known to have hypertension, diabetes or other medical illness.

Generally, he was afebrile with stable vital signs. Left eye examination showed his visual acuity was 6/36 and not improved with pinhole. There was positive RAPD in the left eye. There were occasional cells in the anterior chamber with mild vitritis. The IOP was normal. Fundus examination showed the presence of neuroretinitis characterised by optic disc swelling at the inferotemporal part and temporal margin of the disc, accompanied by star shape arrangement of hard exudates around the fovea manifested as macular star (Fig. 2A). The OCT of the left macula showed increased macular thickness, oedematous of Henle's layer with hard exudates, and presence of SRF (Fig. 2B). Right eye examination was normal. Systemically, there were no lymphadenopathy or skin lesions.

A provisional diagnosis of ocular CSD was made given the patient had a history of cat scratch with neuroretinitis manifestation. Other infective causes for neuroretinitis were also investigated. The patient's erythrocyte sedimentation rate (ESR) was raised (30 mm/hr) and he had a positive *Bartonella henselae* serology test for both

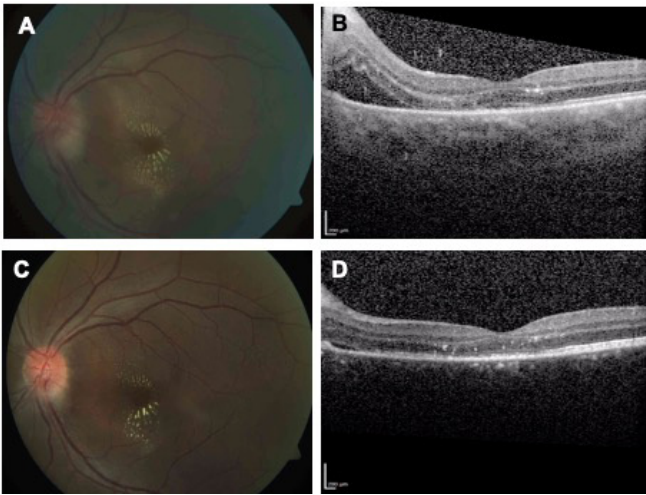


Figure 2: Fundus and optical coherence tomography (OCT) findings for left eye in Case 2. (A) Left fundus showed optic disc swelling at the inferotemporal part and temporal margin of the disc with macular star at presentation. (B) Left eye OCT displayed presence of subretinal fluid (SRF) and oedematous of Henle's layer with hard exudates at presentation. (C) Left fundus showed resolving optic disc swelling and macular star six weeks post treatment. (D) Left eye OCT showed resolution of SRF and Henle's layer's oedema six weeks post-treatment.

IgM and IgG (titres of 1:24 and 1:128, respectively). Other infection screenings were negative.

A final diagnosis of ocular CSD was made based on a positive *Bartonella henselae* serology test. This patient was treated with 200 mg oral doxycycline daily for six weeks and topical dexamethasone every four hours, which then tapered down within four weeks. At six weeks review, the patient's left eye vision improved to 6/9, with resolving optic disc swelling and macular star and resolved vitritis (Fig. 2C). OCT of the left eye showed resolution of Henle's layer's oedema and SRF (Fig. 2D).

Case 3

A 30-year-old woman presented with a painless progressive blurring of vision in the right eye for four days. Prior to the blurring of vision, she had a history of high-grade fever for a few days. She had a vaccinated cat and had no history of cat bites. She had not known to have hypertension, diabetes or other medical illness.

On general examination, she was afebrile with stable vital signs. Right eye examination showed her visual acuity was 6/60 and not improved with pinhole. The RAPD was negative. The anterior segment examination was normal with normal IOP. Fundus examination showed optic disc swelling at the temporal disc margin with macular oedema (Fig. 3A). There were multiple foci of choroiditis at superior and inferior arcades, and a single chorioretinal scar nasal to optic disc without adjacent chorioretinitis. However, there was no vitritis. Left eye examination was normal. Systemically, there

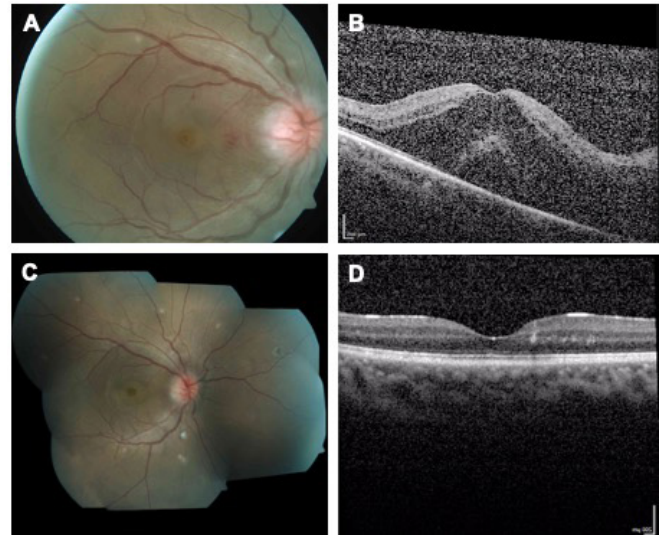


Figure 3: Fundus and optical coherence tomography (OCT) findings for right eye in Case 3. (A) Right fundus showed optic disc swelling at the temporal disc margin with macular oedema, and multiple choroiditis at superior arcuate at presentation. (B) Right eye OCT displayed presence of subretinal fluid (SRF) and oedematous of Henle's layer at presentation. (C) Right fundus showed resolving optic disc swelling and macular star eight weeks post treatment. Multiple choroiditis at superior and inferior arcades and a single chorioretinal scar appeared nasally to optic disc. (D) Right eye OCT showed resolution of Henle's layer's oedema SRF eight weeks post-treatment.

was no lymphadenopathy or skin lesions.

