

***Streptobacillus notomytis* Bacteremia after Exposure to Rat Feces**

Akira Kawashima, Satoshi Kutsuna, Akira Shimomura, Lubna Sato, Honami Ando, Tsutomu Tanikawa, Maki Nagashima, Tohru Miyoshi-Akiyama, Takeshi Inagaki, Norio Ohmagari

Author affiliations: National Center for Global Health and Medicine, Tokyo, Japan (A. Kawashima, S. Kutsuna, A. Shimomura, L. Sato, H. Ando, M. Nagashima, T. Miyoshi-Akiyama, T. Inagaki, N. Ohmagari); Yamazaki Professional College of Animal Health Technology, Tokyo (T. Tanikawa)

DOI: <https://doi.org/10.3201/eid2804.204965>

To determine the source of *Streptobacillus notomytis* bacteremia in a woman in Japan with signs of rat-bite fever, we examined rat feces from her home. After culture and PCR failed to identify the causative organism in the feces, next-generation sequencing detected *Streptobacillus* spp., illustrating this procedure's value for identifying causative environmental organisms.

Rat-bite fever, characterized by fever, rash, and arthritis, is caused by *Streptobacillus moniliformis* and *Spirillum minus*, which are gram-negative, filamentous, bacilli transmitted by rat bites or ingestion of water or food contaminated with rat feces or urine (1). In 2015, *S. notomytis* was reclassified from *S. moniliformis* to the new species (2). We reported a case of rat-bite fever in Japan that was caused by *S. notomytis*, identified by 16S rRNA sequencing after blood culture and most likely transmitted by rat feces.

A 70-year-old woman was admitted to the National Center for Global Health and Medicine (Tokyo,

Japan), reporting left back pain, lower leg myalgia without arthralgia, and a 3-day fever with abdominal discomfort. At the time of admission, she was fully conscious with the following parameters: temperature 37.9°C, blood pressure 132/68 mm Hg, heart rate 112 beats/min, respiratory rate 24 breaths/min, and oxygen saturation 98%. She reported that rats often entered her apartment and that she had noticed the smell of urine over the previous 2 weeks. She had no rash or bite wounds, and her conjunctiva appeared normal. Chest radiographs showed no signs of pneumonia.

Laboratory tests revealed leukocytosis (9.0×10^8 cells/L) and elevated C-reactive protein concentration (16.9 mg/dL). Urinalysis revealed hematuria but no other signs of pyelonephritis. Contrast-enhanced computed tomography of the trunk revealed no kidney abnormalities.

Because hematuria led us to suspect pyelonephritis, we initiated ceftriaxone treatment (2 g/d), after which, the patient's fever rapidly resolved. On day 2, diffuse purpura appeared on both of her legs but rapidly resolved. Blood culture revealed gram-negative bacilli (Figure, panel A). On the basis of her history of rat contact and blood culture results, we provisionally diagnosed rat-bite fever but continued administering ceftriaxone.

Bacterial culture of the patient's blood yielded small, smooth colonies on 5% sheep blood agar and 5% horse blood agar (both Nissui Pharmaceutical, <https://www.nissui-pharm.co.jp>) with addition of healthy serum (provided by one of the authors of this article) and incubation at 35°C under 7% carbon dioxide for 48 h (Figure, panel B). We evaluated the isolate by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry with the Bruker MALDI BioTyper software version 6.903 library database (Bruker Daltonik GmbH, <https://www.bruker.com>). *S. moniliformis* was a candidate,

