



Case Report

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Ataxic Gait and Back Pain in an Immunocompetent 5-Year-Old Boy

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Abstract

Bartonella henselae is a Gram-negative bacterium and the causative agent of Cat Scratch Disease (CSD). Atypical presentations of *B. henselae* that involve musculoskeletal, hepatosplenic, or neurologic systems are rare. In this case report, we describe a case of *B. henselae* osteomyelitis involving the thoracic spine at the level of T2, complicated by both hepatic and splenic granulomas in a 5-year-old generally healthy male patient. Although *B. henselae* is a rare cause of osteomyelitis, it should be considered in patients with a possible cat exposure, who present with fever, pain, and lymphadenopathy.

Keywords

Bartonella, Immunocompetent, Osteomyelitis

Introduction

Bartonella henselae is a Gram-negative bacillus that is known to cause cat scratch disease (CSD), usually in children [1]. The organism can be transmitted by kittens or puppies, but most of the cases are usually from kittens under one year of age [1]. The organism is usually found in the bloodstream of these animals, however, the animals are usually asymptomatic. The mode of transmission is from kittens that are teething, or lose their teeth and lick their paws, and then subsequently break the skin of a human via a scratch or a bite. It is also thought that the cat flea transmits this organism from kitten to kitten, and may directly transmit to humans [2,3].

Children and teenagers make up approximately 80% of patients diagnosed with CSD [4]. *Bartonella* osteomyelitis frequently occurs in the spine and presents with pain or tenderness in the affected area [5]. Osteomyelitis is usually diagnosed via magnetic resonance imaging (MRI) or radionuclide bone scanning. Additionally, clinicians must rely on serologic testing to identify *Bartonella henselae*, since the causative organism does not grow in culture [6]. We present an atypical case of CSD with vertebral osteomyelitis after possible cat exposure in an immunocompetent patient.

Case Report

A healthy 5-year-old male with a non-contributory past medical history, presented with worsening back pain and intermittent tactile fevers, along with acute ataxia and left head tilt. Three weeks prior to his admission he complained

of generalized back pain with difficulty walking. Ibuprofen did not relieve the pain. This continued for 2 weeks, during which time he had intermittent fevers; a painful left groin lump was noticed about a week and a half after the back pain started. The left groin lump did not have any surrounding erythema, fluctuance or drainage.

During his initial ER visit on May 14th, 2019, vital signs were notable for an oral temperature of 98.6 F, pulse of 109, respiratory rate 20, Blood Pressure 89/55, an oxygen saturation of 100% on room air, and weight of 21.7 kg. His exam was notable for generalized tenderness to palpation along the entire back, shotty inguinal lymphadenopathy, a 2 cm × 3 cm tender mass in the left inguinal region, and a 3mm pustule on the left heel with some purulent drainage. He had no focal neurological deficits, and his gait was steady. Basic labs, spinal x-ray and Ultrasound of the left groin mass were obtained (Table 1).

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The family was given an initial diagnosis of lymphadenitis and discharged home.

Following his discharge, he continued to have back pain not relieved with Ibuprofen. Over the course of two weeks, his back pain worsened, such that he was unable to ambulate. Despite round the clock analgesia, he had no relief. He developed a noticeable head tilt and limping gait one week after his first ER visit. Due to the new developments, he was referred to the ER by his primary care provider for immediate evaluation of a malignancy. The family denied any travel history, trauma, neurological deficits, weight loss, night sweats, headache, bowel or urinary incontinence, sick contacts, or any other system involvement. Of note, the family had recently acquired a cat, but denied any scratches or bites.

Upon the second presentation to the ER on May 21, 2019, vital signs notable for a temperature of 97.7 F, pulse of 112, respiratory rate of 24, blood pressure of 104/72, an oxygen saturation of 100% on room air, and weight recorded as 21.8 kg. His exam in the ER was notable for an ataxic gait and left-sided head tilt while ambulating. Additionally, he had a 2 cm × 2 cm tender mass in the left groin, that was mobile, non-tender, and without overlying erythema, edema, warmth, or discoloration. Laboratory tests and additional imaging (Table 2) were done and he was admitted to the General Pediatric Inpatient Unit to rule out a malignancy.

