

Rat-Bite Fever in an Immunocompromised Patient in Israel

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Rat-bite fever (RBF) is a rare zoonotic infection caused by *Streptobacillus moniliformis* or *Spirillum minus*. It is typically transmitted through contact with rats. In the United States, *Streptobacillus moniliformis* is the predominant causative agent, whereas in Asia, cases are more commonly attributed to *Spirillum minus*. We report a case of RBF in Israel, in which the identified pathogen was *Streptobacillus moniliformis*, a pleomorphic, Gram-negative bacillus. The classic clinical presentation of RBF includes fever, rash, and arthralgia, which may be migratory in nature.

In Israel, RBF is not a notifiable disease, and its true incidence remains unknown. A review of the literature revealed only two previously published case reports [1,2], suggesting that RBF may be under-recognized and underreported in our country. In this case communication, we present a case of RBF in an immunocompromised adult patient from the northern part of Israel.

PATIENT DESCRIPTION

A 60 year old man presented with a history of fever (39°C) one day prior to admission, left peri-umbilical abdominal pain, and paroxysmal frontal headaches. Four days prior, he was bitten by a rat on the second toe of his right foot. His medical history was significant for pancytopenia for several months prior to admission. His evaluation for suspected myelodysplastic syndrome (MDS), a bone marrow biopsy, was pending. Physical examination on admission revealed a healthy appearing male, hemodynamically stable and fully alert, with no signs of acute distress. Examination of the affected area on the right foot revealed a bite wound on the second toe, with edema, erythema, and warmth consistent with cellulitis. No purulent discharge observed. Abdominal examination revealed a soft abdomen with tenderness in the lower left quadrant.

Initial laboratory evaluation in the emergency department revealed worsening pancytopenia. The complete blood count marked a leukocyte count of 2000 cells/μL, macrocytic anemia (hemoglobin 9 g/dL, MCV 100 fL), and thrombocytopenia (platelet count 52,000 cells/μL).

Neutropenia was indicated by his

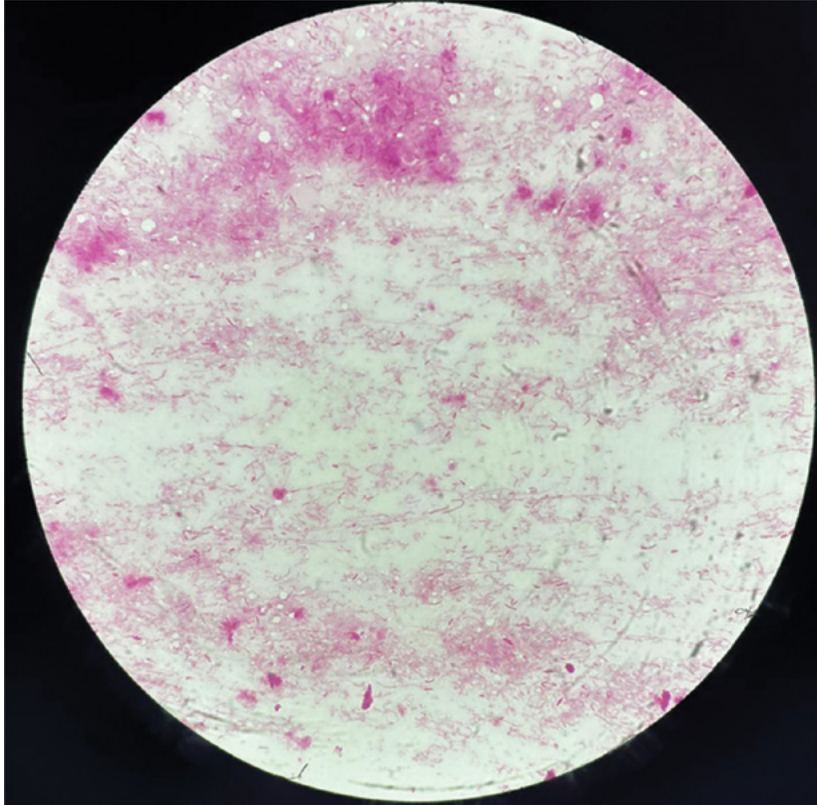
neutrophil count of 890 cells/μL. A peripheral blood smear confirmed true thrombocytopenia, with no schistocytes or spirochetes observed. Basic metabolic panel indicated mild acute kidney injury, mild indirect hyperbilirubinemia, and mild hyponatremia. Urinalysis was positive for protein.

The patient was admitted for further evaluation and management. Empirical intravenous with piperacillin-tazobactam was initiated due to his neutropenic status. Multiple blood cultures were drawn.

A computed tomography scan of the abdomen and pelvis was performed revealing splenomegaly (18 cm) along with increased bone marrow attenuation.

Bacterial growth was detected in blood cultures obtained on admission after 12 hours of incubation. Gram staining revealed elongated, pleomorphic Gram-negative rods arranged in chains and filaments, a morphology raising suspicion for an unusual fastidious organism [Figure 1]. Subcultures demonstrated very slow growth, with small grayish colonies becoming visible only after 48–72 hours on enriched media, including chocolate, blood, and Brucella agar. In this case, the microorganism grew under aerobic

Figure 1. Gram staining revealing elongated, pleomorphic Gram-negative rods arranged in chains and filaments



conditions enriched with 5% CO₂ after 3 days. These features reflect the fastidious nature of *Streptobacillus moniliformis*, which may require up to 7 days of incubation under microaerophilic conditions to achieve visible growth, and whose colonies remain small and nonspecific in appearance, which complicates recognition.

