CASE REPORT

Rat bite fever with osteomyelitis and discitis: case report and literature review

Steven H. Adams¹ and Rahul Mahapatra²,³*

Abstract

Background: Rat bite fever (RBF) is a rare systemic febrile illness transmitted by rats. *Streptobacillus moniliformis* is a pleomorphic Gram-negative bacillus which is the usual etiologic organism for rat bite fever in the United States.

Case presentation: Here we present a case of rat bite fever complicated by vertebral osteomyelitis and discitis. The patient revealed an exposure history of being bitten by pet rats. The patient's symptoms dramatically improved with a six-week course of cephalexin therapy.

Conclusions: It is important to obtain a thorough zoonotic exposure history and maintain rat bite fever in the differential when considering potential causes of discitis and osteomyelitis.

Keywords: Rat bite fever, Vertebral osteomyelitis, Discitis, Case report

Background

Rat bite fever (RBF) is an uncommon systemic febrile illness transmitted by rats. *Streptobacillus moniliformis* is a pleomorphic Gram-negative bacillus which is the usual etiologic organism for RBF in the United States. Osteomyelitis and discitis have very rarely been reported in association with RBF.

Case presentation

A 55-year old male presented to an academic medical center in February 2020 with a six-week history of increasing midline back pain. He had a history of chronic mid- and lower back pain as the result of degenerative disc disease, however his pain had abruptly worsened in the 6 weeks prior to presentation. Pain was worsened with trying to sit up straight or walk. Pain was partially relieved with acetaminophen, ibuprofen, and oxycodone 5 mg tablets taken as needed. He reported no associated fevers, chills, or night sweats. He did not recall a febrile illness prior to the onset of symptoms. He did report anorexia and 15-pound weight loss in the last 6 weeks. His medical history included chronic obstructive pulmonary disease, chronic hepatitis C infection, hyperlipidemia, generalized anxiety disorder, and lumbar degenerative disc disease. His surgical history was notable for cervical spine laminectomy in the remote past. His social history was notable for heavy and ongoing tobacco use with a 60 pack-year smoking history. He denied alcohol or illicit drug use including intravenous drug use.

He was afebrile and hemodynamically stable on presentation. Physical exam revealed a gaunt Caucasian male in moderate distress due to pain. Poor dentition was noted. His cardiopulmonary examination was unremarkable. On spinal examination, no bony tenderness was elicited upon palpation of the thoracic and lumbar spine, however paraspinal tenderness was noted in the lumbar spine. Neurologic examination including strength and sensation of the lower extremities was intact. Babinski reflex was downward bilaterally.

MRI with and without gadolinium contrast revealed abnormal enhancement of the lower endplate of the L2 vertebral body as well as diffuse enhancement of the L3 vertebral body.

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vertebral body with irregularity of the upper endplate. This abnormal enhancement extended to the intervertebral disc. Findings were suggestive of discitis with osteomyelitis not excluded. Additionally, there was enhancement and thickening in the anterior epidural space measuring 2 mm × 4 mm which may represent epidural abscess or hematoma (Fig. 1). Laboratory evaluation including CBC with differential and comprehensive metabolic panel was unremarkable. Sedimentation rate was 36 mm/hr. and C-reactive protein was 30.1 mg/L. Blood cultures were sterile.

Based on initial results of clinical, laboratory, and radiographic evaluation, antibiotic therapy was withheld. CT-guided aspiration of the L2-L3 disc was performed for culture and histopathology. Gram stain revealed Gram variable rods. Histopathology revealed fibrocartilage with degenerative changes and acute inflammation suggestive of discitis (Fig. 2). He was seen in Infectious Diseases outpatient consultation, initially offered intravenous antibiotic therapy however patient requested oral antibiotic therapy for empiric treatment of discitis. He was started on treatment with cephalexin 1 g by mouth three times a day as well as linezolid 600 mg by mouth twice a day. (Initially, prior to the revelation of RBF infection, linezolid was chosen (in addition to cephalexin) because Gram stain revealed Gram-positive rods. The intention was to cover Corynebacterium spp. and coagulase-negative staphylococci, skin flora which tend to have resistance to beta-lactams but susceptibility to vancomycin or linezolid.) Cultures were sent to a reference laboratory, with growth noted on Mueller-Hinton media with 5% sheep blood. The organism was identified as *Streptobacillus moniliformis* by matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF). On further history, it was revealed that patient had two pet rats and had sustained numerous bites in the last 1 year prior to symptom onset. In vitro susceptibility testing using broth microdilution revealed low MIC for penicillin (< 0.06 μg/ml), ampicillin (< 0.12 μg/ml), and ceftriaxone (< 0.06 μg/ml), with elevated MIC > 4 μg/mL for gentamicin. The patient’s symptoms dramatically improved with cephalexin so a decision was made not to switch to oral or IV penicillin. Linezolid was discontinued after 2 weeks once culture results were available. He completed 6 weeks of oral cephalexin therapy with dramatic improvement of back pain. The patient was offered TEE to evaluate for endocarditis. However, he declined to have the test done as this coincided with the onset of CoVID-19 pandemic.

