Prosthetic Valve Endocarditis caused by *Streptobacillus moniliformis*:

A Case of Rat-Bite Fever

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Key words: rat bite, *Streptobacillus moniliformis*, prosthetic valve, endocarditis

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Abstract

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 16S rRNA of *S. moniliformis* was detected in valve specimens by polymerase chain reaction and nucleotide sequencing.
Introduction

Rat-bite fever (RBF) can be caused by *Streptobacillus moniliformis* or *Spirillum minus*. Human gets infections from the bite of infected rodents or ingestion of contaminated food or water (1). RBF is characterized by relapsing fever, arthralgia, and rash, and causes severe metastatic infections (2). Among these complications, endocarditis is rare, but the most lethal form, which most often occurs in persons with underlying valvular diseases (3). Total 19 cases of RBF infective endocarditis have been documented so far (3-5). Here, we report a case of *S. moniliformis* infection resulting from wild rodent bite, which subsequently leads to prosthetic valve endocarditis.
Case report

A 60-year-old female was admitted to a university hospital in Tainan in southern Taiwan, with a history of intermittent fever for two weeks. Symptoms began one week later after a rodent bite over 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 rheumatic mitral valve 17 years ago. She was regularly followed up in cardiac surgical clinic, and took coumadin and trichlormethiazide regularly.

On admission, temperature was 38.1℃, heart rate 82/min, and respiratory rate 18/min. Blood pressure 139/69 mmHg. Physical examinations showed no skin lesions or joint inflammation. The heart sound of mitral mechanical valve was clear, but a new grade 3/6, systolic murmur over left lower sternum border radiating to left apex was noted on cardiac auscultation. Laboratory studies revealed the followings: leukocyte count 15,100/mm$^3$, neutrophil 94%, lymphocyte 4%, hemoglobin 8.2 g/dl, and platelet 134,000/mm$^3$. Electrolytes, renal and liver functions were normal. Serum level of C-reactive protein (CRP) was 162.9 mg/L (normal: < 8 mg/L), and erythrocyte sedimentation rate (ESR) 14 mm/hr (normal: < 15 mm/hr).

Transesophageal echocardiography revealed dehiscence of mechanical mitral valve
with severe posterior eccentric mitral regurgitation, and a fluttering mass located at lateral mitral valve annulus, in a size of 0.8 cm. She received mitral valve replacement for valve dysfunction on the 7th hospital day, and became afebrile after operation. Endocarditis with vegetations was confirmed by pathologic examinations.

With a history of penicillin allergy, empirical antibiotic therapy with parenteral levofloxacin 500 mg daily was started after admission, and then parenteral ceftriaxone 1 g q12h and gentamicin 1 mg/kg q8h, and oral doxycycline 100 mg q12h for culture-negative endocarditis. Three sets of blood cultures (commercial BACTEC™ culture bottle with sodium polyanetholsulfonate as anticoagulant), one before and two after administration of antibiotics, were incubated with BACTEC 9000 system. All were sterile after incubation for at least two weeks.

The diagnosis of *S. moniliformis* infection was made by the 16S rRNA polymerase chain reaction (PCR) assays. Primers 5’-AGAGTTTGATGGCTCAG-3’ and 5’-GGAACGTATTCACCGTAGCA-3’ were used to amplify 16S rRNA conserved genes from the dissected cardiac tissue and vegetations in the removed mechanical valve (6), and an identical 1.4-kb amplicon were obtained from both specimens. By comparison with sequences deposited in the GenBank database, the partial sequences (region of 29 to 854) of two amplified fragments were 100% identical to the 16S rRNA gene of *S. moniliformis* isolate H2730 (accession number
DQ325537), followed by 99.5% identical to 16sRNA gene of *S. moniliformis* ATCC 14647, type strain (accession number Z35305). With the above microbiological information, antimicrobial therapy was shifted to parenteral ceftriaxone 2g daily plus oral doxycycline 100 mg bid for four weeks. She recovered without sequels.
Discussion

It has been well known that *S. moniliformis* accounted for the majority of RBF in the United States and Europe, while *S. minus* caused a significant portion of this disease in Asia (2). Although nasopharyngeal carriage of *S. moniliformis* is reported in 10% to 100% of healthy laboratory rats and 50% to 100% of wild rodents (7, 8), the exact prevalence of *S. moniliformis* infections among human has not been clearly understood. Among countries in southeastern Asia, there was only one formally reported case of *S. moniliformis* infection in Thailand (9). Such a finding suggested possible geographic extension of *S. moniliformis* to the Far East areas. *S. moniliformis* may be a pathogen transmitting between continents due to blooming global trade and increasing lovers of pet-rodents. However, patients with *S. moniliformis* infections were not recognized in Taiwan. A further epidemiological survey among wild or domestic rodents in 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 (3), most of the affected patients presented fever and cardiac murmurs, and their rat-bite history was remarkable, as found in our case. However, embolic phenomena were not frequent findings. Among 16 reported cases, ten died of RBF or associated complications, and those who received non-specific antimicrobial therapy, or inadequate penicillin
dosages, were eventually fatal. Such a finding highlights the importance of appropriate diagnosis and antimicrobial therapy for *S. moniliformis* endocarditis.

Classically, the diagnosis of RBF is based on bacterial cultures. However, this is difficult in routine practice, because *S. moniliformis* is a fastidious gram-negative bacillus, which needs special media and environments for isolation (2). Sodium polyanethol sulfonate as anticoagulant in commercial blood culture bottles limits the growth of *S. moniliformis* (1, 10). Laboratory personnel should be consulted before processing of specimens if *S. moniliformis* is suspected. Moreover, Gram-stained smear of *S. moniliformis* on blood agar medium demonstrating pleomorphic branching gram-negative bacilli provides an 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 the 16S rRNA genes in the detection and identification of *S. moniliformis* infection in human and animals (11). Broad range PCR amplification of a part of the 16S rRNA genes followed by sequencing has also been demonstrated to identify this organism (12-14). 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 of diagnosis, which
is especially important in critical patients and those in which antimicrobial therapy has been started.

Antimicrobial therapy for patients with rat-bite and fever should begin without delay. 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 strain susceptible to penicillin 0.1 µg/ml, combined with or without streptomycin (2, 3, 8). Other drugs for RBF include a tetracycline or streptomycin, if the patient is allergic to penicillin. A cephalosporin is also an alternative, but cross-allergy to penicillin should be taken into consideration (2). A 3-day course of oral penicillin 2 g per day for post-exposure prophylaxis has been advocated (8), although the clinical efficacy is unknown.

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

**Financial support.** No.

**Potential conflicts of interest.** All authors: no conflict.
References


