

Prosthetic Valve Endocarditis Caused by *Streptobacillus moniliformis*: a Case of Rat Bite Fever[▽]

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We report a case of rat bite fever caused by *Streptobacillus moniliformis* in Taiwan. It manifested as prosthetic valve endocarditis, which was cured by cardiac valve replacement and antimicrobial therapy. The DNA sequence of the 16S rRNA gene of *S. moniliformis* was detected in valve specimens by PCR and nucleotide sequencing.

CASE REPORT

A 60-year-old female was admitted to a university hospital in Tainan in southern Taiwan with a 2-week history of intermittent fever. Symptoms began 1 week later, after a rodent bite over her right big toe in her house in early October 2006. Pus was noted initially, and the wound healed subsequently. Associated symptoms were general weakness and body weight loss. She had received mechanical valve replacement for the rheumatic mitral valve 17 years ago. She was regularly followed up in a cardiac surgical clinic and took coumadin and trichloremthiazide regularly.

On admission, her temperature was 38.1°C, her heart rate 82 beats/min, and her respiratory rate 18 breaths/min. Her blood pressure was 139/69 mm Hg. Physical examinations showed no skin lesions or joint inflammation. The heart sound of the mitral mechanical valve was clear, but a new grade 3/6 systolic murmur over the left lower sternum border radiating to the left apex was noted on cardiac auscultation. Laboratory studies revealed the following: leukocyte count, 15,100/mm³; neutrophil level, 94%; lymphocyte level, 4%; hemoglobin level, 8.2 g/dl; and platelet count, 134,000/mm³. Electrolyte levels and renal and liver functions were normal. The serum level of C-reactive protein was 162.9 mg/liter (the normal level is <8 mg/liter) and the erythrocyte sedimentation rate 14 mm/h (the normal level is <15 mm/h). Transesophageal echocardiography revealed a dehiscence of the mechanical mitral valve, with severe posterior eccentric mitral regurgitation, and a fluttering mass with a size of 0.8 cm located at the lateral mitral valve annulus. She received mitral valve replacement for valve dysfunction on the 7th hospital day and became afebrile after the operation. Endocarditis with vegetations was confirmed by pathological examinations.

Due to a history of penicillin allergy, empirical antibiotic therapy with parenteral levofloxacin at 500 mg daily was

started after admission, followed by treatment with parenteral ceftriaxone at 1 g every 12 h, gentamicin at 1 mg/kg of body weight every 8 h, and oral doxycycline at 100 mg every 12 h for culture-negative endocarditis. Three sets of blood cultures, one before and two after administration of antibiotics, were incubated with the BACTEC 9000 system (a commercial BACTEC culture bottle with sodium polyanetholsulfonate as an anticoagulant). All were sterile after incubation for at least 2 weeks.

The diagnosis of *Streptobacillus moniliformis* infection was made by 16S rRNA PCR assays. Primers 5'-AGAGTTTGATG GCTCAG-3' and 5'-GGAACGTATTCACCGTAGCA-3' were used to amplify the conserved 16S rRNA genes from the dissected cardiac tissue and vegetations in the removed mechanical valve (14), and identical 1.4-kb amplicons were obtained from both specimens. By comparison with sequences deposited in the GenBank database, the partial sequences (the region of positions 29 to 854) of two amplified fragments were 100% identical to that of the 16S rRNA gene of *S. moniliformis* isolate H2730 (accession number DQ325537) and 99.5% identical to the 16S rRNA gene of *S. moniliformis* ATCC 14647, the type strain (accession number Z35305). With the above microbiological information, antimicrobial therapy was shifted to treatment with parenteral ceftriaxone at 2 g daily plus oral doxycycline at 100 mg twice daily for 4 weeks. She recovered without sequels.