**Discussion**

Rat bite fever (RBF) caused by *Streptobacillus moniliformis* is transmitted to humans predominantly through rodent bites and scratches. *S. moniliformis* has been commonly detected in wild and pet rats [1]. A diverse array of animals has been implicated to harbor, or suffer from, *S. moniliformis* infections, such as gerbils, squirrels, turkeys, koalas, macaques, dogs, cats, weasels, and ferrets. However, more recent metagenomic data have suggested that streptobacilli in these other rodent species may in fact be separate species altogether [1]. Moreover, novel *Streptobacillus* species (*S. hongkongensis, S. felis*) have been recently described in clinical human and veterinary infections [2].

RBF has historically been a disease of poverty. While prior to 2007 only a small minority (5%) of RBF cases had known pet rat exposure, since 2010 most cases of RBF have been linked to pet rats [3, 4]. This trend is likely attributable to the increasingly popular practice in the United States of keeping rats as house pets [5]. The actual incidence of rat bite fever is unknown as it is not a mandatory reportable disease [4].

*S. moniliformis* is a pleomorphic, non-acid-fast, Gram-negative, facultative anaerobe bacillus which tends to grow in long intermittently-beaded filaments. Difficult to
grow in culture, *S. moniliformis* requires specific growth and incubation conditions [3]. Definitive identification is made by MALDI-TOF [1]. In our case, the isolate was sent to ARUP reference laboratory (Salt Lake City, UT), and species identification was made using MALDI-TOF. It must be mentioned that commercial MALDI-TOF databases do not contain spectra of all *Streptobacillus* species and that it is plausible that MALDI-TOF may not be able to differentiate between *S. moniliformis* and other *Streptobacillus* species [1]. Many hospital laboratories do not have the capabilities for accurate detection of the organism, and therefore diagnosis may be delayed [4]. Exposure to rats may often not be clarified from patient history until after *S. moniliformis* is identified by laboratory testing.

A 2007 review of 65 RBF case reports showed that clinical symptoms are fever (92%), arthralgias (66%), and rash (61%). Nausea and vomiting (40%), headache (34%), and sore throat (17%) were also common. White blood cell count was on average 12.2 \(10^3/\mu L\); only 5 patients demonstrated leukocytosis higher than 15 \(10^3/\mu L\) [3]. Interestingly, these common clinical manifestations were all absent in our patient. (WBC remained under 8 \(10^3/\mu L\) throughout the patient’s clinical course). It is possible that patient’s history of chronic hepatitis C infection may have blunted the patient’s adaptive and innate immune response to *S. moniliformis* infection and thereby led to the atypical clinical presentation.

Reported complications associated with RBF are extensive and include meningitis, mastoiditis, interstitial pneumonia, periarteritis nodosa, pancreatitis, pericarditis, myocarditis, hepatitis, prostatitis, septic arthritis, and abscess formation in various organs [4, 6]. Infective endocarditis due to RBF has a particularly poor outcome with mortality rates of 50% [4, 7].

The standard for treatment for *S. moniliformis* is penicillin G [4]. However, our patient was not switched to penicillin once RBF infection was revealed given his significant clinical improvement with cephalixin.

We performed a literature review for RBF cases with osteomyelitis or discitis. PubMed was searched for the following terms: *Spirillum minus*, *Streptobacillus moniliformis*, *Haverhillia multiformis*, rat bite fever, AND osteomyelitis, discitis. Our literature review uncovered associated with *S. moniliformis*, only 4 cases of osteomyelitis, 1 of possible osteomyelitis, and 4 of discitis, reported globally [6–14]. It is difficult to judge in our case whether the findings on MR imaging represent discitis or rather extension of infection from the L2-L3 endplate. Nonetheless, this is an unusual and rarely reported complication of RBF [13].