There was a wide differential diagnosis (Table 3).

Table 1: This table outlines the initial laboratory testing that was done when the patient first presented to the ER after having symptoms (generalized back pain, and intermittent fevers) for 2 week and a newly presented left groin lump.

Laboratory testing/Radiologic work-up	Results
Complete Blood Count	White blood cell count:10.69 /nL Segmented Neutrophils: 48 % Lymphocytes: 38.4 % Monocytes: 9.8 % Eosinophils: 2.8 % Hemoglobin: 12.3 g/dL Hematocrit: 36.5 %
Complete Metabolic Panel	Sodium: 139 mEq/L Potassium: 4.5 mEq/L Chloride: 101 mEq/L Bicarbonate: 26.5 mEq/L Blood Urea Nitrogen: 9 mg/dL Creatinine: 0.5 mg/dL Calcium: 9.1 mg/dL Glucose: 92 mg/dL Albumin: 4.1 g/dL Total Protein: 6.8 g/dL Total bilirubin: 0.3 mg/dL Alanine Transaminase: 63 U/L Aspartate Aminotransferase: 33 U/L Alkaline Phosphatase: 180 U/L
Spinal X-ray	Normal studies
Ultrasound of the left groin	Enlarged lymph node without a fluid collection

Table 2: This table represents the work-up that was done for the evaluation of this patient's symptoms when he presented to the ER for the second time.

Laboratory Testing/Radiologic Work-Up	Results
Complete Blood Count	White blood cell count: 11.33 /nL Segmented Neutrophils: 57.9 % Lymphocytes: 32.7 % Monocytes: 7.4 % Eosinophils: 1.1 % Hemoglobin: 12.4 g/dL Hematocrit: 37.5 %
Complete Metabolic Panel	Sodium: 141 mEq/L Potassium: 4.5 mEq/L Chloride: 102 mEq/L Bicarbonate: 25 mEq/L Blood Urea Nitrogen: 8 mg/dL Creatinine: 0.4 mg/dL Calcium: 9.9 mg/dL Glucose: 103 mg/dL Albumin: 4.5 g/dL Total Protein: 7.6 g/dL Total bilirubin: 0.2 mg/dL Alanine Transaminase: 56 U/L Aspartate Aminotransferase: 39 U/L Alkaline Phosphatase: 229 U/L
C-Reactive Protein	8.3 mg/L
Erythrocyte Sedimentation Rate	58 mm/h
Heterophile Ab Screen	Negative
EBV Ab Panel	IgM Negative, IgG Positive
Uric Acid	2.4 mg/dL
LDH	359 U/L
CK	96 U/L
Abdominal X-ray	Calcifications in the left upper quadrant
Chest X-Ray	Normal chest radiograph.
Abdominal Ultrasound	Multiple tiny hypoechoic lesions within the spleen, which was not enlarged for the patients age. Suspect 2 hypoechoic lesions in the liver, otherwise liver demonstrates normal size, contour and echotexture.

Pediatric neurology was consulted first, due to the concern of a possible posterior fossa malignancy. On their exam, they noted point tenderness at the level of the second thoracic vertebra and bilateral foot clonus, in addition to a left sided-head tilt. A non-contrast head CT was performed and was negative.

Due to findings of lymphadenopathy, Epstein-Barr virus, cytomegalovirus, QuantiFERON-Gold test, and *B. henselae* antibodies were measured. CT spine was obtained and demonstrated minor soft tissue changes around the T2 vertebra, that was better characterized by an MRI of the spine which showed hyper-intensity of the T2 vertebral body (Figure 1).

As imaging was negative for a possible malignancy, no additional treatment was started. The *B. henselae* titers returned on hospital day 8 and he was started on dual therapy

Table 3: This table outlines the differential diagnosis for the patient when he first arrived at the pediatric inpatient unit.