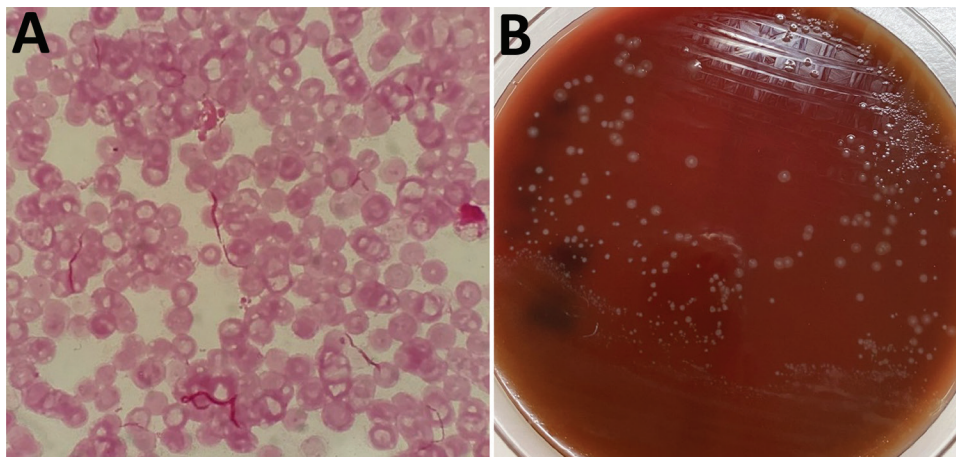


Figure. Results of testing for the causative agent of rat-bite fever in a 70-year-old woman in Japan. A) Gram-stained blood smear showing chain-shaped gram-negative bacilli; original magnification $\times 1,000$. B) Small, smooth colonies in culture of healthy human serum (provided by one of the authors of this article) on 5% sheep blood agar. Further testing identified the bacilli as *Streptobacillus notomytis*.

but its score of 1.49 was considered too low. We determined antimicrobial susceptibility patterns by using broth microdilution. The MIC of oxacillin was <0.12 µg/mL; ampicillin, <0.12 µg/mL; cefazolin, <0.5 µg/mL; imipenem, 0.25 µg/mL; vancomycin, <0.5 µg/mL; clindamycin, <0.06 µg/mL; and levofloxacin, <0.5 µg/mL. To further characterize the isolate, we performed 16S rRNA gene sequencing by using a universal primer pair: 5F (5'-TTGGAGAGTTTGATCCTGGCTC-3' and 1485B (5'-TACGGT-TACCTTGTTACGAC-3'). The sequence showed 100% identity (1,465/1,465 bp) with *S. notomytis* AHL_370-1 (GenBank accession no. KR001919). Therefore, on day 6, we changed treatment to intravenous ampicillin (2 g 4×/d). On day 7, treatment was changed to oral amoxicillin (500 mg 3×/d), and the patient was discharged. She completed a 14-day course of ceftriaxone, ampicillin, and amoxicillin and showed no further signs of bacteremia.

After the patient was discharged, we visited her home and collected rat feces samples. We saw a rat in her home but were unable to capture it. The rat feces were dry, and the target bacteria could not be cultured. Because the causative organism could not be identified by wide-range 16S rRNA PCR due to the large number of species of bacteria, we performed next-generation sequencing of DNA extracts as described previously (3), prepared library NEBNext Ultra II DNA Library Prep Kit (New England BioLabs, <https://www.neb.com>) according to the manufacturer's instructions, and analyzed sequence data by using MiSeq (Illumina, <https://www.illumina.com>). Results confirmed the presence of *Streptobacillus* spp. in the rat feces. We used the *S. notomytis* genome as a reference sequence (GenBank accession no. GCA_00161275.1) for comparison of sequence reads. We performed mapping with a 99% identity setting. Of the 844,070,6 genes read, 177 were mapped and possibly belong to *S. notomytis*.

Three cases of *S. notomytis* infection in humans have been reported; the pathogen was detected in the blood, skin pustules, and synovial fluid (4–6). In the case we report, *S. notomytis* was identified in the blood by using 16S rRNA sequencing. *S. moniliformis* and *S. notomytis* may also cause Haverhill fever, which is epidemic arthritic erythema transmitted by inhalation or ingestion of food and drink contaminated with rat feces and urine (7–10). Because the patient reported here had no history of rat bites, the most likely mode of transmission was aerosol inhalation of dried rat feces or water contamination at the patient's home.