Table 1 summarizes nine cases of RBF associated with osteomyelitis or discitis, all reported from developed nations from 2008 through 2019. Ages ranged from 22-months to 80-years, with 4 females and 5 males. In only seven of the nine cases did the patient acknowledge direct exposure to rats. Four kept rats in their home for reasons including having house pets and a reptile food source. Affected joints included the cervical, thoracic, lumbar, sacral vertebrae and intervertebral discs, as well as hip, ankle, and sternoclavicular joints. Two cases required surgical debridement, while six resolved with antibiotic therapy alone (Table 1). A recent analysis of rat bite fever diagnosis in the United States reveals that the majority of encounters occur in persons aged 0–19
| Year | Country | Study | Age/sex | Exposure | Clinical history and findings | Significant biochemical findings | Site of osteomyelitis/discitis | Identification method of Streptobacillus moniliformis | Cultures | Imaging findings | Surgical treatment | Histological findings | Diagnosis | Antibiotic treatment | Outcome |
|------|---------|-------|---------|----------|-----------------------------|----------------------------------|-------------------------------|---------------------------------|----------|------------------|-------------------|---------------------|-----------|---------------------|---------|
| 2008 | France  | Dubois et al. | 80-year/male | Rooster scratch | History: One week of shaking chills and back pain radiating to both legs on awakening. The pain subsided by time of presentation. | Day 1: WBC 10,000/μl, Hb 10.9 g/dl, platelets 217,000/μl, CRP 0.000 mg/liter, fibrinogen 8.9 g/liter, procalcitonin 13 mg/ml. | TS-T6 and L2-L3 | 16S RNA PCR assay from psoas abscess fluid | Blood specimens inoculated into paired aerobic and anaerobic bottles gave positive results after 1–5 days. | CT thorax revealed pericardial and pleural effusions. CT abdomen showed right iliac psoas abscess communicating with a prosthesis screw. | Bone scan revealed increased signal at L3. | MRI lumbosacral spine revealed psoas abscess and of spondylodiscitis at T5 and T6, and at L2 and L3. | Began with empirical antibiotic therapy parenteral amoxicillin-clavulanic acid (1 g, Q8H) and ofloxacin (200 mg, Q12H). Switched to imipenem-clavulanate (1 g, Q6H), intravenous meropenem (400 mg, Q12H), and teicoplanin (600 mg, Q12H). Then an additional 9-week treatment with intravenous ceftriaxone (200 mg, Q12H), IV dindinidin (600 mg, Q8H), and metronidazole (500 mg, Q8H). | In good health at 8 month follow-up. |
| 2008 | United States | Flannery et al. | 22-month/male | Two pet rats | History: Two days of URI symptoms then 5 days of fever, malaise, with a worsening and blistering rash on all extremities, including palms and soles. Irritability. | Day 1: WBC 10,000/μl, Hb 10.9 g/dl, platelets 217,000/μl, CRP 0.000 mg/liter, fibrinogen 8.9 g/liter, procalcitonin 13 mg/ml. | Right-hip joint 16S rRNA sequencing and DNA mapping | Blood, left-footsynovial fluid, and femoral bone cultures grew Gram-negative rods (though bone culture may have been contaminated). | Ultrasound of right hip revealed joint effusion. | MRI bone marrow edema in the right proximal femoral epiphysis with edema in the surrounding muscles and fascial planes (possibly post-op changes). | Open irrigation and debridement of hip joint | Septic arthritis and possible osteomyelitis | Started on vancomycin and rifampicin for empirical bacterial coverage. Switched to IV piperacillin (250,000 units/kg of body weight/day divided every 4 h). Total of 8 weeks of antibiotics with 4 weeks of intravenous penicillin and 4 weeks of oral amoxicillin. | At one-month follow-up patient remained afebrile with normal inflammatory markers. X-rays of hips and pelvis were normal. Improved weight bearing with physical therapy. Thereafter lost to follow-up. |
| Year | Country | Study | Age/sex | Exposure | Clinical history and findings | Significant biochemical findings | Site of osteomyelitis/discitis | Identification method of Streptobacillus moniliformis | Cultures | Imaging findings | Surgical treatment | Histological findings | Diagnosis | Antibiotic treatment | Outcome |
