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Bartonella Osteomyelitis of the Acetabulum: Case Report and Review of the Literature

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Abstract

Introduction: *Bartonella henselae* commonly involves the mononuclear phagocyte system (MPS), and its most common presentation is lymphadenitis. Rarely, it can cause isolated osteomyelitis. We present a case of a 3 year old with constitutional symptoms and new onset of limp. Previously reported cases of osteomyelitis due to *B. henselae* are also reviewed here, keeping the index case in mind.
Methods: We conducted a Medline search using MeSH subject headings *Bartonella* and osteomyelitis, limited to humans.
Results: The index case is a 3-year-old female who had a subacute presentation with new-onset leg pain and fever. Subsequent imaging demonstrated osteomyelitis of the acetabulum. Multiple diagnostic attempts were unsuccessful, and the patient did not respond to empiric therapy. Despite indeterminate serology, the diagnosis of *Bartonella* osteomyelitis was eventually confirmed by PCR on bone biopsy of the lesion. The literature search revealed 48 publications, which were reduced to 28 when limiting articles to the English language and the pediatric population. After a report of 36 pediatric cases in 2007, there have been an additional 12 pediatric cases since 1998. Generally, these patients had a subacute presentation with relatively mild constitutional symptoms. Most commonly, bone involvement occurred as osteolytic lesions of the axial skeleton. Of the total 48 cases reported, only four reported involvement of the axial skeleton.
Conclusion: We present the first case, to our knowledge, of pediatric osteomyelitis of the pelvis due to *B. henselae* with indeterminate serologic and positive PCR results. *Bartonella* osteomyelitis should be included in the differential diagnosis when typical pathogens are not identified or if the patient is slow to respond to standard therapies. The sensitivity of tissue PCR for *Bartonella* osteomyelitis is now better than the current gold standard of serology, and new management guidelines may need to reflect this.

Key Words: Pediatric osteomyelitis—*Bartonella henselae*—PCR.

Introduction

Bartonella henselae IS THE causative agent of cat scratch disease, usually presenting with regional lymphadenopathy, fever, and mild constitutional symptoms (Al-Rahawan et al. 2012). Osteomyelitis is an unusual manifestation of *Bartonella*, but should be considered when typical pathogens are not identified or the patient does not respond to standard therapies (Al-Rahawan et al. 2012). Most diagnoses of *B. henselae* infection are based upon serologic testing, but newer methods for *Bartonella* detection, such as PCR, are becoming more widely available (Johnson et al. 2003). Here, we describe a case of pediatric *B. henselae* osteomyelitis of the acetabulum with indeterminate serologic and positive PCR results. We also review the literature regarding pediatric osteomyelitis due to *B. henselae.*

Case

A previously healthy 3-year-old girl presented to the emergency department (ED) with a 2-week history of fever and loose stools, and a 5-day history of pain in her right leg and refusal to bear weight. She did not have any associated rash, and there was no history of trauma.

On initial presentation, her vital signs were temperature of 37.9°C, heart rate 105 beats/min, blood pressure 123/76 mmHg, and respiratory rate 20 breaths/min. On general physical exam, she appeared well but uncomfortable. She

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had no significant lymphadenopathy. She had full range of motion at the ankle, hip, and knee joints, and no localized joint swelling or tenderness. The initial workup was significant for a total white blood cell (WBC) count of $12.6\times10^3/mm^3$ (normal $4\times10^3/mm^3$ to $12\times10^3/mm^3$), hemoglobin of 12.6 grams/dL (normal 11.5–14.5 gm/dL), platelets of $619\times10^3/mm^3$ (normal $200\times10^3/mm^3$ to $400\times10^3/mm^3$), and erythrocyte sedimentation rate (ESR) of 90 mm/h (1–8 mm/h). Blood, urine, and stool cultures were obtained. X-rays of the ankle and the tibia/fibula were normal. The patient was discharged home from the ED after consultation with the Orthopedics Department. Her differential diagnosis included viral syndrome, transient synovitis, and early osteoarthritis. The patient was instructed to return if symptoms did not resolve.

