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CASE REPORT

PATHOLOGY/BIOLOGY

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Rat Bite Fever, a Fatal Case of *Streptobacillus moniliformis* Infection in a 14-Month-Old Boy

ABSTRACT: *Streptobacillus moniliformis* is the primary cause of rat bite fever in North America. Children under 12 years of age are primarily infected, presenting with an acute syndrome of fever, rash, and polyarthritis. Common vectors include rats and mice. Transmission is predominantly from a bite or scratch, but contact with or ingestion of food contaminated with feces or saliva has also been reported. We report a fatal case of *S. moniliformis* infection in a 14-month-old-boy. At home, the child was exposed to filthy living conditions and the family had pet ferrets. Autopsy revealed a red-pink, mostly confluent rash and a circumscribed area suspicious for a possible bite mark. Cerebrospinal fluid cultures were positive for *S. moniliformis*. This case highlighted key features, such as the morbiliform rash, but lacked lymphadenopathy or joint manifestations. It is important to consider rat or rodent exposure as a source of infection.

KEYWORDS: forensic science, *Streptobacillus moniliformis*, rat bite fever, *Spirillum minus*, sodoku, Haverhill fever, *Actinobacillus muris*, pediatric

Rat bite fever (RBF) describes two similar but distinct disease syndromes caused by *Streptobacillus moniliformis* or *Spirillum minus*. *S. moniliformis*, also referred to as *Actinobacillus muris* in some reports, is a rare Gram-negative filamentous bacillus and is the primary cause of RBF in North America. *S. minus* causes RBF in Asia, also known as sodoku in Africa. In the U.S., primarily children under the age of 12 years are infected. The acute clinical syndrome is characterized by fever, rash, and polyarthritis (1). Common vectors include rats and mice, which are natural reservoirs. Transmission is predominantly from a bite or scratch, but contact with or ingestion of food contaminated with feces or saliva has also been reported (2). The Haverhill fever was an epidemic outbreak of the disease through contaminated milk in Haverhill, Massachusetts in 1926. The organism, at that time termed *Haverhillia multiformis*, was later shown to be identical to *S. moniliformis* (3). We report a rare confirmed fatal case of *S. moniliformis* infection in a 14-month-old boy.

Clinical Presentation

A previously healthy 14-month-old boy with an unremarkable birth history was in his usual state of health until 1 day prior to presentation, according to the parents. During the evening, the child was noted to have a fever and diffuse rash on his face, trunk, and extremities. The child was empirically treated with one dose of acetaminophen and laid down in his crib. Later that night, the child's mother and grandmother returned to the room and found the child unresponsive. Resuscitative measures were started, and the child was emergently taken to the hospital. Upon arrival, the child was in cardiac arrest and was subsequently declared dead. All other family members including a 2-year-old sibling remained in good health.

Upon further investigation, the house was noted to generally be in a state of disarray. The upstairs bedroom, where the child was found, was especially disheveled and cluttered with two cribs, a full-size adult bed, a microwave oven, a hot plate, and several animal cages adjacent to the cribs containing rabbits, ferrets, and an aquarium with dead fish and algae. The rabbits and ferrets had large amounts of fecal material within their cages. The room was also infested with roaches, flies, and ticks over the floor, walls, ceilings, and all of the bedding.

Forensic Autopsy Findings

The body was a well-developed and well-nourished white male toddler. He weighed 25 pounds (62nd percentile) with a crown-heel length of 29 inches (fifth percentile). A red-pink macular and mostly confluent rash covered almost the entire body surface with prominence on the head including the scalp, neck, anterior and posterior torso, anogenital region, and portions of the thighs (Figs 1–3). There was sparing of the bilateral legs, soles, palms and portions of the forearms, nose and mouth, except the left lateral corner of the mouth. The rash did not involve the buccal mucosa or gums. On the right knee, there was a circumscribed, donut-shaped rash containing multiple, 1/16″ to 3/16″ round to irregular abrasions with a central 2″ in diameter sparing and a 3/16″ abrasion within the spared area (Fig. 4). On the left arm and elbow region were multiple 1/8″ to ½″ irregular abrasions (Fig. 5). The eyes appeared sunken into the orbits with normal sclera and conjunctiva. There was no palpable cervical, axillary, or inguinal lymphadenopathy. No additional external abnormalities were noted on the chest, abdomen, back, genitals, or anus.