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| AB | United Kingdom | Adizie et al. | 29-year/male | Owner of three rats | History: Five days of malaise, feverishness, headache, sore throat, joint swellings with rash. On exam: Pustular, maculopapular and perialarial rash of the extremeties including palms and soles. Right knee and left ankle effusions, right second MCP swelling. | CRP 211, ESR 36, ferritin 417, neutrophils 7.89 | Left ankle | 16S rDNA PCR molecular sequencing | Blood cultures and joint aspirate were initially negative. Repeat joint aspirate showed S. moniliformis on 16S rDNA molecular testing. | Left ankle MRI: considerable marrow edema, moderate thick walled effusion consistent with septic arthritis and associated osteomyelitis. | none | Rash skin biopsy: mild non-specific perivascular inflammation within the subcutis | Septic arthritis and associated osteomyelitis | Initially treated with a broad-spectrum antibiotic changed to i.v. benzylpenicillin, then switched to oral penicillin after 2 weeks. | Good recovery |
| AB | Japan | Nei et al | 72-year/female | Denied any direct contact with rodents. Possibility of contact with contaminated water and/or food. | History: 8 days of feverishness and chills. On exam: T 38.8 °C. Subsequent worsening severe lower back pain which limited ability to ambulate. | WBC 13.3 (99% neutrophils), alkaline phosphatase 1035 IU/L, γ-glutamyl transpeptidase 239 IU/L, CRP 26.92 mg/dL | L3-L4 vertebral and intervertebral disc space | 16S rDNA genotyping | At 2 days of incubation in aerobic culture with 5% CO2 on 5% sheep blood agar, highly pleomorphic, filamentous gram-negative bacilli were visualized. Colonies described as very tiny, transparent and slightly white. | MRI: Vertebral bodies L1 and L4 with low signal on T1WI, high signal on T2WI. Low intervertebral disk with linear T2 high signal. Vertebral endplates at L3, L4 were destroyed with visible high-signal intensity bone marrow edema. | none | n/a | Vertebral spondylodiscitis | Initially treated with ceftriaxone (1 g/day) every 6 h. Switched to ampicillin (3 g/day) and gentamicin (0.75 g/day) due to failed antimicrobial susceptibility tests. | Gradual improvement of lower back pain, gradual recovery of exercise and walking capacity | Discharged on 71st day of hospital stay |
| AB | Japan | Sato et al | 52-year/male | Rats infestation in his home; suspicion of bite during sleep. | History: Four days of diffuse arthralgias beginning in knees and back. Found immobile due to severe arthralgia and was taken to hospital. On exam: Afebrile, HR 110, RR 24. Scars on his fingers and feet. Warm, swollen, and tender joints with pain with passive motion. Tenderness at | WBC 10,300/mL (89% neutrophils), Creatinine kinase 789 U/L, CRP 34.6 mg/dL | L5, S1 vertebral L5-S1 disc space | MALDI-TOF MS suggested S. moniliformis DSM 12112 T (score value was 1.588 – unreliable). 16S rDNA molecular sequencing | Blood cultures positive for gram-negative bacilli at 25 h/35 °C/5% CO2. | T2-weighted MRI: high signal intensity in L5 and S1, destruction of L5-S1 disc space supporting diagnosis of vertebral osteomyelitis | Surgical debridement. Cultures from site were negative. | Vertebral osteomyelitis | Gefranzine, 1 g per 24 h, 6 weeks | Complete resolution of arthralgia and back pain; no long-term sequelae. |
| Year | Country | Study | Age/sex | Exposure | Clinical history and findings | Significant biochemical findings | Site of osteomyelitis/discitis | Identification method of Streptobacillus moniliformis | Cultures | Imaging findings | Surgical treatment | Histological findings | Diagnosis | Antibiotic treatment | Outcome |
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| 2008 | Canada | Akter et al. | 46-year/ female | Pet rat scratch | Day 4 of admission; systolic fell to 70mmHg, septic shock. | WBC 11.1, ESR 76 mm/hr, CRP 149 mg/L. | L5-S1 intervertebral disc | Cultures. (Further info not reported). | Initial blood culture was negative. Repeat cultures grew S. moniliformis. Right ankle synovial fluid sample culture negative. | MRI lumbar spinal spine: enhancement of the vertebral end plates; T1WI showed markedly reduced signal at the L5-S1 level, while T2WI showed increased T2 signal. | none | n/a | Discitis | Initially treated with prednisone, methotrexate, sulfasalazine, and hydroxychloroquine due to erroneous diagnosis of rheumatoid arthritis. When correct diagnosis was realized these were discontinued and was started on i.v. ceftriaxone. Was discharged with 3-month course of i.v. ceftriaxone. |