The patient presented again in the ED 2 days later with progressive worsening of pain and refusal to bear weight, although fever had resolved. She had asthenia and significant pain with knee flexion and hip flexion. The remainder of her exam remained normal. All previous cultures were negative, and repeat investigations revealed WBC $9.0\times10^3/mm^3$, platelets $599\times10^3/mm^3$, ESR 71 mm/h, C-reactive protein 5.9 mg/dL (normal 0.068–8.2 mg/dL), and creatine phosphokinase 137 units/L (normal 20–128 units/L). Hip ultrasound revealed a small hip effusion; aspiration yielded serosanguineous fluid with no organisms on microscopy. She was admitted for suspicion of septic arthritis of the hip joint and started on medical therapy with broad-spectrum antibiotics (vancomycin and ceftriaxone), because surgical access to site of infection was relatively difficult. The patient continued to spike moderate- to high-grade fevers, refused to move her right leg, and had persistent elevation of inflammatory markers. She underwent magnetic resonance imaging (MRI) of the hip, which revealed an osteolytic lesion suggestive of focal osteomyelitis within the right acetabulum, as well as a 4-mm abscess within the bone. After irrigation and debridement, pathological examination of the surgical biopsy revealed granulomas. Purified protein derivative (PPD) for tuberculosis, *B. henselae* serum immunoglobulion M (IgM) and IgG (positive if ≥1:16 and 1:256, respectively), human immunodeficiency virus (HIV) testing, and *Histoplasma* urine and serum tests were performed, all of which were negative, as were all microbiologic cultures.

Further history revealed that the family had received a young kitten as a present about 3 weeks prior to onset of symptoms. The family had removed the kitten from the home after 3 weeks of contact because it was ''always scratching'' the patient. The biopsy specimen was sent to Associated Regional and University Pathologists (ARUP) Laboratories, a national reference laboratory, for qualitative *Bartonella* PCR. The PCR was positive for DNA specific to *B. hensaelae*. Additionally, Steiner staining of the tissue section demonstrated small numbers of short, plump bacilli, consistent with *Bartonella* spp.

The patient's antibiotic regimen was changed to rifampin and azithromycin. She responded well clinically and was discharged home on oral antibiotics to complete a 4-week course. Subsequent repeat *Bartonella* serologies remained indeterminate at 8 weeks after initial testing.

Discussion

B. henselae is a Gram-negative bacillus usually acquired from exposure to infected cats or kittens. Human infection most commonly manifests in immunocompetent hosts as regional lymphadenopathy, referred to as ''cat scratch disease.'' Although any organ system can be involved after bacteremia, osteomyelitis due to *B. henselae* is a rare presentation (American Academy of Pediatrics Committee on Infectious Diseases 2012). Most reports of *Bartonella* osteomyelitis involve vertebral sites, with only one previously reported pediatric case of osteomyelitis of the acetabulum (Solder et al. 1995).

A Medline search using the terms ''*Bartonella*'' and ''osteomyelitis,'' limited to human studies, English language, and pediatric patients, yielded 31 articles. In 2007, Hajjaji et al. (2007) reported 36 pediatric cases, and since then, an additional 13 cases of osteomyelitis due to *B. henselae* have been described, including ours. One case of *Bartonella* osteomyelitis of the acetabulum was reported by Krause et al. in 2000 in a 29-year-old adult male (Krause et al. 2000).

Table 1 lists the clinical features, diagnostic methodologies, and treatments used for the 13 *B. henselae* pediatric osteomyelitis cases since Hajjaji's 2007 review. On the basis of the aggregate data compiling Hajaji's article and Table 1, patients generally had a subacute presentation with mild constitutional symptoms. Seventy-eight percent had fever as part of their initial presentation, and 74% of cases involved the axial skeleton. Thirty-one percent were found to have an abscess contiguous with the site of bone involvement. Concomitant superficial lymphadenopathy was reported in only 59% of patients. For diagnosis, 95% of patients who had serologic studies performed had positive results. Multiple antimicrobials were employed for treatment, and no definitive regimen evolved as the most efficacious.

For our patient, initial empiric therapy was directed toward the most common etiologies of osteomyelitis in her age group. The diagnosis of *B. henselae* usually hinges upon serology by commercially available indirect fluorescence assay (IFA)-based testing, which is highly sensitive and specific (Zangwill et al. 1993, Dalton et al. 1995). ARUP Laboratories used IFA-based serologic testing for our patient. Positive IgM titers strongly indicate acute disease, but the production of IgM is usually very short-lived. This may explain the IgM response in our patient, because she was tested about 3 weeks after last contact. Furthermore, positive IgG titers represent active or recent *Bartonella* infection, but the sensitivity of the IgG assays is suboptimal, and the prevalence of positive serology in 4–6% of the population increases the false positivity rate.