System	Differential Diagnosis	Common Presentation	Investigation	Likelihood in our Patient	Treatment
Neurology	Posterior Fossa Malignancy	-Head-tilt -Headache -Herniation (respiratory depression, bradycardia)	-CT and MRI of the brain	Unlikely - repeat exam noted bilateral foot clonus, ataxic gait and left-sided head tilt, but imaging negative	-Surgery -Chemotherapy and Radiation
Hematology / Oncology	Lymphoma	-Night sweats -Pruritus -Weight loss -Cough -Lymphadenopathy (non-tender)	-CBC (normal or high WBC) -Bone marrow biopsy -Chest x-ray -Excision of the lymph node	Unlikely - patient had regional tender lymphadenopathy, no history of cough, weight loss or night sweats	-Chemotherapy and Radiation -Surgery
	Leukemia	-Bone pain -Weight loss -Fever -Poor appetite -Bleeding -Bruising -Infections	-CBC (high or low WBC, low Hb or Plt) -BMP (high potassium) -LDH (elevated in Tumor Lysis Syndrome) -Uric Acid (Elevated in Tumor Lysis Syndrome) -Bone marrow biopsy	Unlikely - normal white count, slightly elevated LDH to 359, normal uric acid, no weight loss, or change in appetite	-Chemotherapy (induction and maintenance)
	Neuroblastoma with osseous metastases	-Nystagmus -Purple hue to eyelid -Possible ecchymosis to periorbital area -Abdominal Pain	-Elevated ferritin -Elevated LDH -Urine VMA may be elevated -Bone Marrow Biopsy -CT/MRI -MIBG scan	Likely - given age and sex, but without abnormal eye movements, abdominal pain, and abdominal imaging negative for mass	-Surgical Resection -Chemotherapy -Radiation -Antibody medicines (Naxitamab or Omburtamab)
	Spinal Tumor	-Back Pain -Neuropathy from compression -Incontinence -Ataxic Gait	-CT and MRI of the spine	Less likely - given age, no incontinence, although patient had back pain and ataxic gait	-Surgery -Chemotherapy -Radiation
Infectious Disease	Cat-Scratch Disease	-Regional lymphadenopathy +/- drainage -Fever -Scratches or bites -Back Pain	-Bartonella IgM Serology	Likely - had point tenderness at T2, pustule on left heel from first ER visit, left groin lymphadenopathy, possible cat exposure at home, CT showed enhancement at T2	-No need to treat, unless patient is immunocompromised or with severe disease -Treat with macrolides, doxycycline, TMP-SMX, and gentamicin
	Tuberculosis (Pott's Disease)	-Cough -Night sweats -Hemoptysis -Fever -Back Pain -Spinal deformity	-Positive QuantiFERON-Gold test -AFB smears of sputum/secretions -Positive PPD	Unlikely - chest xray and initial spinal imaging negative, no history of exposure, negative quantiferon	-Rifampin -Isoniazid + pyridoxine (for possible neuropathy) -Ethambutol
	EBV	-Sore throat -URI symptoms -Fatigue -Abdominal Pain -Fever -Lymphadenopathy	-Viral Capsid Antigen -Monospot -EBV IgM and IgG titers -CBC (atypical lymphocytes)	Unlikely - patient had regional lymphadenopathy only, no URI symptoms or abdominal pain, EBV serology negative	-Supportive care
	CMV	-Sore throat -URI symptoms -Fatigue -Abdominal Pain -Fever -Lymphadenopathy	-CMV IgM and IgG titers	Unlikely - Patient had regional lymphadenopathy only, no URI symptoms or abdominal pain, and CMV serology negative	-Supportive care