Internal examination revealed a moderately congested liver with mild hepatomegaly. The mesenteric lymph nodes were slightly

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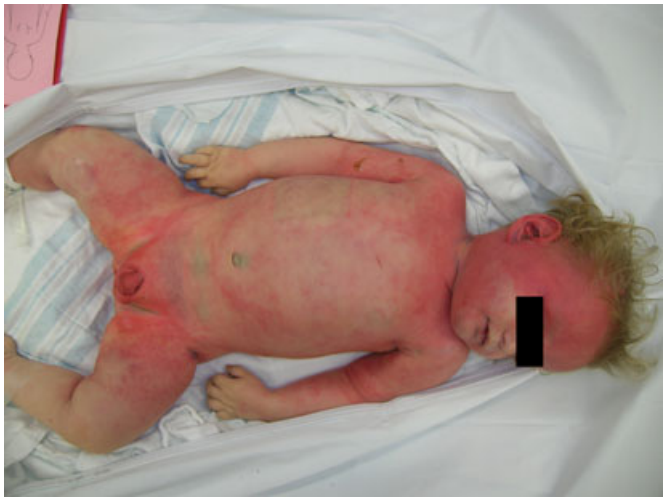

FIG. 1—*Overall frontal autopsy photograph.*

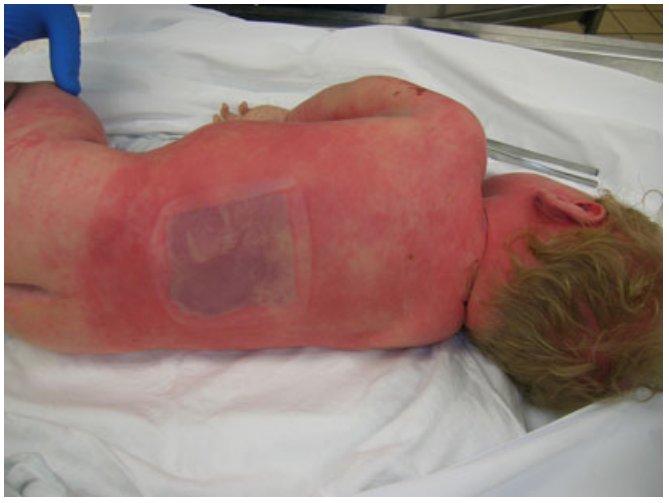

FIG. 2—*Overall posterior autopsy photograph.*

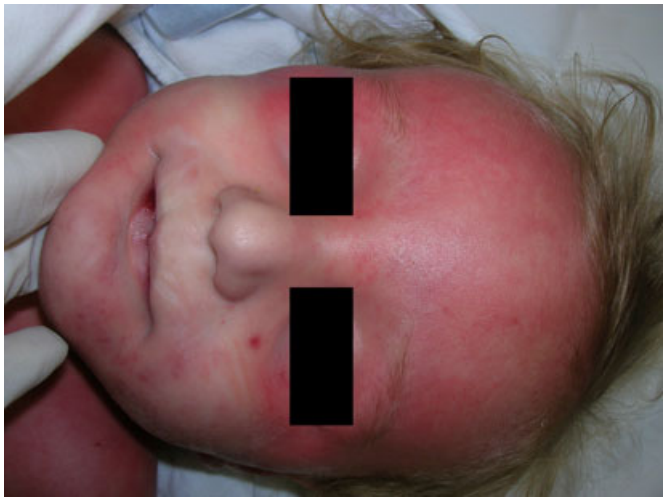

FIG. 3—*Close-up of the head autopsy photograph.*

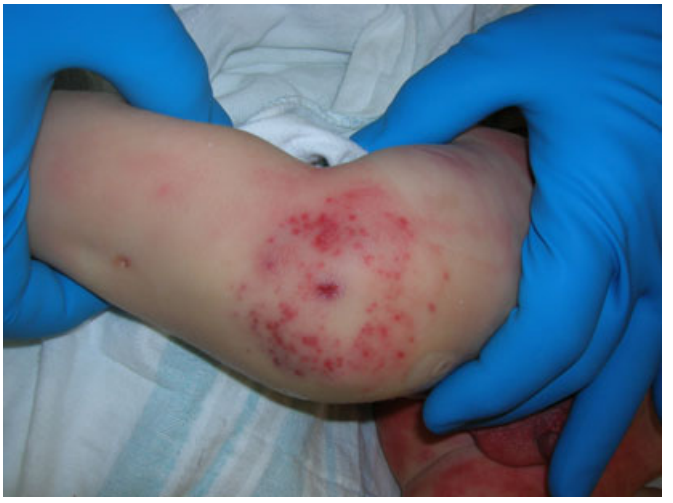

FIG. 4—*Possible bite mark on right knee.*

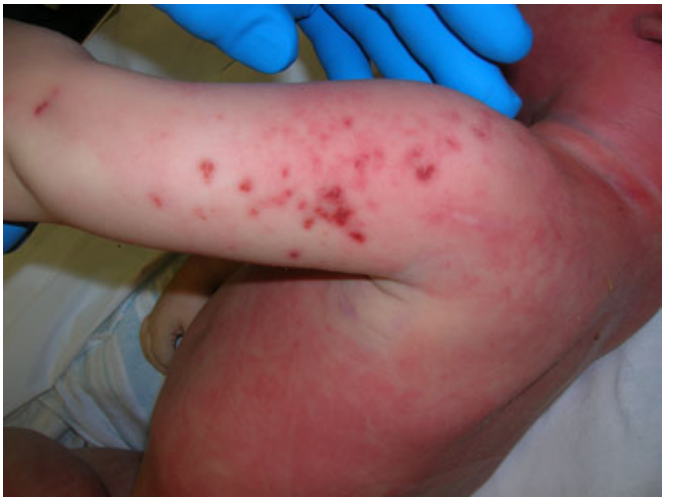

FIG. 5—*Abrasions on left upper arm.*

enlarged. There was mild flattening of the cerebral gyri with mild collapse of the ventricular system.

Microscopic examination of the lungs showed interstitial pneumonitis with rare neutrophils and edema. There were focal areas of gastric aspiration without associated vital reaction. The kidneys had fibrin microthrombi with focal fibrinoid necrosis of the tubules, consistent disseminated intravascular coagulopathy. The middle ears showed focal chronic inflammation. The small and large intestine, liver, thymus, thyroid gland, larynx, and heart showed mild to moderate autolysis, but no other major histopathologic changes. The lymph nodes showed sinus hyperplasia and erythrophagocytosis. Examination of the dura, leptomeninges, cerebral vasculature, left frontal region, hippocampus, pons, cerebellum, and the spinal cord showed no major histopathologic changes. There was no evidence of infection or inflammation with negative silver stain and acid fast stains.

Routine toxicologic analysis of heart blood and liver at the Medical Examiner's toxicology laboratory with mass spectrometry (Agilent 5975 C VL MSD; Palo Alto, CA) and gas chromatography (Agilent 7890 A GC system) revealed diphenhydramine in concentrations of 4.7 mg/L and 4.7 mg/kg, respectively. The diphenhydramine was administered during resuscitation in the

emergency department for presumed allergic reaction. The blood and liver were negative for additional drugs or alcohol. The vitreous was insufficient for electrolyte, vitreous urea nitrogen, and creatinine analysis.

Gram stain on the cerebrospinal fluid showed rare red and white blood cells with no organisms identified. However, microbiologic culture on the cerebrospinal fluid was positive for *S. moniliformis*. Blood cultures were negative. Viral cultures for influenza, parainfluenza 1–3, adenovirus, respiratory syncytial virus, and enteroviruses were negative.

