OBSERVATION

# Suspecting Optic Neuritis, Diagnosing *Bartonella* Cat Scratch Disease

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**Background:** *Bartonella* cat scratch disease is classically a febrile illness, in conjunction with lymphadenopathy and cat exposure.

**Objective:** To report 2 atypical cases of cat scratch disease with only blurred vision and headache.

**Design:** Case reports.

**Setting:** University hospital.

**Patients:** Two young adults with unilateral blurred vision, retro-orbital headache, and a positive *Bartonella henselae* serologic result, without fever or lymphadenopathy.

**Main Outcome Measures:** Funduscopic examination and *B henselae* serologic findings.

**Results:** Both patients had optic disc swelling and a macular star on funduscopic examination, suggestive of infection. Infection was confirmed by positive serologic results.

**Conclusion:** Cat scratch disease should be considered in the differential diagnosis for patients presenting with blurred vision and headache, even in the absence of fever, lymphadenopathy, or both.

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CAT SCRATCH DISEASE (CSD) is most commonly caused by *Bartonella henselae*. More than 30 000 cases of CSD are reported annually in the United States, resulting in more than 2000 hospitalizations.[1] Cat scratch disease is typically characterized by fever and regional lymphadenopathy, with some patients having a skin lesion at the site of inoculation.[2,3] After the lymphatic system, the eye is the most frequently affected organ.[3] Ocular involvement can be subclinical and visual symptoms may not be a common presenting complaint. Neuroretinitis is an optic neuropathy classically characterized by optic disc swelling in the presence of a partial or complete macular star.[4] Its prevalence in CSD is unclear, possibly seen in 1% to 2% of cases.[1] Typically, neuroretinitis presents unilaterally.[2] Bilateral cases have been reported, but they are much rarer.[3,5]

Lymphadenopathy is a diagnostic criterion of CSD. In a study of 1200 patients, Carithers[3] estimated that lymphadenopathy is present in 85% of cases. Fever is also present in most patients.[2,3] We report 2 serologically confirmed cases of CSD. Both patients presented with unilateral visual symptoms and headache but without fever or lymphadenopathy.

## REPORT OF CASES

### CASE 1

A 31-year-old woman with no significant medical history was admitted to the hospital for blurred vision in the left eye and mild frontal headache for 2 days. The patient reported horizontal diplopia and pain on right gaze. Visual acuity in the right eye was baseline (20/20); in the left eye, it was reduced to finger counting (20/200). Color vision was normal bilaterally. Optic disc swelling and retinal exudates were noted bilaterally (**Figure 1**A and B) but more so in the left eye. A partial macular star (Figure 1B) was seen in the left retina. Results of neurological examination were otherwise unremarkable. The patient was afebrile throughout the hospital admission and had no lymphadenopathy.