S. moniliformis infection is usually treated with penicillin, cephalosporins, or tetracyclines (1). *S. notomytis* is also reportedly sensitive to these drugs, but its sensitivity to amoxicillin is reportedly intermediate (4,5). For this patient, ceftriaxone and ampicillin were prescribed. In summary, after conventional methods (culture and PCR) failed to identify the causative organism for this patient's infection, we detected *Streptobacillus* spp. in rat feces by using next-generation sequencing, thereby illustrating the value of this procedure for identifying causative organisms in the environment.

This work was supported by the Health, Labour, and Welfare Policy Research Grants, Research on Emerging and Re-emerging Infectious Diseases and Immunization (grant no. 20HA1006).

About the Author

Dr. Kawashima is a senior resident at the Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan. His primary research interest is the diagnosis of infectious diseases.

References

- Elliott SP. Rat bite fever and *Streptobacillus moniliformis*. Clin Microbiol Rev. 2007;20:13–22. <https://doi.org/10.1128/CMR.00016-06>
- Eisenberg T, Glaeser SP, Ewers C, Semmler T, Nicklas W, Rau J, et al. *Streptobacillus notomytis* sp. nov., isolated from a spinifex hopping mouse (*Notomys alexis* Thomas, 1922), and emended description of *Streptobacillus* Levaditi et al. 1925, Eisenberg et al. 2015 emend. Int J Syst Evol Microbiol. 2015;65:4823–9. <https://doi.org/10.1099/ijsem.0.000654>
- Nagata N, Tohya M, Fukuda S, Suda W, Nishijima S, Takeuchi F, et al. Effects of bowel preparation on the human gut microbiome and metabolome. Sci Rep. 2019;9:4042. <https://doi.org/10.1038/s41598-019-40182-9>
- Fukushima K, Yanagisawa N, Imaoka K, Kimura M, Imamura A. Rat-bite fever due to *Streptobacillus notomytis* isolated from a human specimen. J Infect Chemother. 2018;24:302–4. <https://doi.org/10.1016/j.jiac.2017.10.018>
- Ogawa Y, Kasahara K, Lee ST, Ito T, Hasegawa H, Hirose S, et al. Rat-bite fever in human with *Streptobacillus notomytis* infection, Japan. Emerg Infect Dis. 2018;24:1377–9. <https://doi.org/10.3201/eid2407.171580>
- Kusuda T, Ryoko A, Yoshishige M, Tanaka M, Yoshida A, Kikuchi K, et al. Erosive polyarthritides caused by sepsis due to a novel species of *Streptobacillus notomytis*. Mod Rheumatol Case Rep. 2020;4:95–8. <https://doi.org/10.1080/24725625.2019.1655246>
- Stehle P, Dubuis O, So A, Dudler J. Rat bite fever without fever. Ann Rheum Dis. 2003;62:894–6. <https://doi.org/10.1136/ard.62.9.894>
- Joshi RM, Al Sweih N, Bin Nakhi HA, Al Azemi M, Nair S. *Streptobacillus moniliformis* bacteremia in a child: case report. Med Princ Pract. 2010;19:409–11. <https://doi.org/10.1159/000316383>

9. Nei T, Sato A, Sonobe K, Miura Y, Takahashi K, Saito R. *Streptobacillus moniliformis* bacteremia in a rheumatoid arthritis patient without a rat bite: a case report. *BMC Res Notes*. 2015;8:694. <https://doi.org/10.1186/s13104-015-1642-6>
10. Onodera H, Uekita H, Watanabe T, Taira K, Watanabe C, Saito H, et al. Rat-bite fever due to *Streptobacillus moniliformis* in a patient without bite history: an unexpected cause of consciousness disturbance. *Jpn J Infect Dis*. 2020; 73:85–7. <https://doi.org/10.7883/yoken.JJID.2019.271>

Address for correspondence: Satoshi Kutsuna, Disease Control and Prevention Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo, 162-8655, Japan; email: skutsuna@hosp.ncgm.go.jp

