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CASE REPORT PEER REVIEWED | OPEN ACCESS

A hidden bite: Unveiling rat bite fever in a 17-month-old

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ABSTRACT

Introduction: Rat bite fever is a zoonotic illness that is typically transmitted through rodent bites or consuming contaminated water or food, though some cases have also reported transmission by body fluids. Organisms involved can include *Streptobacillus moniliformis*, *Streptobacillus notomytis*, and *Spirillum minus*. The organism did not grow in hospital lab culture after three days and was sent to State Lab, was detected on day 7 by polymerase chain reaction (PCR).

Case Report: We report a case of a 17-month-old unimmunized male brought to the emergency department with change in behavior, fever, decreased oral intake, and hand and foot pain due to a suspected animal bite. His condition deteriorated over the course of admission from persistent low-grade fevers, dehydration and rash to include evidence of sepsis, and the development of acute kidney injury and respiratory distress. Although the initial gram stain of blood cultures was positive, the cultures revealed no growth.

Conclusion: Rat bite fever is rare and is often caused by difficult-to-detect *Streptobacillus moniliformis*. Blood cultures commonly yield negative results. It is imperative to prioritize complete exposure history in suspected cases, and empiric treatment with cephalosporin antibiotics should be started as soon as possible until definitive identification of the organism is achieved, as delays in treatment can result in serious complications.

Keywords: Pediatric, Rat bites, Rat bite fever, Sepsis, *Streptobacillus moniliformis*, Zoonoses

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INTRODUCTION

Rat bite fever is a zoonotic illness that is typically transmitted through rodent bites or consuming contaminated water or food, though some cases have also reported transmission by body fluids. The average incubation period is five days [1, 2]. Organisms involved can include *Streptobacillus moniliformis*, the most common cause in Europe and North America, or *Streptobacillus notomytis* and *Spirillum minus*, which are common in Asia [3, 4].

S. moniliformis is a fastidious gram-negative bacillus facultative anaerobe residing as normal flora of pet, laboratory, and wild rodents in the upper respiratory tract. This bacterium is often difficult to grow in routine media due to its inert nature which may necessitate polymerase chain reaction (PCR), immunohistochemistry, or rRNA sequencing for proper identification. Typical presentation of rat bite fever includes a triad of fever, rash, and arthritis [5, 6].

CASE REPORT

A 17-month-old unimmunized male without significant past medical history was brought in by his mother to the emergency department with complaints of change in behavior, fever, decreased oral intake, and hand and foot pain for two days prior. The mother reported that they were sleeping in the basement on a floor mattress when the child woke up crying at 3 am, and the mother noticed 3 puncture wounds to the sole of the left foot with minor bleeding two days prior to presentation. His mother

suspected an animal bite as they live in a basement with known mice infestation, and there were no sharp objects in the area. The child's symptoms developed shortly afterward as his mother subsequently noticed a decreased level of energy, decreased interest in food, and decreased ambulation throughout the day. He would cry when his hands or feet were touched, even accidentally. He developed a non-blanching rash on his face, arms, torso, and legs one day prior to presentation that was not associated with a change in detergent, lotions, or soap. His urine output was reported as less than usual for the prior two days. He was also reported to have had 1 bout of emesis and 1 bout of diarrhea each day.

There was no history of sick contacts or recent travel, and his 6 other siblings remained well. There were no pets in the home. The mother treated the child with ibuprofen at home. In addition to having no significant past medical history, there was no surgical history and no previous episodes of illness with similar complaints. The child had no known allergies, and there was no significant birth or family history. He is the youngest of 6 siblings. All his siblings are healthy and alive. None of them had similar complaints, and all are fully vaccinated.

Vital signs on initial presentation showed a temperature of 37.4 °C, heart rate was 153 beats/minute consistent with tachycardia, a mildly elevated blood pressure of 127/67 mmHg, and an elevated respiratory rate of 34 breaths/minute with oxygen saturation of 96% at room concentration.

On examination the child was fussy but consolable. Physical examination revealed capillary refill time of 3–4 seconds with signs of moderate dehydration and multiple areas of non-blanching, pinpoint, faint maculopapular rash on his face, torso, arms, and legs but sparing palms and soles. He also was noted to have non-pitting edema of the hands and feet. The rest of his physical examination was unremarkable.