Results of brain imaging studies (head computed tomography, brain magnetic

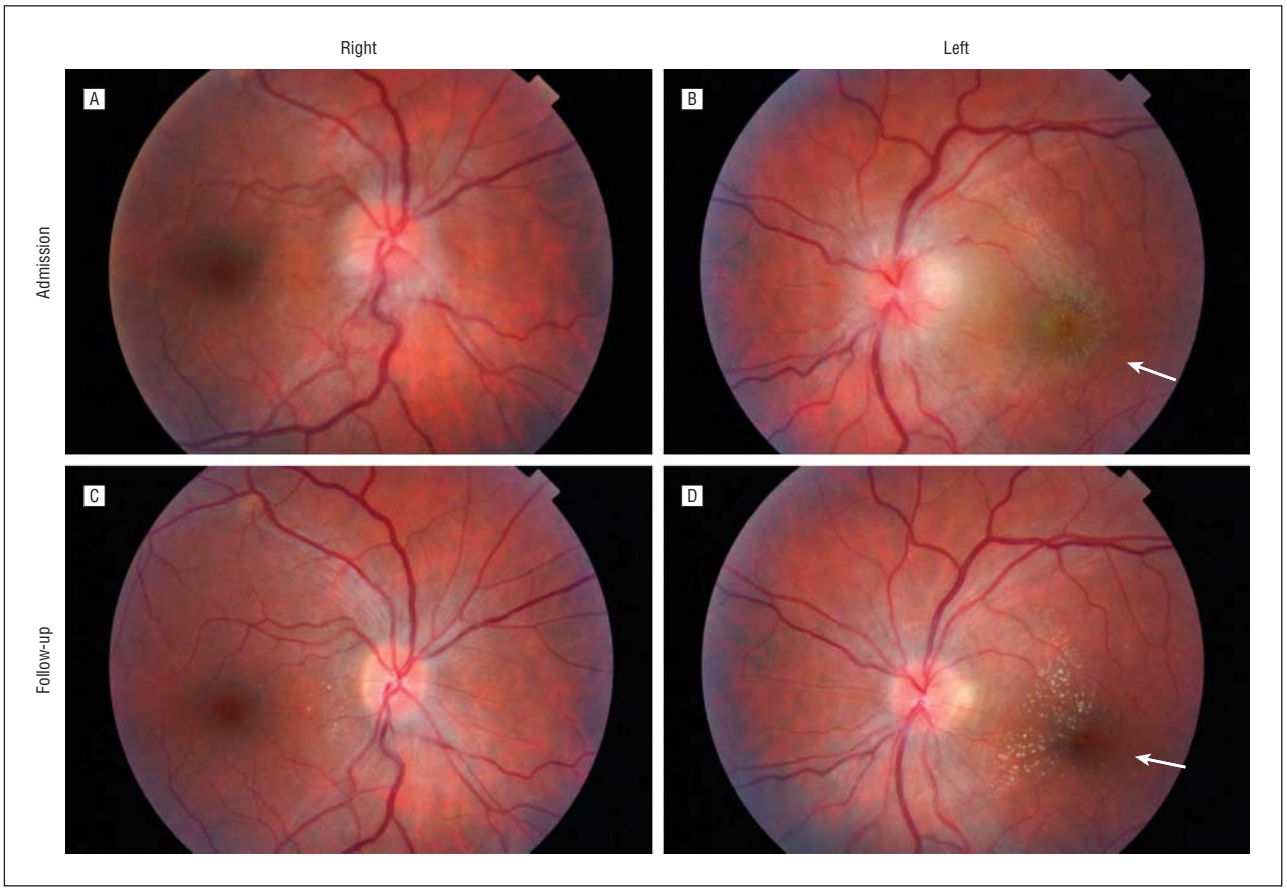


**Figure 1.** Patient 1. Color fundus views of the right (A) and left (B) eyes at hospital admission and 7 weeks later, right (C) and left (D) eyes. Note optic disc swelling that is present bilaterally, at hospital admission, but resolved at 7 weeks. A partial macular star is seen in the left eye at admission and follow-up (arrows).

resonance imaging, and brain magnetic resonance venogram) were normal. The results of routine blood tests were normal; the levels of glycated hemoglobin, thyrotropin, and B12 were normal as well. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated at 3.9 mg/dL and 48 mm/h, respectively (to convert CRP to nanomoles per liter, multiply by 9.524). Lumbar puncture opening pressure was 175 mm $H_2O$. Cerebral spinal fluid (CSF) had an elevated white blood cell count (10 000/μL) (to convert to $\times 10^9$/L, multiply by 0.001), with a differential cell count of 2% polymorphonuclear leukocytes, 64% lymphocytes, 0% eosinophils, 0% basophils, and 34% macrophages (to convert all the percentages to a proportion of 1.0, multiply by 0.01). Red blood cell count ($9.0\times 10^9$/L) (to convert to $\times 10^{12}$/L, multiply by 1.0) and protein (29 mg/dL) (to convert to grams per liter, multiply by 10.0) and glucose (61 mg/dL) (to convert to millimoles per liter, multiply by 0.0555) levels were within normal limits. A chest radiograph was normal and tuberculosis skin test (purified protein derivative) was nonreactive. Results of serum angiotensin-converting enzyme, antinuclear antibody (ANA), anti–neutrophil cytoplasmic antibodies (pANCA or cANCA), and human immunodeficiency virus testing were negative. Serologic results for serum rapid plasma reagin, Lyme, *Borrelia*, and toxoplasmosis antibody titers were all negative, as were CSF culture, VDRL test, polymerase chain reaction for *Bartonella* and Lyme DNA, and multiple sclerosis (CSF) panel (myelin basic protein, oligoclonal bands, IgG index).