| 2009 | Germany | Eisenberg et al. | 59-year/ male | Snake keeper who bred rats for snake food | History: 15 days of fever and arthralgia without rash, inability to stand and acute progressive onset of dyspnea. On exam: T 39°C. Was initially sedated and placed on ventilator. With discontinuation of sedation, exam showed cervical pain, fascia tautness, sensitivity at the T4 level, knees and left wrist swollen with joint effusion. | WBC 15 (predominantly neutrophils); C-reactive protein 125 mg/L. | C5–T1 vertebral | 16S rRNA gene sequencing from synovia | Blood cultures showed negative results. Culture-negative inflammatory liquid and uric acid crystals found in joint effusions. | Fat-saturated, contrast-enhanced T1-weighted MRI spine Sagittal view of the cervical spine shows: intradiscal protrusion with C5–T1 compression. | none | n/a | Vertebral osteomyelitis and an epidural abscess with consecutive compression of the spinal cord (C5–T1). | Complete resolution of arthritis, marked improvement of back pain, normal inflammatory markers, and resolution of discitis on repeat MRI at 3 months followup. |
| Year | Country | Study | Age/sex | Exposure | Clinical history and findings | Significant biochemical findings | Site of osteomyelitis/discitis | Identification method of Streptobacillus moniliformis | Cultures | Imaging findings | Surgical treatment | Histological findings | Diagnosis | Antibiotic treatment | Outcome |
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| 2019 | United Kingdom | Abusalameh et al | 62-year/female | Denied history of rat bite; acknowledged exposure to live rats and rats droppings. | History: Four days of diarrhea and vomiting followed by severe onset of diffuse hot, swollen joints with severe lower back pain. Hx of seropositive RA (positive anti-CCP), controlled with MTX and tocilizumab. | CRP 218 mg/l, creatinine 2.37 | L5/S1 intervertebral disc | 16S rRNA PCR | Knee, ankle, wrist, and L5/S1 disc needle aspirates grew a gram-negative organism. | MRI spine edema of L5/S1 intervertebral disc. | Discitis | Initially on benzyl penicillin and clindamycin. Later changed to 12-week course of oral amoxicillin and clindamycin. | Disc edema improvement after weeks of antibiotic treatment. |
| 2019 | Portugal | Pena et al | 75-year/female | Rat bite | History: Four day history of fever, myalgias, headache. On exam: Subfebrile, hypotensive, incised wounds on two fingers of left hand. Neck stiffness. On day 3 of admission patient developed worsening neck pain and quadripareisis. | WBC 14,670/μL (86.3% neutrophils), CRP 334 mg/dL, normal LP | C5, C6, and C7 vertebral left SC joint | 16S rRNA PCR and Sanger sequencing | Two blood cultures BD BACTEC Plus Aerobic/F medium grew gram-negative bacteria after 3 days incubation. | Normal CT brain. MRI T2WI: High signal intensity in C5, C6, and C7 vertebrae with meningeal enhancement and high signal intensity the left SC joint, consistent with diagnosis of vertebral osteomyelitis and septic arthritis. | n/a | Vertebral osteomyelitis and septic arthritis | Empirically treated on day 1 of hospitalization with i.v. ceftriaxone (2 g/day); completed 26 days of i.v. ceftriaxone followed by 8 months of oral amoxicillin-clavulanate after discharge. | Complete resolution of neck pain and quadripareisis. |
Our case highlights the need to consider the diagnosis in older adults as well.

This case underscores the importance of obtaining a thorough zoonotic exposure history and maintaining a broad differential that includes RBF when considering potential causes of discitis and osteomyelitis.

Abbreviations
RBF: Rat bite fever; MIC: Minimum inhibitory concentration; TEE: Transesophageal echocardiography; MALDI-TOF: Matrix-assisted laser desorption/ionization

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Authors’ contributions
S.H.A. and R.M. equally contributed to this manuscript. The author(s) read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
Our case report does not meet criteria for required review by SUNY Upstate’s (our institution) IRB (https://www.upstateresearch.org/compliance/committees/institutional-review-board-irb/case-reports/).

Consent for publication
Written consent for publication was obtained from the patient. A copy of the written consent form can be made available for the editor to review under reasonable request.

Competing interests
The authors report no competing interests.

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