

CASE REPORT

Infective Endocarditis after Multiple Rat Bites in a Patient with Diabetic Neuropathy: If not *Streptobacillus moniliformis*, What Else Should be Suspected?

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Abstract

Painless rat bites in patients with diabetic neuropathy are very rare occurrence and may result in foot ulcers, amputations, or rat bite fever. Infective endocarditis complicating rat bites are extremely rare and almost exclusively a complication of rat bite fever caused by *Streptobacillus moniliformis* (a common microbial flora of the rat mouth). To the best of our knowledge, this is the first report of *Staphylococcus aureus* (another common flora of rat teeth) native valve endocarditis complicating rat bite.

Key words: Diabetic neuropathy, Rat bite, Infective endocarditis, *Staphylococcus aureus*, *Streptobacillus moniliformis*

Introduction

Diabetic neuropathy (DNP) denotes a spectrum of diverse clinical manifestations that affect different parts of the nervous system. DNP can manifest in different ways such as sensory neuropathies, focal and multifocal neuropathies and autonomic neuropathies. Chronic distal symmetric sensorimotor polyneuropathy is the most common form of DNP and can manifest with chronic sensory symptoms in the feet and legs in 50% of patients or can be asymptomatic in the remaining 50% (1). It has been shown that somatic sensorimotor neuropathy is an independent predictor of all cause mortality and diabetes-related mortality in patients with type 2 diabetes (T2DM) (2). Various morbidities can complicate sensorimotor neuropathy such as neuropathic foot ulcers, osteomyelitis, Charcot joints and increased risk of amputation. Common external injuries that may trigger these complications include walking barefoot and stepping on a sharp object, or simply wearing ill-fitted shoes (3,4).

Rat bites typically happen in children less than 5 years of age with face or arms being the most common sites for bite (5). Although rare, rat bites in diabetic patients with sensory neuropathy are increasingly recognized with

various complications such as ulcers, amputations, rat bite fever and death, been reported in literature (6).

Infective endocarditis complicating rat bites is extremely rare and almost exclusively a complication of rat bite fever caused by *Streptobacillus moniliformis* (a common microbial flora of rat mouth). It typically occurs in patients with prior valvular abnormalities (7,8). We here report a case infective endocarditis of native valve complicating rat bite with unique features.

Case report

A 45-year old man presented to our hospital with fever and hypotension three days after multiple rat bites in his feet that resulted in partial amputation of the left second toe (Figures 1a and 1b). The patient described the incident as absolutely painless and he awakened up in morning to find multiple rats eating his feet with blood oozing from the wounds. His wounds were cleaned and dressed in a local clinic on the same day. Three days later, he was admitted for high-grade fever and hypotension (85/60).

Physical examination revealed multiple bite marks in his feet with partial amputation of the left second toe. He had enlarged and tender left inguinal lymph nodes.



Figure 1a



Figure 1b

Figures 1a and 1b. Multiple rat bites in the feet resulting in partial amputation of the left second toe

Lower limb examination revealed absent pain, fine touch and vibration sensations with loss of ankle reflexes. Cardiovascular and other system examination was unremarkable.

Laboratory investigations revealed neutrophilic leukocytosis of $15.3 \times 10^3/\text{ul}$ with anemia (Hb 9.8 g/dl) and thrombocytopenia ($128 \times 10^3/\text{ul}$). Serum lactic acid was high (2.89 mmol/l) with evidence of disseminated intravascular coagulation (prolonged INR and APTT). Five sets of blood culture (including aerobic and anaerobic) grew Methicillin sensitive *Staphylococcus aureus* (MSSA). His glycemic control was poor (Hb A1C 8.8%). Transesophageal echocardiography revealed a vegetation of 0.9 x 0.8 cm attached to the mitral valve and other smaller vegetations attached to the aortic cusps. 2 grams of intravenous Cloxacillin every 4 hours were started after blood culture result. On the fourth day post admission, he developed sudden loss of vision in the right eye. Ophthalmologic evaluation revealed right branch retinal artery occlusion. Magnetic resonance imaging and angiography (MRI and MRA) of the brain demonstrated a right occipital infarct with normal blood vessels (Figure 2). The patient condition improved significantly on antibiotics. Fever subsided and repeated blood cultures after 10 days from initiating cloxacillin

did not grow any organism. Valvular vegetations disappeared on repeated echocardiography after 3 weeks of treatment. Cloxacillin was continued for 6 weeks and he was discharged home in a good condition.

