Grand Rounds
A 31-year-old man with bilateral blurry vision and floaters

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Summary
We report a case of bilateral multifocal retinochoroiditis and bilateral optic disc edema in a patient with cat-scratch disease from Bartonella henselae. The patient initially had negative serologic testing. Repeat testing showed a markedly increased IgG and IgM convalescent titer and the development of a branch retinal artery and vein occlusion. In patients for whom there is a high clinical suspicion of cat-scratch disease, a convalescent titer should be obtained 2–3 weeks following a negative initial result.

History
A 31-year-old male presented to Stony Brook University with bilateral blurry vision and floaters. The vision loss was of sudden onset, but the patient denied ocular pain. He had a history of flulike illness with malaise, fever, myalgia, and upper respiratory symptoms 1 week earlier.

Examination
On examination, best-corrected visual acuity was 20/20 in each eye. Slit-lamp examination was remarkable for 1+ anterior chamber cell in both eyes, 3+ anterior vitreous cell in the right eye and +1 in the left eye. Dilated fundus examination disclosed bilateral disc edema, more prominent on the right more than the left, and multifocal deep retinal and choroidal yellowish infiltrates 100–300 μm in diameter (Figure 1).

Ancillary Testing
Laboratory workup for bilateral uveitis and multifocal retinochoroiditis included negative serology for Lyme IgM and IgG; Bartonella IgM and IgG; Epstein-Barr virus; hepatitis A, B, and C; toxoplasma; syphilis; HIV; anti-nuclear antibody; anti-neutrophil cytoplasmic antibody; anti–double stranded DNA; and complement levels. He had a slightly elevated angiotensin converting enzyme (ACE) titer (74 U/L; normal range, 12–68 U/L). Because of his borderline ACE and to rule out sarcoidosis, he underwent chest computed tomography, which did not show any evidence of hilar adenopathy or interstitial lung disease.

Treatment
The patient was started on 60 mg oral prednisone daily, which was tapered over 1 month. At 1 month after the initial presentation, his visual acuity was 20/20 in each eye. He had mild vitreous cells and mild disc edema bilaterally. In addition, he had developed stellate macular exudates (macular star) in the right eye, retinal vasculitis, and a branch retinal artery and vein occlusion in the left eye (Figure 2). A repeat Bartonella titer was positive at IgG > 1/2560 (negative, <1/320) and IgM 1/200 (negative, <1/100). On further questioning, the patient mentioned he had recently been exposed to a cat. He was started on doxycycline and rifampin. Two months later, his visual acuity remained 20/20, and the disc edema had resolved. The vitritis and macular exudates had cleared completely, but he had developed nasal choriretinal scars (Figure 3). On his most recent examination, 1 year after initial presentation, his visual acuity was 20/20 in each eye.
Differential Diagnosis

For unilateral granulomatous conjunctivitis (Parinaud syndrome), the main differential diagnosis includes tuberculosis, syphilis, tularemia, and chlamydia.\(^1,2\)

For neuroretinitis the main differential includes Lyme disease, malignant hypertension, syphilis, and idiopathic stellate neuroretinitis.

For the isolated retinal or choroidal infiltrates, the differential includes the white dot syndromes, particularly multiple evanescent white dot syndrome\(^3\) and toxoplasmosis, which, unlike Bartonella infections, classically have infiltrate adjacent to chorioretinal scarring and are not multifocal.\(^4\)

Our patient’s differential diagnosis included white dot syndromes such as multifocal choroiditis, sarcoidosis, syphilis, lyme, and infectious and idiopathic neuroretinitis.

Diagnosis and Discussion

Cat-scratch disease is usually a self-limited infection, most commonly caused by an intracellular Gram-negative rod, *Bartonella henselae*. The estimated incidence of the disease in the US is 9.3/100,000.\(^5\) Although *Bartonella* infection was historically reported in children,\(^1\) 45% of patients in the database were >18 years of age.\(^5\) The bacteria is transmitted from a young cat through a bite, scratch, or previous break in the skin,\(^1\) although fleas can transmit the disease directly.\(^6\) A non-pruritic papule, usually <1 cm, develops at the inoculation site 3–5 days after exposure, accompanied by flu-like illness.\(^1\) Regional lymphadenopathy occurred in 100% of 1,200 cases within 1–2 weeks.\(^1\) It is at this point that bacteremia can rarely lead to systemic complications, which have been reported to occur in every organ system,\(^7\) including encephalitis in 0.2%.\(^1\)

After regional lymphadenopathy, ocular *Bartonella* infection is the most common manifestation of the disease. Both the presenting and final visual acuity can vary greatly, from 20/20 to counting fingers.\(^8\) The most common ocular presentation is unilateral Parinaud ocu-loglandular syndrome, consisting of preauricular lymphadenopathy and follicular conjunctivitis, which was reported in 48 of 1,200 patients (4%).\(^1\) The second most common ocular finding is chorioretinal infiltrates, reported in 16 of 37 (43%) and 29 of 35 cases (83%) of ocular...
Bartonella infection. Neuroretinitis (optic disc edema accompanied by a stellate pattern of exudative maculopathy) sometimes with peripapillary or equatorial dot-blot hemorrhages, is a classic finding. Although neuroretinitis only occurs in 1%–2% of cases of systemic Bartonella infection, a frequently cited study reported neuroretinitis caused by Bartonella in 9 of 14 cases (64%).