Laboratory studies showed a blood urea nitrogen (BUN) of 71 mg/dL, creatinine of 0.95 mg/dL, direct bilirubin of 0.40 mg/dL with total bilirubin of 1.10 mg/dL, aspartate aminotransferase (AST) 41 unit/L, total protein 5.4 g/dL, serum sodium 133 mmol/L, serum bicarbonate 13 mmol/L, total CO_2 13.3 mmol/L, hemoglobin of 10.9 g/dL, hematocrit 32.4%. White blood count (WBC) count was within normal limits with a differential of neutrophils 50%, lymphocytes 40%, monocytes 8%, and platelets of 47,000/mm^3. Peripheral blood smear showed microcytes, burr cells, tear cells, acanthocytes, and poikilocytes.

Serum potassium, chloride, calcium, glucose, anion gap, albumin, alkaline phosphatase (ALP), alanine transaminase (ALT), red blood cell counts (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW) were within normal limits for the age. The child was admitted to the pediatric ward under a working diagnosis of dehydration, acute kidney injury, and thrombocytopenia due to rat bite fever. He was given 2 boluses of 250 mL each of normal saline in the emergency department and then started on maintenance intravenous fluids. The next day, he remained tachycardic with a heart rate in the 150 s/min with mild hypertension for age as blood pressure was 115/71 mmHg. He also continued with an elevated respiratory rate of 38 breaths/min with normal oxygen saturation of 97% at room concentration. He showed signs of mild respiratory distress, and the rash had spread to his palms and soles.

On repeat evaluation the following day, the serum sodium normalized at 139 mmol/L, chloride become elevated (113 mmol/L), CO_2 remained unchanged at 13.6 mmol/L, BUN improved but remained elevated (57 mg/dL), creatinine normalized to 0.59 mg/dL, total protein remained decreased, WBC count was 11,160/mm^3, red blood count (RBC) count decreased from 4.09 to 3.73 M/mm^3, hemoglobin decreased to 9.9 g/dL, hematocrit decreased to 30.4%, platelet count increased to 70,000/mm^3, and prothrombin time (PT) and international normalized ratio (INR) were increased (15.4 s and 1.2 respectively). The procalcitonin was elevated to 7.9 ng/mL, total bilirubin increased to 1.20 mg/dL, and serum bicarbonate remained 13 mmol/L. Arterial blood gas analysis showed a severe metabolic acidosis with normal anion gap and respiratory compensation.

Serum potassium, calcium, lactate, glucose, albumin, ALP, ALT, MCV, MCHC and RDW remained within normal limits for the age. Urine analysis revealed +2 heme, trace ketones, +1 protein, with presence of RBCs and WBCs.

He remained tachypnoeic and tachycardic with mildly elevated blood pressure, and capillary refill time was <2 seconds.

In the pediatric unit, a blood culture was sent before initiation of antibiotics (Ampicllin/Sulbactam), and a lumbar puncture was performed. He also underwent a brain magnetic resonance imaging (MRI) under general anesthesia. Due to concern for progressive sepsis, he subsequently received intravenous Vancomycin and Ceftriaxone empirically.

The day after admission to the pediatric ward, he developed a fever to 39.0 °C as well as signs of increasing respiratory distress, and his respiratory support was advanced to high flow nasal cannula with a requirement for supplemental oxygen (45%) and a flow rate of 20 L/min to maintain an oxygen saturation of 97%. He was therefore transferred to the pediatric intensive care unit (PICU) where he stayed for 5 days. Over the course of several days, his platelet count increased to 1321 K/mm^3 and aspirin was started.

The gram stain of his blood culture was read as gram-negative rods, but there was no growth on culture. As a result of this gram stain, his antibiotics were broadened to include Piperacillin/Tazobactam. To attempt to identify the organism, the sample was sent to the Maryland state laboratory for further analysis. Via polymerase chain reaction (PCR) testing, it was subsequently identified as *S. moniliformis*. However, the organism did not grow on culture so that susceptibility testing was not possible.

