CASE REPORT

RAT-BITE FEVER CAUSED BY *STREPTOBACILLUS MONILIFORMIS*

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Rat-bite fever, a rare disease, is an acute febrile illness acquired from the bite of a rat, mouse, or other rodent. The causative agent can be either *Streptobacillus moniliformis* or *Spirillum minus* (Robertson, 1924). The former was reported to cause Haverhill fever (erythema arthriticum epidemicum) (Parker and Hudson, 1926), while the latter causes Sodoku.

In Thailand, rat-bite fever was first reported in 1938. All the three cases were affected by *Spirillum minus* (Vardhanabhuti, 1938). To our knowledge, this is the first report on the disease affected by *Streptobacillus moniliformis* in this country.

A 24 year old Thai male laborer from Bangkok, complained of fever, multiple joint pain and skin rash for 10 days. He was bitten on the right foot by a rat while he was entering a store room. Four days later, he developed diarrhea which was successfully self-treated with an antidiarrheal drug. The next day, he began to have high fever, malaise and headache which was temporarily relieved by dipyrone. A non-pruritic generalized erythematous rash accentuated on palms and soles was noted on the day after. Simultaneously, he developed pain over shoulder, knee, ankle and wrist joints. The patient was treated by a local hospital doctor without any improvement. Four days later, the patient came to Siriraj Hospital and was treated for drug allergy in the Outpatient Department. His symptoms of fever, malaise, joint pain and skin rash continued. He was admitted to the hospital 6 days later.

Physical examination revealed a temperature of 38.8°C, pulse rate 100/minute, respiratory rate 20/minute and blood pressure 130/90 mmHg. The patient was conscious, not pale, nor icteric. Erythematous macules were found over abdomen, arms and legs, more accentuate on palms and soles. A pustule of 3 mm in diameter on an erythematous base was also noted at the right elbow. The cardiovascular, respiratory and nervous system were unremarkable. Inflammation of both shoulders, elbows, wrists knees and ankle joints, including the left 1st metacarpophalangeal joint, the right 2nd metacarpophalangeal and the right 2nd proximal interphalangeal joints was detected. The differential diagnosis was rat-bite fever, septic arthritis or enteropathy associated arthritis.

Laboratory investigations revealed hematocrit of 42%, white cells 29.5×10^9/l, neutrophils 92%, lymphocytes 4%, monocytes 4%, normal red cell morphology and normal platelet count. Urinalysis and stool examination were normal. Examination of pus from the right elbow was negative for bacteria. Blood culture and tapping of the right knee joint were carried out. Three ml of cloudy yellowish joint fluid were obtained. It contained white cells 5.7×10^9/l, neutrophils 85%, lymphocytes 15%; no bacteria were found. The patient was then given penicillin G sodium 2.5 million units every 4 hours intravenously.

After penicillin G sodium was administered, fever disappeared in 24 hours and polyarthritis subsided in a week with a dramatic improvement of his general condition. Ten days after admission, the results of blood and joint fluid culture were obtained. All six consecutive blood cultures taken on admission yielded small, pleomorphic gram negative rods subsequently identified as *Streptobacillus moniliformis*. The patient was given penicillin G sodium for 2 weeks and discharged from the hospital. He remained well after a follow up period of one month.

The following technique was employed in our diagnostic bacteriology laboratory for the isolation of microorganism from blood. Five ml samples of blood were inoculated into hemoculture bottles containing 50 ml brain heart infusion broth, incubated at 37°C and observed daily for evidence of growth. After 48 hours incubation the bacteriologic growth characteristics in fluid medium of microorganisms isolated from this patient exhibited typical features of *Streptobacillus moniliformis*. It produced

fluffball-like, greyish-white granules on the surface of sedimented red blood cells and the side of the glass bottles. No turbidity or surface growth of the broth were observed. The fluffball-like colonies were removed by pipette and transferred to slide and blood agar for microscopic examination and aerobic culture respectively. Characteristic microscopic morphology revealed very striking pleomorphic, small, 0.4-0.6 μm wide by 1-5 μm long, non-branching, non-acid fast, gram negative rods with rounded or pointed ends occurring singly and as irregular chains and very long looped or curved filaments up to 150 μm in length, growing in inter woven masses. Some filaments showed spherical, oval, fusiform or club-shaped swellings occurring terminally, subterminally, or in some other part along the length of the filament. These candida-like swellings were 2-5 times the diameter of the filament and may project from one side only (Fig 1).

The colonines on blood agar which appeared in 2 days were small, 0.2-0.3 mm in diameter, circular, convex, almost water-clear with smooth glistening surface, entire edge, butyrous consistency easily emulsifiable and no increase in size on further incubation.

The identification of *Streptobacillus moniliformis* was based on the following biochemical tests. The organism was non-motile and oxidase and catalase tests were negative. Nitrate was not reduced to nitrite. Lysine decarboxylase activity was absent and urease was not produced. Glucose, salicin and maltose were utilized if cystine trypticase agar containing 1% carbohydrate and 1 drop of serum per tube was used (Rogosa, 1985).

The antimicrobial susceptibility test was performed by the paper disk method. The organisms were susceptible to all antibiotics except co-trimoxazole.