On a second medical history intake, patient 1 revealed sporadic contact with a cat, most recently 2 weeks prior to hospital admission. She denied having been scratched or bitten. No skin lesions, scratches, or bite marks were found. She denied recent fever or any sick contacts. Patient 1 was treated empirically with a combination of oral doxycycline hyclate, 100 mg, and rifampin, 300 mg, twice daily for 7 weeks, on the basis of funduscopic examination. Five days after hospital discharge, *B henselae* serologic results demonstrated IgM and IgG detectable at a dilution of 1:512, indicating current infection (indirect fluorescent antibody enzyme-linked immunosorbent assay (ELISA); ARUP Laboratories, Salt Lake City, Utah). She reported slightly improved visual acuity in the left eye. After 7 weeks, headache had resolved, and visual acuity returned to baseline (20/20 OS). A partial macular star remained (Figure 1D).

## CASE 2

A 37-year-old man with no significant medical history was admitted for blurred vision in the right eye and accompanying retro-orbital headache for 2 days. Secondary complaints included recurrent sinus pain and subjective fever (intermittent self-perception of abnormal warmth or coldness) that he attributed to his typical si-

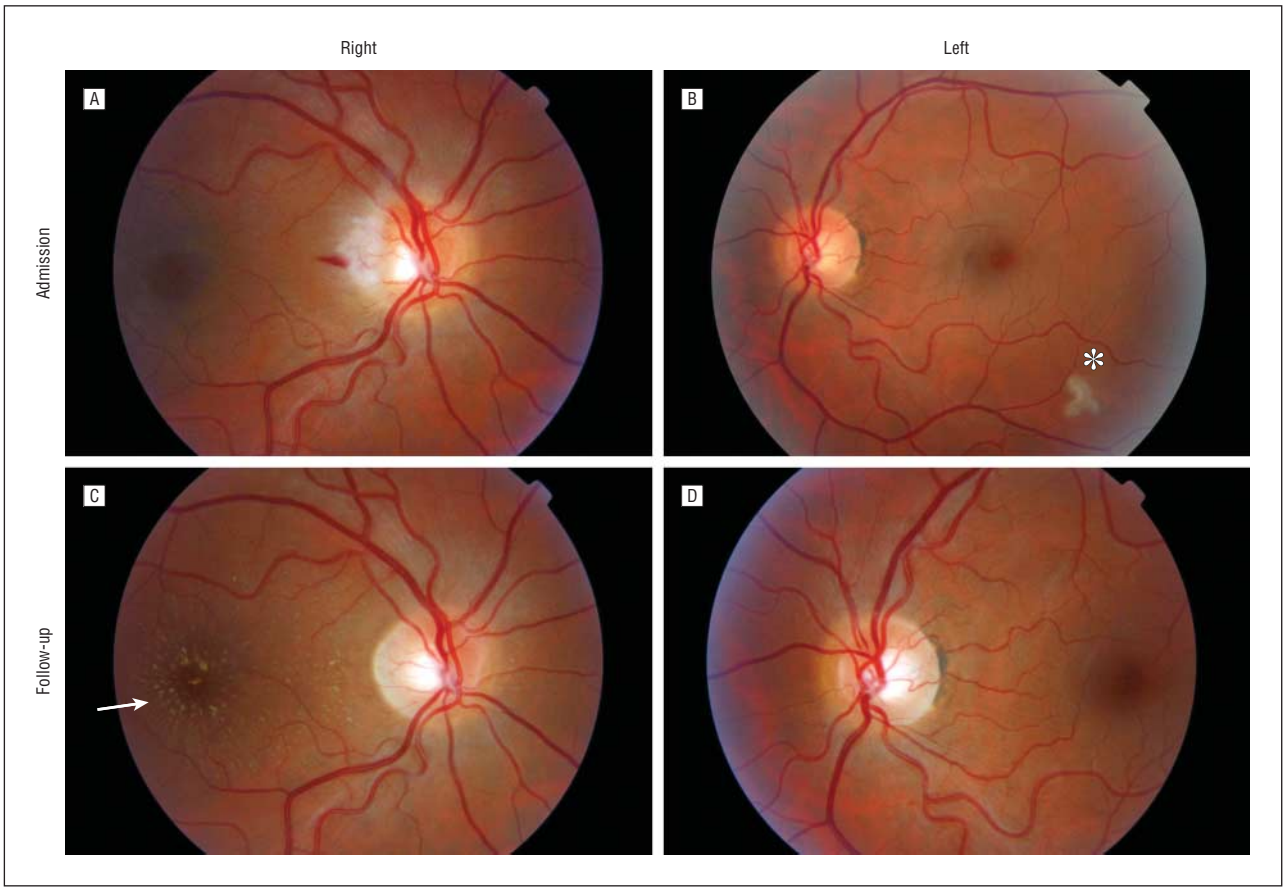


**Figure 2.** Patient 2. Color fundus views of the right (A) and left (B) eyes at hospital admission and 8 weeks later, right (C) and left (D) eyes. Note optic disc swelling and a small hemorrhage near the optic disc are present in the right eye but not in the left eye. There is a cotton-wool spot in the left eye at hospital admission (*), the area is not visualized at 8 weeks. A macular star is seen in the right eye at follow-up (arrow), whereas optic disc swelling has resolved.