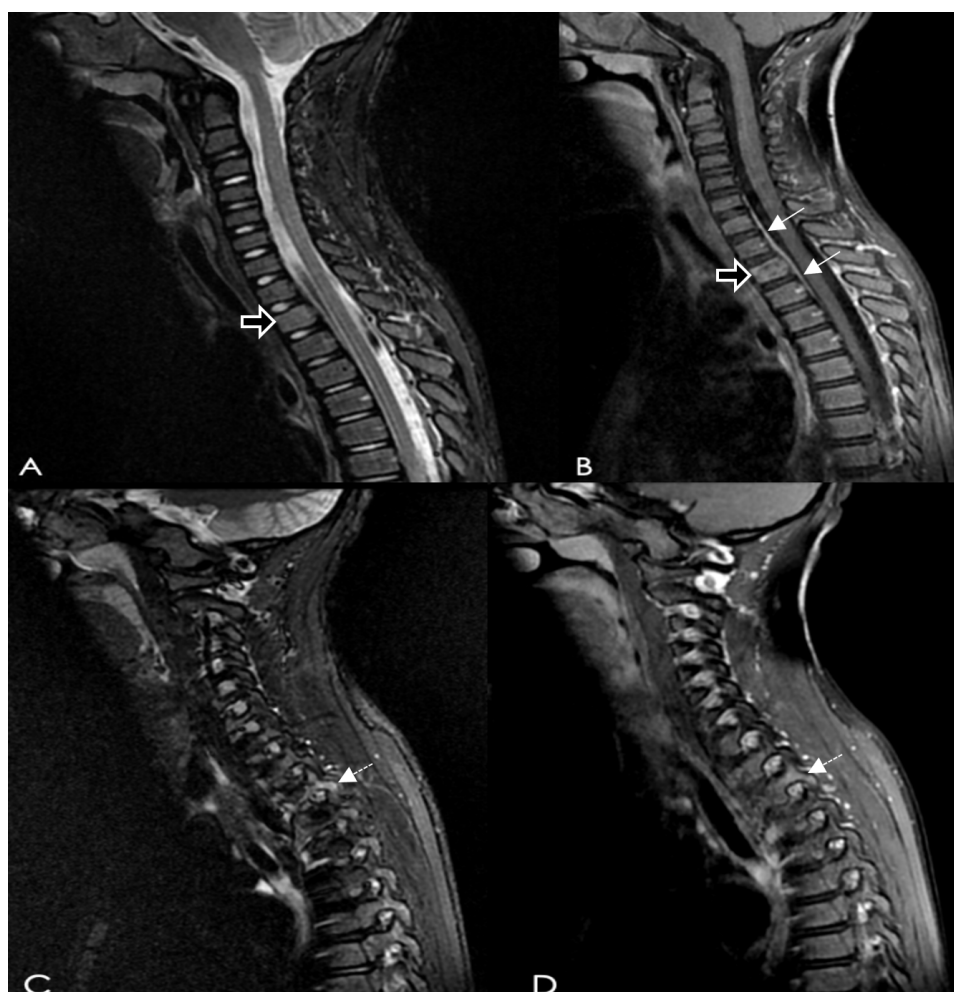


Figure 1: Images A and B are Sagittal midline MRI images of the cervical spine (fat suppressed inversion recovery and fat suppressed T1 weighted image following the administration of intravenous contrast) demonstrate high signal indicating subtle edema and enhancement of the T2 vertebral body respectively (open →). The intervertebral discs demonstrate normal height and signal. Linear enhancement along the anterior dural space (solid →) from C6 to T3 represents engorged dural veins reactive to the process at T2. Images C and D represent the sagittal right of midline MRI images of the cervical spine (fat suppressed inversion recovery and fat suppressed T1 weighted image following the administration of intravenous contrast) demonstrate similar high signal in the right inferior facet of T3 (dashed →).

