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Case report

Cat scratch disease: Pediatric case series for varying presentations of *Bartonella henselae*

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ABSTRACT

Cat scratch disease (CSD) typically presents as regional lymphadenopathy, following inoculation via scratch, bite, or lick to an open wound by a young cat. Annual prevalence is 22,000 cases in the United States. Although CSD is self-limiting in the majority of cases, CSD can manifest in varying presentations and affect multiple organ systems. Serology testing for *Bartonella henselae* antibodies is a practical diagnostic tool but has limitations. Therefore, it is important for medical providers to recognize CSD in its multiple forms, as antibacterials are indicated in certain presentations. The following cases focus on cardiac and ophthalmic manifestations, as well as delayed seroconversion.

Introduction

Cat scratch disease (CSD) presents as a local cutaneous and regional lymphadenopathy disorder in approximately 85–90% of pediatric cases [1]. CSD is caused by *Bartonella henselae*, a fastidious Gram-negative bacillus. Approximately 22,000 cases are diagnosed annually in the United States [2,3]. Cats serve as the main reservoir for *Bartonella henselae* [4]. Kittens or stray cats are more likely to be bacteremic [1]. Transmission from cat to cat occurs via the cat flea *Ctenocephalides felis* [1,5]. Humans become infected through inoculation by cat scratch, bite, or lick at broken skin [1,6]. In two thirds of cases, a papule or pustule forms within 12 days at the inoculation site, followed by regional lymphadenopathy in 1–2 weeks [1,5]. Patients may experience constitutional symptoms including fever, malaise, and fatigue [7].

Although CSD is self-limited in 90–95% of pediatric cases [1,6], CSD can manifest in varying presentations. In certain cases, antibacterial therapy is warranted. Although serology testing is important for diagnostic purposes, antibody detection has limitations [1,8]. Therefore, it is imperative for providers to recognize CSD to avoid prolonged work-up and delay in treatment. The following case series will explore varying manifestations of CSD.

Case 1

An 8-year-old female, with no significant past medical history (PMH), presented to the Emergency Department (ED) for evaluation of 1-month painful left inguinal lymphadenopathy. A 6-month-old kitten had scratched her legs prior to symptom onset. She had experienced fever and night sweats over 2–3 weeks. Blood tests, collected 2–3 weeks into illness, were significant for *Brucella* immunoglobulin M (IgM) positive, *Brucella* immunoglobulin G (IgG) negative, *Bartonella* serologies negative, Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) serologies negative, and tuberculosis (TB) quantiferon gold negative. At ED presentation, she had already completed 5 days of cephalexin, 10 days of clindamycin, and 5 days of azithromycin.

Fever recurred at time of ED presentation. Physical exam was significant for bilateral inguinal and right submandibular lymphadenopathy. COVID-19 test was positive. Notably, total *Brucella* antibody was negative. *Bartonella henselae* IgG and IgM were positive (IgG >1:1024, IgM 1:256). Fever and elevated inflammatory markers were attributed to COVID-19 infection. Supportive care was continued without further therapy, as patient had already completed 5 days of azithromycin. At 1 week follow-up, lymphadenopathy persisted with mild tenderness.

Case 2

A 13-year-old female, with no significant PMH, presented to ED for 3 weeks of worsening left eye pain with new neck and jaw pain. She had recently completed cefdinir and trimethoprim-sulfamethoxazole for possible bacterial conjunctivitis. A 9-month-old kitten had scratched her

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neck 2 weeks prior to pain onset. Physical exam was notable for left conjunctival injection, and left preauricular and cervical lymphadenopathy. There was no vision change or pain with eye movement. Ophthalmic exam was notable for nodular scleritis with conjunctival granuloma of the left eye, concerning for Parinaud's Oculoglandular Syndrome (POGS). Azithromycin was prescribed.

After completion of 14 days of azithromycin, lymphadenopathy, pain, and ocular symptoms resolved. *Bartonella henselae* serologies from the ED were negative. Despite initial negative *Bartonella* serologies, history and physical exam were consistent with POGS. When redrawn at approximately 4 weeks after symptom onset, *Bartonella henselae* IgM returned borderline positive (1:20). Additionally, testing showed recent EBV infection: EBV Nuclear antigen antibody IgG positive, EBV Early antigen IgG positive, EBV viral capsid antigen (VCA) negative; EBV VCA IgG positive. Approximately 8 weeks after symptom onset, repeat *Bartonella henselae* serologies returned IgG positive (1:64) and IgM negative.