nus problems. The patient's hospital admission temperature was 37.4°C, and he had a single maximum temperature of 37.6°C throughout his hospital stay. No lymphadenopathy was found. Reduced right eye visual acuity (20/60 OD), optic disc swelling, retinal exudates, small hemorrhages (**Figure 2**A), and a central scotoma were noted. Visual acuity was normal in the left eye (20/20), and funduscopic examination demonstrated a lone cotton-wool spot (Figure 2B). He had normal color vision in both eyes. Results of the neurological examination were otherwise unremarkable. Patient 2 had scratches on his arms from direct contact with 2 cats.

Head computed tomography showed a small mucous retention cyst in the left maxillary sinus. Brain magnetic resonance imaging demonstrated multiple small T2 and fluid-attenuated inversion recovery hyperintensities within the bilateral subcortical white matter, as well as centrum semiovale, suggesting the possibility of demyelinating disease. Results of the magnetic resonance venogram were normal. Results of routine blood tests and $B_{12}$ level were normal. Lumbar puncture opening pressure was 200 mm $H_2O$. Cerebrospinal fluid had normal levels of white blood cells (2000/μL), red blood cells ($1.0\times10^9$/L), protein (36 mg/dL), and glucose (76 mg/dL). A chest radiograph was normal. Results of serum angiotensin-converting enzyme, antinuclear antibody, anti–neutrophil cytoplasmic antibodies (pANCA and cANCA), rapid plasma reagin, Lyme, and human immunodeficiency virus testing were negative, as were CSF routine culture, VDRL test, angiotensin-converting enzyme, *Bartonella* and Lyme polymerase chain reaction, and a multiple sclerosis panel.

Suspecting optic neuritis, a 5-day course of intravenous methylprednisolone was initiated, following which the patient's vision greatly improved. Erythrocyte sedimentation rate decreased from 44 mm/h on day 2 of methylprednisolone treatment to 29 mm/h on discharge day 5. The CRP level was 0.4 mg/dL, tested on day 3 of methylprednisolone treatment. On the day of hospital discharge, a preliminary report of *B henselae* IgM suggested infection (indirect fluorescent antibody ELISA; ARUP Laboratories), and a combined course of oral doxycycline hyclate, 100 mg, and rifampin, 300 mg, twice daily for 8 weeks was started.

After discharge, *B henselae* IgM serologic results returned positive at 1:16, whereas the IgG titer was equivocal at 1:64. Three weeks later, *B henselae* IgM was not detected (<1:16), but IgG was suggestive of recent infection (1:256).

Four weeks after hospital discharge, a macular star (Figure 2C) had developed in the right eye, not previously present during the hospital admission (Figure 2A). Visual acuity had improved significantly. The patient was experiencing occasional subjective

fevers but was afebrile at clinic visits. At 8-week follow-up, the subjective fever had fully resolved, although he still experienced occasional mild right periorbital headache. Visual acuity in the right eye had improved but not to baseline.