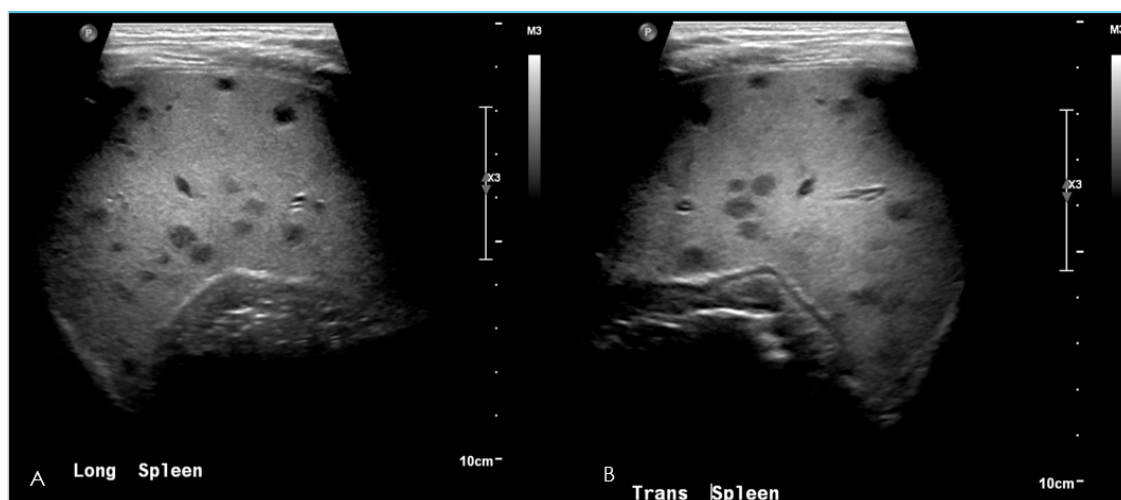


Figure 2: Longitudinal (a) and transverse (b) grayscale sonographic images of the spleen demonstrate multiple hypoechoic nodules representing granulomas related to Bartonella henselae infection.

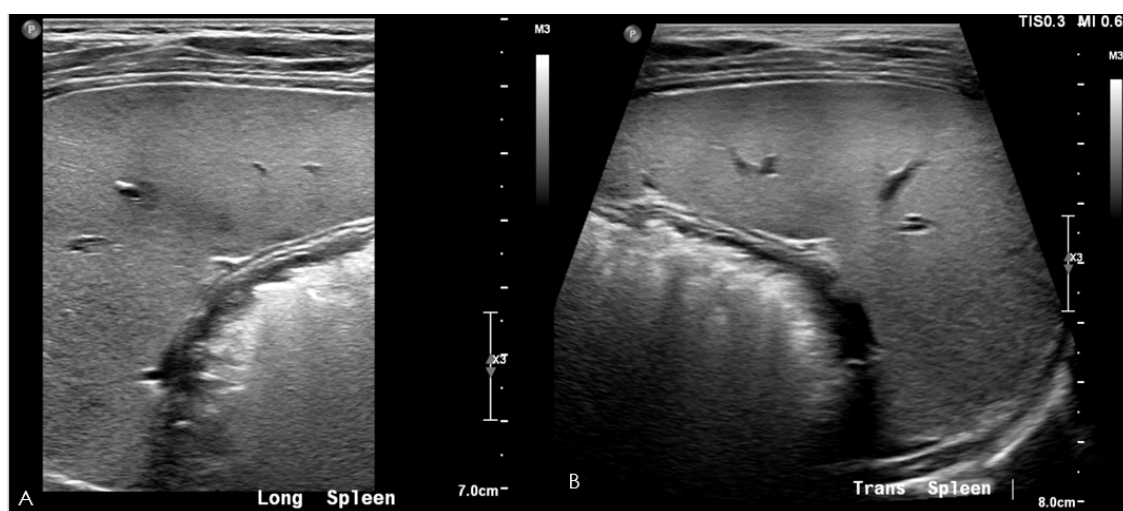


Figure 3: Longitudinal (a) and transverse (b) grayscale sonographic images of the spleen obtained 7 weeks after initiation of treatment demonstrate near complete resolution with interval decrease in size and conspicuity of the nodules.

of Rifampin and Azithromycin, as his titers were suggestive of an infection (IgG > 1:1024, IgM > 1:20). Due to the possible hepatic involvement of *B. henselae* a repeat abdominal ultrasound was performed showing multiple liver and splenic lesions, compatible with disseminated *B. henselae* infection (Figure 2).

This confirmed the granulomatous inflammation that is seen with atypical CSD. Due to disseminated infection, he was started on Azithromycin and Rifampin. His back pain improved and he was discharged home on hospital day 11 to complete a total 8-week course of treatment. He and his mother were happy with his improvement.

He had regular follow-up visits with Infectious Disease and had a repeat abdominal ultrasound on week 7 of treatment, showing near complete resolution of the splenic and liver nodules (Figure 3), consistent with resolving infection. Additionally, repeat *Bartonella henselae* serology testing performed at week 7 were notable for negative IgM titers (< 1:20), and positive IgG titers (\geq 1:1024) which was suggestive of a resolving infection.