Autochthonous *Leishmania infantum* in Dogs, Zambia, 2021

David Squarre,¹ Herman M. Chambaro,¹ Kyoko Hayashida,¹ Lavel C. Moonga, Yongjin Qiu, Yasuyuki Goto, Elizabeth Oparaocha, Chisoni Mumba, Walter Muleya, Patricia Bwalya, Joseph Chizimu, Mwelwa Chembensofu, Edgar Simulundu, Wizaso Mwasinga, Nelly Banda, Racheal Mwenda, Junya Yamagishi, King S. Nalubamba, Fredrick Banda, Musso Munyeme, Hirofumi Sawa, Paul Fandamu

Authors affiliations: University of Edinburgh, Edinburgh, Scotland, UK (D. Squarre); Ministry of Fisheries and Livestock, Lusaka, Zambia (D. Squarre, H.M. Chambaro, P. Bwalya, F. Banda, P. Fandamu); Hokkaido University, Sapporo, Japan (H.M. Chambaro, K. Hayashida, L.C. Moonga, Y. Qiu, J. Chizimu, J. Yamagishi, H. Sawa); Central Veterinary Research Institute, Lusaka (H.M. Chambaro, F. Banda); University of Tokyo, Tokyo, Japan (Y. Goto); Showgrounds Veterinary Clinic, Lusaka (E. Oparaocha); University of Zambia, Lusaka (C. Mumba, W. Muleya, M. Chembensofu, E. Simulundu, W. Mwasinga, N. Banda, R. Mwenda, K.S. Nalubamba, M. Munyeme); Macha Research Trust, Macha, Zambia (E. Simulundu); Global Virus Network, Baltimore, Maryland, USA (H. Sawa)

DOI: <https://doi.org/10.3201/eid2804.212378>

¹These authors contributed equally to this article

Leishmaniasis are neglected tropical diseases of humans and animals. We detected *Leishmania infantum* in 3 mixed-breed dogs in Zambia that had no travel history outside the country. Our findings suggest presence of and probable emergence of leishmaniasis in Zambia, indicating the need for physicians and veterinarians to consider the disease during diagnosis.

Leishmaniasis, a neglected tropical disease of humans and animals, is estimated to affect ≤ 1 million persons annually (<https://www.who.int/health-topics/leishmania>). The disease is caused by intracellular protozoan parasites of the genus *Leishmania* (Trypanosomatida: Trypanosomatidae), which are vectored by female sand flies of the genera *Phlebotomus* in the Old World and *Lutzomyia* in the New World (1). Although leishmaniasis is endemic to several resource-poor countries in eastern, western, and northern Africa, there is a dearth of information on the epidemiology of the disease in southern Africa, largely caused by weak surveillance systems (1,2).

In Zambia, human visceral leishmaniasis was reported in 1973 in the Eastern Province (3) and subsequently in 1976 in the same area (4). In 1994, a case of canine visceral leishmaniasis was reported in a dog in Lusaka Province (5). We report detection of canine leishmaniasis caused by *Leishmania infantum*, suggesting possible reemergence or reintroduction of the disease in Zambia.

The study was approved by the Department of Veterinary Services, Government of the Republic of Zambia. In June 2021, two female mixed-breed shelter dogs (case 1 and case 2) rescued in Southern Province of Zambia during 2020 were brought to a veterinary clinic in Lusaka. These 2 dogs had chronic weight loss, generalized alopecia, and ulcerative and exfoliative dermatitis (Figure, panel A). The dogs had been previously treated for tickborne and helminth infections but showed no improvement. Physical examination showed that the prescapular and popliteal lymph nodes were enlarged. Case 1 had onychogryphosis (Figure, panel A) and focal corneal opacity in the left eye (Figure, panel B).

Biochemistry profiles for both dogs showed increased levels of serum proteins (>93.3 g/L) and hyperglobulinemia (>74.9 g/L) and hypoalbuminemia (<14.7 g/L), which are common manifestations suggestive of canine leishmaniasis. Giemsa staining of fine-needle lymph node aspirate identified *Leishmania* spp. amastigotes (Figure, panel C).

We performed serologic analysis of *Leishmania* antibodies by using *L. donovani* soluble lysate antigen from cultured promastigotes and recombinant