For our patient, convalescent serologic studies did not show a significant rise in the titer, even 2 months after the initial presentation. There are a few case reports of less common species of *Bartonella* that cause cat scratch disease that do not lead to serologic cross reactivity with *B. henselae* antigen (Kordick et al. 1997, Margileth and Baehren 1998). There is a possibility that the primers/probes to amplify *B. henselae* DNA could also amplify other genetically closely related *Bartonella* spp. Another possibility is that our patient had a weak, but technically four-fold, increase in titers that was undetected by the assay available in the ARUP Laboratory at the time. *Bartonella* is a very fastidious organism to culture. Further typical histopathology findings of granulomas or plump bacilli on Warthin–Starry or similar silver staining (*e.g.*, Steiner) may not be present during the initial inflammatory phase. Additional tests, including PCR-based

Table 1. Pediatric Cases of *Bartonella henselae* Osteomyelitis Since Review by Hajjaji et al. 2007

Author	*Year*	*Age*	*Location*	*Fever*	*LNPy*	*Additional findings*	*Diagnostic modality*	*Antimicrobials*
Puri et al.	2013	3 years	Right acetabulum	Y	N	R leg pain/refusal to bear weight	Tissue PCR +, serology −	Azithromycin and rifampin
Al-Rahawan et al. 2012	2012	7 years	Thoracic vertebra, T7 collapse, paraspinal abscess	N	N	Back pain	Tissue PCR +; serology +	Azithromycin
Boggs et al.	2011	11 years	Left ulna	Y	N	Headache, anorexia, left wrist pain	Serology +	Azithromycin
Boggs et al.	2011	NS	Right proximal ulna, right proximal femur	Y	N	Right arm and leg pain	Serology +	Azithromycin
Cheung et al.	2010	6 years	Mastoid	Y	Post-auricular; cervical	Chronic otitis media, postoperative wound drainage	Tissue PCR +; serology +	Rifampin and clarithromycin
Tasher et al.	2009	5 years	Cervical vertebrae and epidural abscess	Y	Cervical, submandibular	Tonsillar enlargement, torticollis, neck pain	Tissue PCR +; serology +	Gent/azithromycin and rifampin
Ridder-Schroter et al.	2008	12 years	Humerus	Y	Axillary, epitrochlear	Cough	Serology +	Clarithromycin and clindamycin and rifampin
Kodama et al.	2007	11 years	T3, L4–L5 vertebrae, right femur	Y	N	Malaise	Tissue PCR +; serology +	Azithromycin and minocycline
Rozmanic et al.	2007	11 years	T8 and right ilium	Y	Inguinal	None	Serology +	Azithromycin and rifampin
Maman et al.	2007	8 years	Vertebrae and rib	NS	NS	NS	Serology or PCR, not specified	NS
Hussain et al.	2007	3 years	T12, with psoas abscess and epidural abscess	Y	Submandibular	Initially got better, then worsened 3 weeks into therapy, when fluid was sampled and diagnosis was made	Fluid PCR +; serology +	Clindamycin and gent, then TMP-SMX
Vermeulen et al.	2006	9 years	C4–C6, with paravertebral abscess	Y	N	Proximal right arm paresis	Tissue PCR +;serology +	Amox/clav
de Kort et al.	2006	9 years	Left humerus, clavicle and elbow	N	N	Symptoms recurred 6 months later and she was retreated without subsequent problems	Fluid PCR +; serology results not reported	Rifampin and TMP-SMX

LNPy, lymphadenopathy; Y, Yes; N, No; NS, not stated; gent, gentamicin; TMP-SMX, trimethoprim-sulfamethoxazole; amox/clav, amoxicillin-clavulanic acid.

assays, are now commercially available through multiple laboratories and can be even more sensitive than serologic studies (Matar et al. 1999, Sander et al. 1999, Murakami et al. 2002, Metzkor-Cotter et al. 2003). PCR of tissue is specific, but sensitivity again is variable, ranging from 40% to 70%. Timing of sample collection affects yield, with greater chance of negative PCR results in the first 6 weeks after exposure. Our patient's diagnosis was confirmed by PCR testing of the bone specimen.

Conclusions

In summary, *B. henselae* is a rare cause of pediatric osteomyelitis that should be considered in patients who have had cat exposure or who do not respond as expected to typical therapies for osteomyelitis. The diagnosis has historically rested upon serologic evidence of infection, but newer testing modalities such as PCR-based techniques may be more sensitive in cases with indeterminate or negative serology but strong clinical suspicion.

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Author Disclosure Statement

No competing financial interests exist.

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