Rat bite fever (RBF) can be caused by *S. moniliformis* or *Spirillum minus*. Humans get this infection from the bite of infected rodents or ingestion of contaminated food or water (11). RBF is characterized by relapsing fever, arthralgia, and rash and causes severe metastatic infections (6). Among these complications, endocarditis is rare but is the most lethal form, occurring most often in persons with underlying valvular diseases (10). In total, 19 cases of RBF infective endocarditis have been documented so far (2, 9, 10). Here, we report a case of *S. moniliformis* infection resulting from a wild-rodent bite, which subsequently led to prosthetic valve endocarditis.

It has been well known that *S. moniliformis* accounted for the majority of RBF cases in the United States and Europe, while *S. minus* caused a significant number of cases of this

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disease in Asia (6). Although nasopharyngeal carriage of *S. moniliformis* is reported in 10% to 100% of healthy laboratory rats and 50% to 100% of wild rodents (1, 13), the exact prevalence of *S. moniliformis* infections among humans has not been clearly determined. Among countries in southeastern Asia, there was only one formally reported case of *S. moniliformis* infection in Thailand (5). Such a finding suggested a possible geographic extension of *S. moniliformis* to the Far East areas. *S. moniliformis* may be a pathogen transmitted between continents due to blooming global trade and increasing numbers of pet rodents. However, patients with *S. moniliformis* infections were not recognized in Taiwan. A further epidemiological survey among wild or domestic rodents on this island may be warranted.

Endocarditis is a rare but severe complication of *S. moniliformis* infections. In a review of 16 cases of endocarditis from 1915 to 1991 (10), most of the affected patients presented fevers and cardiac murmurs, and their rat bite histories were remarkable, as found in our case. However, embolic phenomena were not frequently found. Among the 16 reported patients, 10 died of RBF or associated complications, and those who received nonspecific antimicrobial therapy or inadequate penicillin dosages eventually died. Such a finding highlights the importance of appropriate diagnosis and antimicrobial therapy for *S. moniliformis* endocarditis.

Classically, diagnosis of RBF is based on bacterial cultures. However, this is difficult in routine practice, because *S. moniliformis* is a fastidious gram-negative bacillus that needs special media and environments for isolation (6). Sodium polyanethol sulfonate as an anticoagulant in commercial blood culture bottles limits the growth of *S. moniliformis* (8, 11). Laboratory personnel should be consulted before processing of specimens when *S. moniliformis* is suspected. Moreover, a Gram-stained smear of *S. moniliformis* on blood agar medium demonstrating pleomorphic branching gram-negative bacilli provides evidence for early diagnosis.

Because of difficulties in microbiological diagnosis of *S. moniliformis* infection, molecular techniques have been developed to identify this fastidious bacterium. A previous study reports the use of PCR-restriction fragment length polymorphism analysis with primers for 16S rRNA genes in the diagnosis and identification of *S. moniliformis* infection in humans and animals (4). Broad-range PCR amplification of parts of the 16S rRNA genes followed by sequencing has also been demonstrated to identify this organism (3, 7, 12). Herein, we used this method to identify *S. moniliformis* in valve tissue in the case of culture-negative prosthetic valve endocarditis. These PCR techniques offer a novel alternative tool for diagnosis, which is

especially important in critically ill patients and those for whom antimicrobial therapy has been started.

Antimicrobial therapy for patients with RBF should begin without delay. The recommended therapy for *S. moniliformis* endocarditis is 20 million units of aqueous penicillin daily for 4 weeks or 4.8 million units of procaine penicillin G intramuscularly for a strain susceptible to penicillin at 0.1 µg/ml, with or without streptomycin (6, 10, 13). Other drugs for RBF include tetracycline or streptomycin, for patients allergic to penicillin. Cephalosporin is also an alternative, but cross-allergy to penicillin should be taken into consideration (6). A 3-day course of oral penicillin at 2 g per day for postexposure prophylaxis has been advocated (13), although its clinical efficacy is unknown.

In summary, diagnosis and empirical treatment for RBF and related complications are critical, especially for persons with fevers after rat exposure. The molecular diagnostic tool may improve the diagnosis of this disease and further reduce the relevant mortality and morbidity.

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