Case 3

A 9-year-old female presented to the ED from the Optometry office for blurry vision in the right eye and papilledema. She played with an approximately 1-year-old outdoor kitten. A 1-cm soft, mobile posterior cervical node was present. Ophthalmic exam was significant for right eye unilateral optic disc swelling with macular star appearance, concerning for neuroretinitis. Brain MRI and MR orbit papilledema were both reassuring. Patient was prescribed 14 days of doxycycline and rifampin. Testing returned positive for *Bartonella henselae* IgG (1:1024). After completion of antibacterials, patient had improvement of blurry vision.

Case 4

A 10-year-old female, with repaired tetralogy of Fallot and pulmonic valve replacement, presented to the ED for evaluation of presumptive subacute endocarditis. Symptoms included fever, fatigue, rhinorrhea, and abdominal pain. Inflammatory markers were elevated with c-reactive protein (CRP) of 28.11 mg/L and sedimentation rate of 80 mm/hr. Echo was significant for new possible vegetation on bioprosthetic pulmonic valve. Blood culture was negative. She had a cat less than 1 year old at home.

A III/VI systolic murmur was noted on examination, located predominantly at the left upper sternal border; otherwise, physical exam was unremarkable. EKG was unchanged from baseline. As fever and new vegetation were concerning for endocarditis, cefepime and vancomycin were initiated. Regimen was later narrowed to ampicillin-sulbactam and gentamicin for culture-negative infective endocarditis. Symptoms improved. CRP and sedimentation rate down trended. No vegetation was visualized on repeat echo. Multiple blood cultures returned with no growth. *Bartonella* IgG was positive 1:1024, with IgM negative. Doxycycline was added to 6-week intravenous antibacterialregimen to treat presumed *Bartonella* endocarditis.

Case 5

A 9-year-old female, with no significant PMH, presented to the ED for 10 days of worsening right jaw swelling, despite completing 7 days of cephalexin. Family reported exposure to a 5-year-old cat. Patient had multiple large submandibular lymph nodes. Submandibular abscess was visualized on CT scan. Bedside incision and drainage was performed for standard cultures. Patient was prescribed 10 days of amoxicillin-clavulanic acid.

At 1-week follow-up, submandibular region was red, swollen, and painful, concerning for abscess and fistula development. *Bartonella* IgG (1:256) and IgM (1:64) titers returned positive; cultures and other studies returned negative. Family discovered patient had played with a kitten at a friend's party in the prior month. Due to persistence of symptoms, patient was prescribed 5 days of azithromycin and rifampin. At 3-week follow-up, submandibular lesion had drained with resolution of swelling.

Discussion

History limitations

Patients with CSD often recall contact with "apparently healthy cats, especially kittens [1]." In Cases 1–4, there was known scratch by a young cat. However, history can be negative for classic exposure, even with careful history taking [8]. In Case 5, patient's history was initially negative for exposure to a young cat.

Limitations in serology diagnosis

Serology tests are used for *Bartonella* antibody detection [1,8–10]. Early antibody detection can prevent extensive hospitalization and evaluation [8]. Medical providers must recognize limitations to serology testing, including delay in seroconversion as seen in Cases 1 and 2. Furthermore, sensitivity of IgM is low [4]. Case 2 was notable for both borderline serology and late-onset of antibody seroconversion, which was previously described [11,12]. Additionally, serology in Case 2 was evident for recent EBV infection. Acute EBV infection may have caused immune dysregulation in Case 2, leading to delay in *Bartonella* IgM detection. EBV infection reducing specificity of *Bartonella* serology testing has been described [13].

Cross-reactivity to *Coxiella burnetti, Brucella, Chlamydophila, non-henselae Bartonella* also occurs [3,4,14]. Case 1 was initially *Brucella* IgM positive and *Bartonella* negative. *Brucella* detection was determined to be false positive, as patient had negative *Brucella* serology and positive *Bartonella* serology on repeat testing [15].