Phenotypically, the isolate was identified as a Gram-negative bacillus, catalase-negative and oxidase-negative. However, repeated attempts at identification by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry failed, as none of the major commercial databases contain reference spectra for

S. moniliformis. This limitation is well recognized in the literature and underscores the restricted utility of MALDI-TOF for rare organisms not represented in manufacturer databases [3]. In addition, the Clinical and Laboratory Standards Institute does not provide specific antimicrobial susceptibility testing guidelines for *S. moniliformis* due to its rarity and growth requirements [4].

Historically, serologic assays and slide hemagglutination tests have been used in animal studies and, to a limited extent, in humans. Although sufficiently sensitive, these assays are no longer available for clinical use in humans, and their role has been largely supplanted by the demand for rapid molecular di-

agnostics. Molecular methods such as polymerase chain reaction (PCR) have shown promise and have been successfully applied in both humans and laboratory animals. A PCR assay specific for *S. moniliformis* uses primers designed based on 16S rRNA gene sequence data from both human and rodent strains.

In our case, definitive species level identification was achieved by 16S rRNA gene sequencing, which confirmed the pathogen as *S. moniliformis*. This finding highlights the indispensable role of molecular diagnostics in confirming infections caused by rare or fastidious bacteria that remain difficult to identify by conventional microbiological methods.

During hospitalization, the patient made a full recovery, with complete defervescence and resolution of his presenting symptoms. After he had remained afebrile for 48 hours, he was discharged and advised to complete a 10-day regimen of oral doxycycline.

Observed worsening of pancytopenia was likely reactive to the acute infectious process. Further outpatient hematological workup was recommended, with MDS/myeloproliferative neoplasm overlap syndrome or a lymphoproliferative disorder remaining as primary differential diagnoses.

COMMENT

Our case highlights several important aspects of *Streptobacillus moniliformis* infection. First, RBF should be considered in patients presenting with unexplained febrile illness, especially when accompanied by a history of rodent exposure, even if seemingly minor. The classic triad of fever, rash, and polyarthralgia may not always be present,

as demonstrated in our patient, who presented with neutropenic fever and atypical abdominal symptoms.

At the patient's presentation with fever, neutropenia, and a history of a rat bite, a broad differential diagnosis was considered. This research included skin and soft tissue infections originating from the bite site as well as zoonotic diseases such as RBF and leptospirosis.

The diagnostic challenges posed by *S. moniliformis* are well documented [3]. Its fastidious growth requirements and often non-distinct phenotypic characteristics can hinder identification by routine laboratory methods, as seen with the unsuccessful MALDI-TOF attempts in our case. In this case as in other published case reports, identification was achieved by 16S rRNA gene sequencing. This investigation underscores the critical role of molecular diagnostics, specifically 16S rRNA gene sequencing, in providing a definitive diagnosis for unusual or difficult-to-culture pathogens, allowing for targeted therapy.

Last, the interplay between the acute infection and the patient's

pre-existing hematological condition is noteworthy. While the worsening pancytopenia during the acute febrile illness was likely reactive, *S. moniliformis*, acute infection can cause hematological abnormalities, including anemia, leukocytosis, and thrombocytopenia. At admission with neutropenic fever, broad-spectrum antimicrobial therapy was promptly initiated. This immediate treatment may have contributed to the rapid resolution of symptoms and potentially prevented the development of serious complications such as arthritis or osteomyelitis, as described in previous studies [5].

CONCLUSIONS

In our case communications, we describe a challenging diagnosis of *Streptobacillus moniliformis* bacteremia in a patient presenting with worsening pancytopenia. We emphasize the importance of a thorough exposure history, maintaining a high index of suspicion for zoonotic infections, and leveraging advanced molecular diagnostic tools when conventional methods are insufficient. Prompt recognition and appropriate antibiotic

therapy with agents like doxycycline or penicillin are crucial for successful outcomes in RBF.

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Capsule

Blood pressure levels and outcomes in type 2 diabetes mellitus

Wang et al. conducted a comprehensive dose-response meta-analysis to characterize the relationship between blood pressure levels and clinical outcomes in individuals with type 2 diabetes mellitus. The investigators analyzed data from 5.87 million participants enrolled in multiple prospective cohort studies. The analysis demonstrated a nonlinear (J-shaped) relationship between blood pressure and adverse outcomes. Cardiovascular and mortality risks increased progressively with higher systolic blood pressure levels, while excessively low blood pressure was also associated with increased adverse outcomes, particularly among high-risk patients. The lowest overall

risk was observed within an intermediate blood pressure range rather than at the lowest achievable values. For most cardiovascular outcomes, maintaining moderately controlled systolic blood pressure was associated with the greatest reduction in risk. Very aggressive blood pressure lowering did not consistently provide additional benefit and, in some populations, was associated with an increased risk of adverse events, supporting concerns regarding overtreatment.

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