Based on this identification, the patient's antibiotics were changed to intravenous Ampicillin/Sulbactam.

He had a long hospital course but did slowly and steadily improve, and inflammatory markers (procalcitonin and CRP) also slowly but steadily improved, as did his thrombocytosis. In total, he was treated for 14 days with intravenous antibiotics and was discharged home after completion of his antibiotic course in good condition with no obvious morbidity.

His workup included excluding other potential diagnoses such as measles, Rocky Mountain spotted fever, Kawasaki disease, other rickettsial illnesses such as Lyme disease or Ehrlichiosis, viral illnesses, idiopathic thrombocytopenic purpura, autoimmune thrombocytopenia, and leptospirosis based on laboratory and clinical findings.

DISCUSSION

Although rat bite fever transmission to humans is rare, it can occur after a bite or scratch from rodents such as a rat, handling of rodents, or exposure to rodent saliva or excreta. There have been limited case reports due to non-obligatory infection report filings. Based on data from 2001 to 2015, it is estimated that 12,700 rodent bites per year are treated in emergency departments in the United States [7]. Rat bite fever in infants is believed to be rare.

The usual presentation of rat bite fever includes fever, headache, rash, and migratory polyarthritis [8]. Other symptoms may include myalgias, lymphadenopathy, chills, malaise, vomiting, and nausea [8]. The rash can vary from erythematous vesiculopapular, petechial, morbilliform, pustular, or purpuric and typically occurs 3–10 days following exposure [8]. In many cases reported the cultures were negative [8]. When the culture was positive, the time for positive blood cultures ranged from 20 hours to 7 days. In review of the literature, there has been reported use of Ceftriaxone, Doxycycline, Ampicillin, Penicillin G, Piperacillin/Tazobactam, and/or Amoxicillin/Clavulanate for varying durations leading to recovery [4]. Despite being a gram-negative bacterium, *S. moniliformis* is susceptible to most antibiotics that cover gram-positive organisms that include penicillin, cephalosporins, tetracyclines, macrolides, clindamycin, and aztreonam [8]. First-line treatment is recommended to be intravenous penicillin. In most cases, antibiotic treatment for 1–2 weeks is sufficient, although if there are systemic complications longer treatment duration may be required. In our case, after the organism was identified, Ampicillin/Sulbactam was utilized and the child recovered uneventfully.

S. moniliformis is a pleomorphic, non-motile, fastidious, microaerophile, gram-negative rod and requires specific culture conditions for growth. This leads to growth delays if not failures of cultivation [5, 6]. Anaerobic blood culture media contains sodium polyanethole sulfonate that can inhibit *S. moniliformis* growth. For this reason, blood culture is an insufficient diagnostic test for this organism and culture failure rates of up to 33% have been observed even in cases of bacteremia. In such cases, use of rRNA sequencing, PCR, or immunohistochemistry is required for proper identification [5, 6].

Progression and complications of the disease can include persistent rash, focal abscesses, migratory polyarthritis, pericarditis, hepatitis, pneumonia, serositis, nephritis, systemic vasculitis, sepsis, meningitis, and death [8, 9]. Delays in identification and treatment can lead to lethal outcomes and cardiac complications such as endocarditis and valvular dysfunction [4]. The prognosis for rat bite fever depends upon effective and early antibiotic therapy [4].

CONCLUSION

Rat bite fever is rare and is caused by difficult-to-detect *S. moniliformis*. Blood cultures commonly yield negative results. It is imperative to prioritize complete exposure history in suspected cases. Prompt identification and management of rat bite fever could be enhanced by diagnostic methods, like PCR or rRNA sequencing, to minimize delays in treatment. Empiric treatment with cephalosporin antibiotics should be started as soon as possible until definitive identification of the organism is achieved, as delays in treatment can result in serious complications or death.

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Author Contributions

Chinwendu N Ezeoru – Conception of the work, Design of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Scott Penfil – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

ABOUT THE AUTHORS

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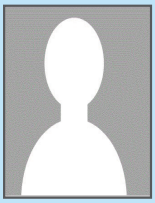

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