General treatment

Two-thirds of CSD cases present as a papule at inoculation site [1], followed by regional lymphadenopathy [1,5]. Commonly affected lymph nodes are "axillary, epitrochlear, cervical, supraclavicular, or submandibular [6]." Skin over areas of lymphadenopathy may become erythematous and indurated. 10–20% of lymph nodes become suppurative [1]. To note, only 30% of CSD cases present with low grade-fever [1].

Antibacterial therapy is generally not indicated in immunocompetent children [1]. Lymphadenopathy typically self-resolves in 2–4 months [1]. 5 days of azithromycin may be considered in mild to moderate cases [6], such as in Cases 1 and 5. Incision and drainage or surgical excision of lymph nodes is not recommended. Such invasive approaches may slow healing or lead to sinus tract formation [1,6], seen in Case 5. Surgical intervention is recommended only if diagnosis is uncertain, or if disease course is significantly prolonged (>16 weeks) [16,17].

Ocular presentations

5–10% of CSD cases present with ocular manifestations. POGS is the most common ocular presentation [1,3,7]. In addition to cat bite or scratch, inoculation may occur directly from rubbing eyes after bacteremic cat exposure [7]. Eye irritation and watery discharge often develop 2 weeks after inoculation [7]. Cases are often misdiagnosed as bacterial and viral conjunctivitis [7], as seen in Case 2. Permanent ocular damage may occur without antibacterial treatment. While standard antibacterial regimen for immunocompetent patients is not established, current guidelines recommend 5 days of azithromycin. Doxycycline plus rifampin or azithromycin for 14 days may also be used to treat POGS [7].

1–2% of CSD cases develop neuroretinitis [2]. Optic disc edema and lipid exudates, also known as "macular star," cause acute painless vision

impairment [1,2,5], seen in Case 3. Antibacterials are recommended for this vision-threatening presentation of CSD. There is currently no established antibacterial regimen. Doxycycline, azithromycin, erythromycin, ciprofloxacin, trimethoprim-sulfamethoxazole, gentamicin, or rifampin may be used for treatment of neuroretinitis [3]. Doxycycline and rifampin are the most commonly used drugs [1], regardless of age. Almost all reported cases of neuroretinitis have recovery of vision to 20/40 or better [1,2].

Culture negative endocarditis

Culture negative infective endocarditis comprises 3–36% of clinically diagnosed endocarditis cases [18]. Common organisms implicated in culture negative infectious endocarditis are *Abiotrophia*, *Granulicatella, Bartonella, Tropheryma whipplei, Coxiella burnetti (*Q fever) and *Brucella* [18]. Although positive *Bartonella henselae* IgG does not completely rule in *Bartonella* endocarditis in Case 4, patient's presentation, ultrasound findings, and cardiac history were consistent with *Bartonella* endocarditis.

Conclusion

In conclusion, CSD is a generally a self-limited disease in immunocompetent children but requires treatment for severe systemic infection. Early recognition of moderate to severe presentations of disease is necessary to prevent delay in treatment. Prompt recognition may also prevent prolonged hospitalization and invasive diagnostic testing for other etiologies, such as malignancy and tuberculosis [8]. While serology testing is practical for diagnosis of CSD, there are limitations to testing, including delay in seroconversion and cross-reactivity.

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Ethical approval

Case Report.

Consent

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CRediT authorship contribution statement

Dr. Sallie Lin collected data, drafted initial manuscript, and reviewed and revised manuscript. Dr. Frances Saccoccio collected data, and reviewed and revised manuscript. All authors approved final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors have indicated they have no conflicts of interest relevant to this article to disclose.

Data availability

This is a descriptive study of CSD. Therefore, no supporting data is available for release.

References

[1] Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH. Bartonella henselae (Cat-Scratch Disease). In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, (Eds.) Red book: 2021–2024 report of the Committee on Infectious Diseases, Committee on Infectious Diseases, American Academy of Pediatrics. 32nd ed. American Academy of Pediatrics; 2021: p. 226–9.

[2] Holdeman NR, Ma L, Tang RA. Cat scratch neuroretinitis. Int J Ophthalmol Clin Res 2017;4(2):071. ⟨https://clinmedjournals.org/articles/ijocr/international-journal-of-ophthalmology-and-clinical-research-ijocr-4-071.php⟩.