Solley et al reported unilateral optic disc edema in 16 of 35 (46%) of ocular Bartonella cases. Chi et al reported bilateral disc edema in only 9 of 53 patients (17%). In their unilateral cases, an afferent pupillary defect was common, occurring in 40 of 44 cases (91%). Optic disc edema progressed to neuroretinitis in 28 of 62 cases (45%). Neuroretinitis is thought to be segmental inflammation of superficial optic nerve head arterioles leading to exudative disc edema, which spreads into the outer plexiform layer. Purvin et al reported unilateral neuroretinitis in 65 of 69 cases (94%). The exudates appear 1–3 weeks after the disc edema and take 2–3 months to resolve.

Omerod noted up to 27 central retinal or choroidal white dots (bilateral in an estimated 75% of cases), usually clearing completely but sometimes leaving pigmented scars: retinal disease was associated with vitritis in 50% and nongranulomatous anterior uveitis in <15% of their cases. Retinal biopsy can confirm that the lesions contain Bartonella colonies. In a relatively large study (n = 35), Solley et al reviewed photographs to determine the depth of infiltrates: 30% occurred in the superficial retina; 49%, in deep retina; 14% were full-thickness; and 7% were in the choroid.

Branch retinal artery occlusion has been reported as frequently as in 11% of 35 cases of ocular Bartonella.
There is a case report of a branch retinal venous occlusion and combined central retinal artery and vein occlusion. Less common ocular complications include optic nerve head vasoproliferative, granulomatous angiomas that are composed of superficial abnormal vascular networks in 5% of cases. Peripapillary serous retinal detachments, thought to be caused by spreading of fluid from the disc edema, occurred in 20% of 35 cases. The subretinal fluid usually resolves after 2 months. Cases of macular holes and a choroidal detachment have also been reported.

*Bartonella henselae* is difficult to culture. It can be identified with the Warthin-Starry stain, but it is uncommon and usually unnecessary to culture a lymph node. Serum indirect fluorescent antibody (IFA) with a titer ≤1:64 is 88% sensitive and 94% specific, except in immunocompromised patients, where the sensitivity is <70%. Seroconversion requires 2–3 weeks, and a four-fold rise in titers strongly suggests the diagnosis, although this only occurs in 66% of cases. Although enzyme-linked immunosorbent assay (ELISA) is available to distinguish between IgG and IgM and was initially reported to be 95% sensitive and 100% specific, others report that ELISA is not accurate because of high false negatives. The combination of a papule, regional adenopathy, and a positive IFA is 95% sensitive. Tissue polymerase chain reaction can be used as a confirmatory test, because it was reported to be 100% specific and 76% sensitive.

Ancillary testing beyond antibody testing may offer evidence in support of positive diagnosis. Optical coherence tomography can be used to demonstrate optic disc edema and peripapillary subretinal fluid. The chorioretinal infiltrates are hypofluorescent early and hyperfluorescent late on fluorescein angiography but hypofluorescent throughout indocyanine green angiography.

Recommended antibiotics include ciprofloxacin (azithromycin in children), sulfamethoxazole with trimethoprim, and rifampin. A randomized control trial to determine the efficacy of any treatment for ocular Bartonella has not yet been reported. Although investigators have reported using antibiotics for 2–4 weeks with or without steroids, neither appear to improve the visual outcome. One study showed that the final median visual acuity in both treated and nontreated groups was 20/20. The only cases consistently reported to require treatment are immunocompromised patients, who are at higher risk for symptomatic bacteremia. Immunocompromised patients should be treated for at least 1–4 months.

Finally, visual visual acuity depends on the extent of posterior segment involvement. Chi et al reported that of 53 cases with disc edema and a mean presenting visual acuity of 20/160, 36 (68%) had a final visual acuity of 20/40 or better, and 3 (6%) had final visual acuity of 20/200 or worse. While the progression from disc edema to neuroretinitis or a serous retinal detachment does not appear to affect final visual acuity, the presence of a vascular occlusion involving the disc or macula limits the visual outcome. Purvin et al reported that disc edema and macular edema led to a central visual field deficit in 88% of tested cases, but these deficits may not persist after disease resolution. Reed et al reported a case series where all 7 patients finished with final visual acuity of 20/20 to 20/30: subtle residual deficits were detected 2 years later in all 3 of those patients who were tested, including decreased contrast sensitivity, a 30% reduction in the visual evoked potential amplitude, and decreased color vision.

The present case demonstrates the different stages of ocular manifestation of a patient with Bartonella. Unlike previously reported cases, where artery occlusion was noted simultaneous to the retinal infiltrates, our case showed an unusually progressive course. In addition, initial Bartonella serology for both IgG and IgM were negative, but repeat convalescent titers were positive for both. In patients for whom there is a high clinical suspicion of cat-scratch disease, a convalescent titer should be obtained 2–3 weeks following a negative initial result.

### References