## COMMENT

The classic presentation of CSD is a febrile illness, in conjunction with a history of feline exposure, lymphadenopathy, and cutaneous lesions. Fever and lymphadenopathy have been considered diagnostic criteria of CSD.[2,3] Cases of CSD neuroretinitis lacking lymphadenopathy have been reported.[3,6] No criterion standard exists for the definitive diagnosis of *B henselae* infection, and diagnostic testing relies heavily on a positive serologic test result. Tissue biopsy, culture, or polymerase chain reaction has variably demonstrated lower specificity and sensitivity.[2,7] While there is variability in multiple studies of *B henselae* IgG and IgM indirect fluorescent antibody and ELISA serology, typical sensitivity values are approximately 50% to 80%, whereas specificity is 90% to 100%. Sensitivity increases when there is a higher clinical index of suspicion for CSD, when IgG and IgM are tested in combination, and when serologic testing is repeated several weeks apart (as antibody production varies through the disease course).[2,7] Tsuneoka and Tsukahara[6] found that up to 16% of patients serologically diagnosed as having CSD presented with no lymphadenopathy. Three of 30 such individuals were also afebrile. However, unlike the cases reported herein, 2 of these patients had symptoms suggestive of systemic illness.[6] A large retrospective study by Carithers[3] demonstrated that as many as 41% of patients with CSD may have no documented fever. However, the collective absence of systemic symptoms, fever, lymphadenopathy, and cat scratch marks in CSD is either rare or underreported. Presenting approximately 1 year apart, these patients illustrate that CSD presenting solely with visual complaints (neuroretinitis) and headache is not rare. Likely, *Bartonella* CSD is underdiagnosed when symptoms are limited to blurred vision and headache. On point, when Suhler et al[8] screened 14 patients with neuroretinitis, 9 of 14 had elevated titers of *B henselae* IgM or IgG.

Neuroretinitis is highly suggestive of infection, whereas optic neuritis is an isolated inflammatory optic neuropathy secondary to demyelination.[9] The funduscopic examination is important in raising the index of suspicion for CSD and did so in the aforementioned patients. Additionally, elevation in inflammatory markers (ESR and CRP) is atypical for optic neuritis.[9] Differentiation of neuroretinitis and optic neuritis (**Table**) is necessary for initiation of appropriate and prompt treatment and impacts eventual prognosis. The most worrisome outcome is the risk of permanent vision loss. Typical *Bartonella* serology time delay can necessitate therapeutic decisions prior to the availability of results.

Intravenous methylprednisolone does not change the long-term prognosis of optic neuritis, but it does hasten short-term visual recovery.[10] Recommended treatment for CSD neuroretinitis is a combination of oral doxycycline and rifampin. There are no controlled clinical trials comparing a nontreatment group with those given antibiotics. However, retrospective case series consistently associated antibiotics with hastened visual recovery and improved visual outcome.[2,5] Corticosteroid use in CSD with eye involvement has had mixed results. There was good response in multiple studies,[11,12] but conversely, recent case reports have found no improvement in symptoms with corticosteroids.[2]

In the cases reported herein, classic signs of CSD were either obscured or absent. Patients sought medical attention with only complaints of blurred vision and headache. Similar abnormalities in relatively young patients, statistically at risk for multiple sclerosis, could be misinterpreted as demyelinating optic neuritis.[9] Reliance on serologic testing, whereas specific,[2,6] can delay diagnosis and treatment. Classic funduscopic examination and elevated inflammatory markers can suggest *B henselae* as the cause, dictating the initiation of antibiotics. Considering CSD, even in the absence of fever, lymphadenopathy, or obvious scratches, will aid in making the diagnosis.

**Table. Typical Presentation and Management of Neuroretinitis vs Optic Neuritis**

| Variable | Neuroretinitis | Optic Neuritis |
|---|---|---|
| Typical age | Children, young adults | Young adults |
| Sex, M/F | 1:1 | 2:1 |
| Retro-orbital headache | Variable | Pain in >90% |
| Onset | Hours to days | Hours to days |
| Visual complaint | Unilateral | Unilateral |
| Funduscopic examination findings | Macular star, disc swelling, exudates, bilateral abnormalities possible | Normal in 2 of 3 patients, rarely bilateral |
| Visual field defect | Variable | Central scotoma |
| Lymphadenopathy | More likely | Not likely |
| Fever | More likely | Not likely |
| Inflammatory markers | Elevated ESR and CRP, variable CSF pleocytosis | Normal ESR and CRP, 1 of 3 patients have CSF pleocytosis |
| MRI | Normal or variably abnormal | Inflammation of optic nerve, other lesions suggestive of MS |
| Treatment | Doxycycline hyclate and rifampin | Methylprednisolone, IV |

Abbreviations: CRP, C-reactive protein; CSF, cerebrospinal fluid; ESR, erythrocyte sedimentation rate; IV, intravenously; MRI, magnetic resonance imaging; MS, multiple sclerosis.

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and Perloff. *Critical revision of the manuscript for important intellectual content:* Gan, Mandell, Otis, Holmuhamedova, and Perloff. *Administrative, technical, and material support:* Gan and Perloff. *Study supervision:* Mandell, Otis, and Perloff.

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