Discussion

In the U.S., 55% of *S. moniliformis* infection cases occur in children <12 years of age (4). The demographics of the victims have broadened to include children, pet store workers, and laboratory technicians, because the rats have become popular pets and study animals (2). RBF is rare in the U.S. with over 200 documented cases. However, as RBF is not a reportable disease, the true incidence of the infection could be much higher (1,5). The incubation period ranges from 3 days to 3 weeks, with symptoms evident most often within 7 days. Clinical presentation consists of a systemic viral-like illness characterized by fever, rigors, and migratory polyarthalgias with associated morbiliform rash. The rash, which is found in 75% of cases, usually appears between the first and fifth day. It is usually maculopapular, with hemorrhagic vesicles that can be present on the distal extremities and petechiae, which can be present on the plantar surface of the feet. Our case showed a diffuse, mainly confluent rash without petechiae or hemorrhagic vesicles. As in this case, the fever has a rapid onset, and it may be intermittent or relapsing with rigors. In addition, lymphadenopathy and polyarthritis of small and large joints can occur in 50% of cases, which can be suppurative. There are 16 reported cases of septic arthritis with positive cultures for *S. moniliformis* in synovial fluid since 1985 (4,6). In this case, there was no significant lymphadenopathy, and the joints were not examined for evidence of gross or microscopic infection. Complications can include anemia, endocarditis/myocarditis, vasculitis, meningitis, bronchopneumonia, and septicemia. Recommended therapy is penicillin or tetracycline in the case of penicillin allergy. Mortality is estimated at 7–13% without treatment (1,5).

The nonspecific clinical presentation yields a broad differential diagnosis including meningococcemia, *Staphylococcus aureus* or *Streptococcus pyogenes* septicemia, Rocky Mountain spotted fever or other rickettsial diseases, enterovirus infection, disseminated gonorrhea, Lyme disease, ehrlichiosis, brucellosis, leptospirosis, and secondary syphilis. Given this differential of more common entities, laboratory identification is essential to proper diagnosis and was vital in the identification of this unsuspected infection. *S. moniliformis* is a Gram-negative, nonmotile, highly pleiomorphic rod. Various culture conditions can yield filaments or chains with individual rods showing lateral bulbar swellings. It is extremely fastidious requiring 20% blood serum or ascitic fluid supplementation and grows optimally under microaerophilic conditions at 35–37°C. The most common problem with identification is that routine blood cultures contain the anticoagulant sodium polyanethol sulfonate (SPS) that inhibits *S. moniliformis* growth. The lack of *S. moniliformis* growth in blood cultures submitted for this case may be explained by the presence of this anticoagulant. The cerebrospinal fluid was submitted in a sterile redtop tube without any additives. Anaerobic or trypticase soy broth–based cultures that lack SPS may show growth. Identification of the organism can be fully determined by biochemical analysis and by chromatographic fatty acid profiles (2,3,5).

The patient's exposure to multiple potential animal vectors and dirty living conditions warrants discussion about *S. moniliformis* sources. It was suspected that the donut-shaped lesion on the right knee and the abrasions on the left arm could have been caused a recent animal bite mark or scratch. Common vectors include rats and mice, which are natural reservoirs. *S. moniliformis* is a commensal organism in the upper respiratory tract of rats. Domesticated or laboratory rats show 10–100% colonization rates, and wild rats show more frequent colonization at 50–100%. However, *S. moniliformis* has also been detected in ferrets, guinea pigs, gerbils, and rare, isolated cases in cats and dogs. Transmission is predominantly from a bite or scratch, but contact with or ingestion of food contaminated with feces or saliva has also been reported. The risk of infection after a single rat bite is estimated at 10%. If there is a bite, it quickly heals with minimal associated induration or adenopathy (2). Per report, testing of the pet ferrets was negative for *S. moniliformis*.

Conclusion

RBF is a systemic infection characterized by abrupt onset of fever, rigors, generalized rash, and migratory polyarthritis. The infection is associated with a mortality rate of 7–13%, if untreated. The actual rate of infection may be much higher, because it is not a reportable disease. Although easily treatable with antibiotics, the diagnosis and treatment can be delayed because of a broad differential diagnosis and difficulties to culture the organism. In all suspected cases, a complete autopsy should be performed, and the microbiology laboratory should be contacted for guidance in submitting blood, cerebrospinal fluid, and probably synovial fluid in appropriate media to prevent growth inhibition of *S. moniliformis*.

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