Discussion

CSD has a variable presentation from regional lymphadenopathy distal to the site of inoculation, fever of unknown origin (FUO), to various organ involvement, which can lead to an atypical presentation. One's immune status can play a role in how a disease may present. Perinatal and postnatal exposures to environmental agents have been thought to affect the immune system "programming" and consequently may effect disease presentation [7]. In an immunocompetent person, the predominant manifestation of CSD is regional lymphadenopathy [8]. Based on history obtained and review of the medical record, there was no evidence for this patient's immune status being compromised [7]. Atypical presentations range from abscesses, Parinaud oculoglandular syndrome, osteomyelitis, encephalitis, or a rash [9,10]. Approximately 10% of patients with CSD will develop hepatosplenic disease, and bone involvement occurs in up to 0.27% in all cases of CSD [11]. Our patient initially presented with fever of unknown origin (defined as fever >

38.3 °C (101°F) of at least 8 days duration, in which no diagnosis is apparent after initial outpatient or hospital evaluation, that includes a careful history and physical examination and initial laboratory assessment) [12].

Although there was denial of a cat scratch or bite, the pustule on the left heel could have been from a minor injury from the cat at home that was not brought to the mother's attention. The location of the pustule and the left groin lymphadenopathy is consistent with the expected regional lymphadenopathy with the initial presentation CSD. The incubation period of *B. henselae* from the time an individual is scratched to the appearance of a lesion is 3-12 days, and from there, lymphadenopathy can occur, on average, after 12 days [1]. Our patient's initial presentation to the ER with regional (inguinal) lymphadenopathy, was a typical presentation of CSD, however, the diagnosis was missed as the history was misleading.

CSD-related osteomyelitis is uncommon, however, when it does occur, it commonly affects the pelvic girdle and vertebral column as was seen in our patient.

In addition, our patient also had radiographic evidence of lesions in the liver, which could have been bacillary angiomatosis. This occurs when certain *Bartonella* spp, such as *B. henselae* cause angioproliferative lesions which are made up of proliferating endothelial cells and bacteria. Although it is still not clear what role Bartonella plays at the molecular level, the resolution of these lesions after the initiation of antibiotic treatment, points toward Bartonella's primary role in their formation [13].

The diagnosis is usually suspected based on the history, especially if there is involvement of a kitten. The diagnosis of CSD is confirmed with positive Bartonella IgM serology. The elevation of IgM is often short lived and IgM titers may remain normal during the course of the disease. As such, elevated IgM is only identified in 50% of people due to its short duration. IgG titers are often greater than 1:256 and are typically indicative of previous or active disease [14].

Bartonella IgG may remain seropositive for up to a year (in 25% of patients), making it difficult to determine if there is an active or previous infection. At present, confirmation of the diagnosis is via PCR testing, as it is nearly 100% specific [5].

When treated with antibiotics or surgery, the prognosis is excellent [15,16]. Treatment options include trimethoprim-sulfamethoxazole, erythromycin, clarithromycin, azithromycin, rifampin, doxycycline (if over 8 years old), ciprofloxacin, and gentamicin [1].

Conclusion

In conclusion, *B. henselae* is a rare cause of pediatric osteomyelitis and disseminated disease and should be considered in those patients who have had possible exposure to a kitten. CSD can have a varied presentation and is usually considered the primary diagnosis where there is possible cat exposure. However, it often goes undiagnosed due to non-specific signs and symptoms associated with the disease, and its usually self-limited course. Our patient's history of significant cat exposure, elevated anti-*B. henselae* IgG and IgM titers, imaging confirming involvement of bone, spleen and liver, supported our diagnosis of CSD. To our knowledge, this is the first case report evaluating the efficacy of Azithromycin and Rifampin in the treatment of a patient with confirmed *Bartonella* osteomyelitis and hepatosplenic involvement.

Author Disclosure

Drs. Miller, Lakkunarajah, and Goldwasser have disclosed no financial relationships relevant to this article to disclose. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device. Dr. Lakkunarajah's current affiliation is Medical College of Wisconsin Affiliated Hospitals, Department of Pediatrics, Division of Adolescent Medicine, Milwaukee, WI. Dr. Miller's current affiliation is New York-Presbyterian Hospital Weill Cornell, Department of Pediatrics, Division of Neonatal-Perinatal Medicine, New York, NY.

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