An initial diagnosis of right ocular toxoplasmosis was made based on a history of contact with cats and the presence of chorioretinal scar together with optic disc swelling and choroiditis. The patient was treated with 960 mg oral sulfamethoxazole and trimethoprim twice per day while waiting for the result of infective screening.

At one week after the presentation, there was a mild improvement of right eye vision. Fundus examination showed the presence of macular star characterised by star shape arrangements of hard exudates around the fovea. OCT of the right macula showed increased macular thickness with oedematous of Henle's layer and presence of SRF (Fig. 3B). Serology for toxoplasmosis was negative. However, *Bartonella henselae* serology was positive for both IgM and IgG with titres of 1:24 and 1:128, respectively. Her ESR was raised (76 mm/hr), and other infection screenings were negative.

Finally, a diagnosis of ocular CSD was made. In view of improvement of vision, the patient was continued with 960 mg oral sulfamethoxazole and trimethoprim twice per day to be completed for six weeks. Her right eye vision improved to 6/9, with the resolution of optic disc swelling and macular star at eight weeks post-treatment (Fig. 3C). OCT findings of the right eye showed resolution of Henle's layer's oedema and SRF (Fig. 3D).

DISCUSSION

Neuroretinitis is associated with varieties of infective agents. The most common infective cause is CSD. The incidence of CSD is 4.7 per 100,000 people age lesser than 65 years old. Estimation of 12 500 patients in the USA is diagnosed annually with CSD (3). In various studies, the seroprevalence of antibodies to *Bartonella henselae* ranging from 3.8% to 50% worldwide (4,5). In Eastern China, the seroprevalence ranges from 2.0 to 32.38% (6).

A history of contact with infected animals (cats, kittens or cat fleas) through scratched skin lesions and inoculation with *Bartonella henselae* is an important point to note (2). Although two of these patients gave no history of cat bites or scratches, some reported cases show merely having contact with cats is enough to get infected by the pathogen. Another mode of entry is via mucous membranes, such as conjunctiva or nasal mucosa. Along with eye rubbing after contact with cats can lead to direct inoculation of this pathogen to allow *Bartonella henselae* to spread systemically (7). Even though the cats are vaccinated, there is no feline vaccine against *Bartonella henselae* developed to date, thus not protective against the pathogen (8).

Typical CSD is characterised by regional lymphadenitis, associated with fever, malaise and night sweats (9). Atypical CSD spreads haematologically causing extranodal manifestations which include musculoskeletal, neurological, dermatological, hepatosplenic and ophthalmic manifestations (10). A combination of granulomatous conjunctivitis and periocular lymphadenopathy is described as Parinaud's oculoglandular syndrome (11).

The posterior segment findings of the eye reported in various studies are neuroretinitis, optic neuritis, focal retinitis, choroiditis, chorioretinitis, exudative maculopathy, serous retinal detachment and vitritis (11,12). All of the patients in this case series presented with a blurring of vision. The ocular symptoms were preceded by fever in two of them. Neuroretinitis is present in all cases. Other aetiological infective agents for neuroretinitis include tuberculosis, leptospirosis and syphilis (13). Neuroretinitis may mimic optic neuropathy such as papilledema, ischemic optic neuropathy, optic neuritis, compressive lesions of the optic nerve, toxic/nutritional deficiencies (14) or vascular retinopathy such as malignant hypertensive retinopathy and diabetic papillopathy (15). Pain, characteristic of visual loss (particularly visual field defects) and abnormalities of retinal vessel help to differentiate the cause of neuroretinitis between optic neuropathy, vascular retinopathy and infective type.

The diagnosis of CSD-associated neuroretinitis is based on the clinical findings; history of contact with

cats, typical neuroretinitis, systemic symptoms, and positive serology (16). Serologic testing is the best way to confirm the diagnosis of *Bartonella henselae* (2). Indirect fluorescent antibody testing for *Bartonella henselae* has high specificity and sensitivity. An increase in IgM titres with a significant increase in IgG antibody titres can imply an acute Bartonella infection (17). All three patients in our case series had positive *Bartonella henselae* serological test results. A positive serology with negative infection screening for other infective causes further supports the diagnosis of Bartonella infection in this case series.

The usual course of treatment for CSD is oral doxycycline 200 mg/day given for 14–28 days. However, the disease can also be self-limiting, only requiring treatment to hasten recovery. Other antibiotics that have been used in CSD treatment include rifampin, ciprofloxacin, trimethoprim/sulfamethoxazole and gentamicin (10, 18). With proper treatment, a favourable visual outcome may be achieved, although spontaneous visual recovery exists in cases of Bartonella neuroretinitis.

In immunocompetent patients, gradual resolution of optic disc oedema and hard exudates may occur within a few weeks or months and most patients regained a normal visual acuity (19). Some immunocompromised patients may have severe ocular complications especially those with intraocular inflammation (20). In our case series, all patients responded well to their treatment options with improved vision and resolved ocular signs.

CONCLUSION

Neuroretinitis is a typical ocular presentation of CSD. Although the disease is self-limiting, various treatment options can hasten disease recovery with good visual outcomes.

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