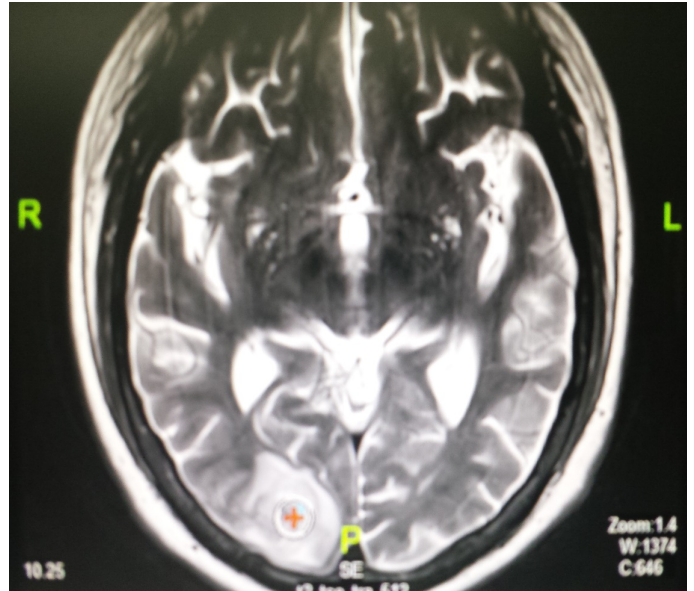


Figure 2. MRI of the brain showing right occipital infarct.

Discussion

Rat bites commonly occur while the victim is asleep at night. They can result in serious complications such as death, tetanus, rabies, leptospirosis, rat-bite fever and plague (9,10). Factors associated with increased incidence of rat bites are urban deterioration, poverty, unemployment and rat infestations. Children less than 5 years of age and infants are typically prone to rat bites possibly because they lack the ability to respond to pain and tend to sleep more often than adults (5). In adults, diabetic patients with peripheral neuropathy are at increased risk of rodent bite injuries particularly in areas with large rodent populations. In a study of 34 patients with type 2 diabetes who had rodent bites, all these patients turned to have diabetic neuropathy and all bites occurred during sleep. Patients who delayed seeking medical attention were significantly more likely to develop gangrene. Seventeen patients underwent minor or major amputation and four patients died. Complete healing occurred in 30 (88%) patients (6).

Infective endocarditis after rat bite is extremely rare condition. Almost all reported cases of infective endocarditis after rat bite happened as complication of “rat bite fever disease” caused by the Gram negative bacilli “*Streptobacillus moniliformis*” (a commensal flora of the rat upper respiratory tract). The disease manifests with systemic illness characterized by relapsing fever, rash, migratory polyarthralgia and can be complicated by hepatitis, nephritis, systemic vasculitis and rarely infective endocarditis. The later carries the highest mortality if untreated (11). Majority of cases of infective endocarditis due to *Streptobacillus moniliformis* had underlying valvular abnormalitis. Native valve endocarditis is extremely unusual (7,8). In a recent review of 23 cases of infective endocarditis caused by *Streptobacillus moniliformis*, the clinical presentation was nonspecific in majority of cases with fever, rashes, polyarthrits and murmur. Confirmation of the diagnosis in these cases was achieved by history of rat bite, positive echocardiography for vegetations, positive blood culture for *Streptobacillus moniliformis* or a positive polymerase chain reaction (8). *Staphylococcus aureus*

infective endocarditis is a common cause of endocarditis in patients with risk factors such as prosthetic heart valves, predisposing cardiac abnormalities, intravenous drug use, intravenous catheter infection and bacteremia of unclear origin. In comparison with community acquired methicillin sensitive *Staphylococcus aureus* (CA-MSSA) bacteremia, community acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) bacteremia is more likely to be associated with superficial skin and soft-tissue infections (12,13). Embolic stroke (such as in this patient), can complicate up to 45% of *Staphylococcus* endocarditis cases (14). The diagnosis of infective endocarditis is generally based on clinical, microbiologic and echocardiographic findings. The Duke criteria are the reference criteria for diagnosis with sensitivity and specificity of more than 80% (15,16). Our patient had CA-MSSA bacteremia and definite infective endocarditis (based on Duke Criteria) after multiple painless rat bites attributed to his diabetic neuropathy. It is well known that microbiological diagnosis of *Streptobacillus moniliformis* can be difficult in certain laboratories due to the fastidious nature and inhibition of its growth by sodium polyanethol sulfonate (an anticoagulant commonly added to aerobic blood culture bottles). Anaerobic bottles, Trypticase soy agar or resin bead culture system may be used to demonstrate its growth (11). Blood cultures performed at Hamad General Hospital laboratory (accredited by the College of American Pathologists) follow standard operative procedure in a BACTEC aerobic and anaerobic bottles. All the five blood culture sets sent over seven days in this case included anaerobic bottles with the possible diagnosis of rat bite fever stated clearly on the request. This makes the possibility of missing fastidious organism such as *Streptobacillus moniliformis* in our laboratory very slim (11). Although it has been demonstrated in previous studies that *Staphylococcus aureus* is the second most common normal flora of rat teeth after bacillus species (17), an important limitation of this case report is that it remains unclear whether the source of Staphylococcal bacteremia in this patient was the rat teeth or the patient's skin (with rat bites forming a portal of entry for these organisms to the blood). Despite the complicated course of our patient's illness (severe sepsis and systemic embolization), he was treated successfully with intravenous antibiotics and fluid resuscitation and discharged home in a good condition.

To the best of our knowledge, *Staphylococcus aureus* infective endocarditis after rat bite has not been previously reported. We suggest that, in addition to *Streptobacillus moniliformis*, *Staphylococcus aureus* should be an etiologic possibility in cases of infective endocarditis associated with rat bites.

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