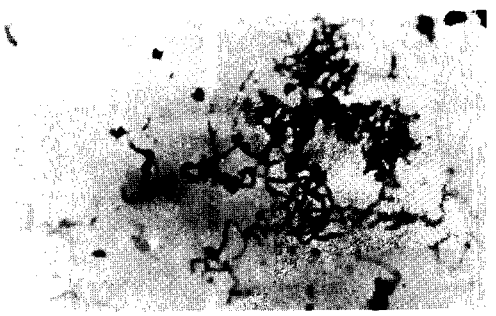

Fig 1–Many irregular filaments of *Streptobacillus moniliformis* with yeastlike swelling obtained from culture.

Rat-bite fever is produced by either *Streptobacillus moniliformis* or *Spirillum minus*. Although these organisms are found world wide, *S. moniliformis* is responsible for most cases of rat-bite fever (Haverhill fever). In Thailand, this is the first rat-bite fever case reported which was caused by *S. moniliformis*. A previous report of 3 cases of rat-bite fever in Thailand showed the etiologic agent was *Spirillum minus* (Vardhanabhuti, 1938). *Streptobacillus moniliformis* naturally inhabits the rodent's respiratory tract but is rarely transmitted to humans. Although the disease is usually transmitted by the bite of the rat or mouse, there may be no such history. An epidemic in Haverhill, Massachusetts, in 1916 was traced to milk (Parker and Hudson, 1926), contaminated with rat-waste products. Another outbreak in Britain (Shanson *et al,* 1983) was also believed to be related to the ingestion of raw milk and cases were reported in laboratory animal handlers (Anderson *et al,* 1983; Hamberger and Knowles, 1953).

The present patient had many typical symptoms of acute rat-bite fever from *S. moniliformis* including the sudden onset of malaise, high fever, headache with progression of polyarthralgia, arthritis and non-pruritic generalised erythematous rash accentuated on palms and soles (Table 1). Diagnosis of a *S. moniliformis* infection can be difficult from both a clinical and laboratory standpoint. First, *S. moniliformis* infection can mimic other systemic infections or disorders. As in our patient, the major manifestation is arthritis, confusion with gonococcal arthritis, rheumatoid arthritis and other non-infection can be made. Presentation with polyarthropathies, fever and rash can mimic systemic lupus erythematosus, drug reactions, viral infections, rickettsial infections, secondary syphilis and disseminated gonococcal infection. Second, atypical presentations such as endocarditis (Mc Cormack *et al,* 1967), pericarditis (Carbeck *et al,* 1967), soft tissue abscess (McBrown and Nunemaker, 1942), brain abscess (Dijkmans *et al,* 1984), and amnionitis (Faro *et al,* 1980) had been reported. Third, laboratory features are nonspecific. Peripheral white blood cell count may range from normal to greater than 30,000/mm^3. One quarter of patients have a biological false positive reaction for syphilis. However, the diagnosis of rat-bite fever in our patient was not difficult because of the history of being bitten by a rat and a typical manifestations of rat-bite fever as described.

Table 1

A relatively distinct syndrome of rat-bite fever caused by *Streptobacillus moniliformis* or *Spirillum minus* (from Gunning, 1976).

	S. moniliformis	*S. minus*
Mode of transmission	Rat bite or ingestion	Rat bite
Bite wound	Rapidly healing	Chancre-like lesion develops
Regional signs	Mild lymphadenitis	Prominent lymphadenitis with lymphangitis
Fever-Character	Irregularly relapsing	Regularly relapsing
Onset	2 to 3 days	14 days
Arthritis	Common	Rare
Rash-Character	Morbilliform to purpuric	Macular, often confluent
% affected	75%	50%
False-positive VDRL	25%	50%
Untreated mortality	12.7%	6.5%

From a microbiologic standpoint, difficulties exist in both isolation and identification of *S. moniliformis*. The microbiologic diagnosis of *S. moniliformis* is usually first suggested by its morphology. The organism is a non-encapsulated, non-motile, non-acidfast, highly pleomorphic, gram-negative bacillus. *S. moniliformis* can be isolated only on certain microbiologic culture media. Growth of this organism requires media supplemented with either blood, serum or ascitic fluid and its generally takes two to six days for evidences of growth (McBrown and Nunemaker, 1942; Savage, 1984). In our patient, six consecutive blood cultures were positive for the microorganism after 48 hours exhibited features of *S. moniliformis*. It produced fluffball-like, greyish-white granules on the surface of sedimented red blood cells and the side of the glass bottles.

In untreated *S. moniliformis* infection, up to 10 percent of patients die, usually from endocarditis (Roughgarden, 1965). Penicillin is the drug of choice for treatment (Roughgarden, 1965). In uncomplicated cases, oral penicillin or 600,000 units of intravenous penicillin G sodium may be given every six hours for 10-14 days. Tetracycline is the best alternative in penicillin allergic patients. Endocarditis requires treatment with 20 million units of penicillin G sodium per day for four to six weeks.

In our patient, acute polyarthritis developed by *S. moniliformis* (rat-bite fever) can mimic disseminated gonococcal infection. This infection should be included in the differential diagnosis of a wide variety of clinical syndromes mentioned especially among farmers, laboratory workers, and urban residents exposed to rats. Cooperation between the clinician and microbiology laboratory is essential in making the diagnosis of this uncommon but readily treatable condition.

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