[3] Ksiaa I, Abroug N, Mahmoud A, Zina S, Hedayatfar A, Attia S, et al. Update on Bartonella neuroretinitis. J Curr Ophthalmol 2019;31(3):254–61. ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6742623/⟩.

[4] Otsuyama KI, Tsuneoka H, Yoshidomi H, Haraguchi M, Yanagihara M, Tokuda N, et al. Utility of *Bartonella henselae* IgM Western blot bands for serodiagnosis of cat scratch disease. J Clin Microbiol 2017;56(1). e01322-17, ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5744212/⟩.

[5] Klotz SA, Ianas V, Elliott SP. Cat-scratch disease. Am Fam Physician 2011;83(2):152–5. https://www.aafp.org/afp/2011/0115/p152.html.

[6] Baranowski K, Huang B. Cat scratch disease. [Updated 2021 Jun 25]. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. ⟨https://www.ncbi.nlm.nih.gov/books/NBK482139/⟩.

[7] Arjmand P, Yan P, O'Connor MD. Parinaud oculoglandular syndrome 2015: review of the literature and update on diagnosis and management. J Clin Exp Ophthalmol 2015;6(443):2.

[8] Weinspach S, Tenenbaum T, Schönberger S, Schaper J, Engers R, Rueggeberg J, et al. Cat scratch disease–heterogeneous in clinical presentation: five unusual cases of an infection caused by *Bartonella henselae*. Klin Padiatr 2010;222(2):73–8. ⟨https://pubmed.ncbi.nlm.nih.gov/19790029/⟩.

[9] McGill SL, Regnery RL, Karem KL. Characterization of human immunoglobulin (Ig) isotype and IgG subclass response to *Bartonella henselae* infection. Infect Immun 1998;66(12):5915–20. ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC108749/⟩.

[10] Rodino KG, Stone E, Saleh OA, Theel ES. The brief case: *Bartonella henselae* endocarditis-a case of delayed diagnosis. J Clin Microbiol 2019;57(9):e00114–9. ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6711904/⟩.

[11] Kymionis GD, Siganos CS, Pallikaris IG. Late onset of serologic positive titers in a patient with Parinaud's oculoglandular syndrome. Semin Ophthalmol 2004;19(3–4):125–6. ⟨https://pubmed.ncbi.nlm.nih.gov/15590554/⟩.

[12] Starck T, Madsen BW. Positive polymerase chain reaction and histology with borderline serology in Parinaud's oculoglandular syndrome. Cornea 2002;21(6):625–7. ⟨https://pubmed.ncbi.nlm.nih.gov/12131048/⟩.

[13] Zbinden R, Ströhle A, Nadal D. IgM to Bartonella henselae in cat-scratch disease and during acute Epstein-Barr virus infection. Med Microbiol Immunol 1998;186(4):167–70. ⟨https://pubmed.ncbi.nlm.nih.gov/9574898/⟩.

[14] La Scola B, Raoult D. Serological cross-reactions between Bartonella quintana, Bartonella henselae, and Coxiella burnetii. J Clin Microbiol 1996;34(9):2270–4 (Sep), ⟨https://www.ncbi.nlm.nih.gov/pmc/articles/PMC229230/⟩.

[15] Jindan RA, Saleem N, Shafi A, Amjad SM. Clinical interpretation of detection of IgM anti-*Brucella* antibody in the absence of IgG and *Vice Versa*; a diagnostic challenge for clinicians. Pol J Microbiol 2019;68(1):51–7. ⟨https://pubmed.ncbi.nlm.nih.gov/31050253/⟩.

[16] English R. Cat-scratch disease. Pediatr Rev 2006;27(4):123–8. https://doi.org/10.1542/pir.27-4-123.

[17] King KY, Hicks MJ, Mazziotti MV, Eldin KW, Starke JR, Michael M. Persistent cat scratch disease requiring surgical excision in a patient with MPGN. Pediatrics 2015;135(6):e1514–7. https://doi.org/10.1542/peds.2014-2923.

[18] Baltimore RS, Gewitz M, Baddour LM, Beerman LB, Jackson MA, Lockhart PB, et al. Infective endocarditis in childhood: 2015 update: a scientific statement from the American Heart Association. Circulation 2015;132(15):1487–515. ⟨https://www.ahajournals.org/doi/10.1161/cir.0000000000000298⟩.