Fever and a rat bite

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A 70-year-old previously healthy man presented to the emergency department with a three-day history of fever. Two weeks before, while working in the kitchen of his restaurant, he captured a rat. The rat bit him on his right thumb, prompting the man to kill the rat and dispose of it in the garbage. He saw his family physician, who gave him a topical antibiotic ointment and a tetanus booster. The wound healed and the patient felt well until 10 days later when he developed fever, chills and sweats. At the same time, his thumb became painful, swollen and erythematous. The wound dehiscenced spontaneously. He returned to his family physician, who prescribed oral cloxacillin and referred him to the emergency department.

Upon arrival at the emergency department, his temperature was 39.1°C and his oxygen saturation was 90% on room air. Blood and wound swab cultures were obtained. The patient was given a second tetanus booster and a consultation with the infectious diseases service was requested.

The patient was from China and had lived in Canada since 1996. He had not travelled outside Canada since his arrival. His vaccination history was unknown. There was no history of arthralgias, myalgias or rash.

On physical examination by the infectious disease service, his blood pressure was 110/80 mmHg, his heart rate was 70 beats/min and regular, and his temperature was 36.7°C. His oxygen saturation was 97% on room air. There was no cervical adenopathy and his conjunctiva were normal. His neck was supple. Cardiovascular and abdominal examinations were normal. Auscultation of his chest revealed bibasilar inspiratory crackles. There was no rash, petechiae, jaundice or clubbing. His right thumb was swollen and erythematous to the base. There was a superficial puncture

Figure 1) Erythematous thumb with margins demarcated and open puncture site

wound on the ventromedial aspect of his thumb (Figure 1). There was no drainage. His thumb was tender and indurated. There was also evidence of lymphangitis on the dorsal aspect of his right forearm.

Initial laboratory investigations revealed a white blood cell count of $9.5 \times 10^9/L$, and normal electrolyte, renal and liver profiles. Two sets of blood cultures were negative. A Gram stain of the sample from the wound showed Gram-negative bacilli on microscopy, but the culture was negative. Radiographs of his chest and hand were normal.

What is your diagnosis and how would you treat this patient?

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DIAGNOSIS

A diagnosis of rat bite fever was made and the patient was treated with 14 days of amoxicillin/clavulanic acid. He became afebrile and was discharged 48 h after starting antibiotics, at which time the erythema, pain and edema in his right thumb had improved and the lymphangitis had resolved. At follow-up two weeks later, he felt generally well and his thumb was not swollen or tender, but there was some residual erythema and induration surrounding the area of the bite. The initial blood cultures (taken 24 h after starting oral cloxacillin) and wound swab culture were negative. Universal bacterial 16S ribosomal RNA polymerase chain reaction of the wound swab was negative.

DISCUSSION

Rat bite fever is a rare but well described clinical syndrome. It is caused by two different pathogens that are commonly found in the oropharynx of rodents – *Streptobacillus moniliformis* and *Spirillum minus*. Originally described as 'sodoku' in Japan, cases of rat bite fever have been reported worldwide.

S. moniliformis is a microaerophilic, Gram-negative bacillus that accounts for most cases of rat bite fever in North America (1). It was previously known as *Haverhillia multi-formis*, named after the epidemic of rat bite fever that occurred in Haverhill, Massachusetts in 1926 (2). *S. minus* (also a Gram-negative bacillus) accounts for most cases of rat bite fever in Asia. Artificially induced spirillar fever, or 'sodoku inoculata', was used in the 1930s for the treatment of dementia paralytica (neurosyphilis). Affected individuals were inoculated with blood from guinea pigs and developed symptomatology that resembled that of clinical rat bite fever (3).

Rat bite fever has been reported in a number of populations, including urban poor communities, rural communities, laboratory workers and children with pets (1). The infection typically follows a rat bite or scratch, although cases have been reported from contact with squirrels, mice, dogs and cats (4). Furthermore, rat bite fever can follow the ingestion of food or water that has been contaminated with rat excrement. This was demonstrated by the outbreak of rat bite fever in Haverhill, Massachusetts in 1926, when a contaminated milk source led to infection in 86 individuals (2).

The clinical features of this syndrome typically appear one to two weeks after the initial bite. Patients report an initial asymptomatic period followed by the abrupt onset of fever, chills, nausea and headache. Many people also develop myalgias and arthralgias. A maculopapular or petechial rash may form on the soles of the feet or palms of the hands of affected individuals. If untreated, the symptoms resolve

TABLE 1
Clinical features of rat bite fever

<i>Streptobacillus moniliformis</i>	<i>Spirillum minus</i>
North America	Asia
Onset within 10 days	Onset in one to four weeks
Wound heals, inapparent	Wound inflamed, reopens
Arthralgias common	Arthralgias uncommon
No lymphangitis	Lymphangitis
Rash on hands and feet	Typically no rash

spontaneously within days, although relapses may occur weeks to months later. Rare complications of rat bite fever include endocarditis, pneumonia, septic arthritis, myocarditis, amnionitis and abscess formation. The mortality rate of untreated patients has been reported to be 13% (4). *S. moniliformis* is almost the exclusive cause of rat bite fever in North America and Europe, while *S. minus* is responsible for rat bite fever in Asia. The amount of time from bite to the onset of symptoms tends to be longer in cases of *S. minus*. Other distinguishing features include the presence of rash, arthralgia and myalgia in *Streptobacillus* infections. *Spirillum* infections are characterized by reopening and eventual ulceration of the wound after it has healed, as well as regional lymphangitis and lymphadenitis (Table 1) (5). The present case is more typical of *S. minus* than *S. moniliformis*. It is possible, however, that the presenting syndrome was caused by a staphylococcal or streptococcal species that frequently causes skin and soft tissue infections.

Diagnosis of rat bite fever relies largely on history and physical examination. Laboratory diagnosis is frequently difficult. *Streptobacillus* requires culturing on enriched media, and *Spirillum* does not grow on culture media. *Spirillum* can be diagnosed only by direct visualization of the typical motile organisms. Both organisms are susceptible to penicillin, and the recommended treatment includes a 10- to 14-day course of antibiotics along with suitable tetanus prophylaxis. Postexposure rabies prophylaxis is not recommended for the treatment of rat bites (6).

Most cases of rat bite fever reported in the North American literature were caused by *S. moniliformis*, the majority of which occurred in laboratory workers, pet owners or people who lived in areas that were infested with rats. It is estimated that 50% of laboratory and wild rats in North America harbour *Streptobacillus* in the oropharynx (7). The most recently reported case of rat bite fever in Canada occurred in 1964 in a female graduate student who was bitten by a laboratory rat (8). *Streptobacillus* was eventually cultured on enriched media. In 1951, two cases of rat bite fever were reported in children who lived together in urban Vancouver, British Columbia and who had been bit-

ten by a rat. *Streptobacillus* was cultured from the blood of both patients. The symptoms recurred periodically for several months. There were eight other cases of rat bite fever reported in Canada before 1940. Seven of those cases occurred in urban Montreal, Quebec (mostly in children), and the other case occurred in rural Nova Scotia. Cultures

did not reveal any pathogenic organisms, although in three cases, *S minus* was reportedly visualized in the blood (9).

We describe the first reported case of rat bite fever in Canada since 1964. This distinct clinical syndrome should be considered in anyone who presents with fever and may be at risk of exposure to rats.

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