

Murine Typhus with Pneumonitis and Pleuropericarditis : A Case Report

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Abstract

Murine (endemic) typhus is a zoonotic disease with worldwide distribution. We report a case of middle-aged female who presented with persistent fever with chills, severe headache, and myalgia. The diagnosis of murine typhus is based on clinical suspicion and confirmatory serology. The purpose of this report is to review the epidemiologic and clinical features, with particular reference to Taiwan.

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Key Words : Murine typhus, Endemic, Pneumonitis, Pleuropericarditis

Introduction

Murine typhus was identified in 1926 as a distinct clinical and epidemiologic entity among the typhus fevers. In 1931, it was recognized as a worldwide zoonosis carried by rats and spread by fleas ¹. It is prevalent in temperate and subtropical seaboard regions, where rat reservoirs (*Rattus* spp.) and the flea vector (*Xenopsylla cheopis*) are found. The disease is transmitted by inoculation of infected flea feces into the area of a pruritic flea- bite. Cases are recognized year round, but are particularly common during the summer and early fall ¹. The etiologic agent of murine typhus, *Rickettsia typhi*, is an obligate intracellular bacterium that infects endothelial cells in mammalian hosts and midgut epithelial cells in fleas ². A new rickettsial agent, *Rickettsia felis*, has been recognized as sharing some antigenic genetic components with *R. typhi*, and has been identified as in association with cat fleas and opossums ³. Because of lack of specificity of clinical findings, it is difficult to be diagnosed.

Case Report

A previously healthy 42 year-old female was admitted on 14 August, 2003, complaining of fever for one week. Her temperature had varied between 38°C and 39°C, accompanied with chills, headache, myalgia and lower abdominal pain. There was

no cough, sore throat, nasal discharge, or diarrhea. She was at first admitted to a regional hospital two days earlier, but her symptoms did not improve and she was transferred to our hospital. She was a housewife living in southern Taiwan. She denied a history of foreign travel or any outdoor activity in the previous 2 weeks. Her family members were free of similar symptoms. She stated she had contact with domestic rats in her home.

On admission, her temperature was 36.7°C, pulse 84 per minute, respiratory rate 20 per minute, and blood pressure 110/70 mmHg. She was alert. Her sclerae and conjunctivae were normal and her neck was supple. No cervical lymph nodes were palpable. The respiratory and cardiovascular examinations were normal. The abdomen was soft; there was mild tenderness in the lower abdomen but no rebound tenderness. There was no skin rash. Her initial laboratory data showed a hemoglobin of 10.1 gm/dl, white blood cell count 2600/cu mm (4000-10000/cu mm), neutrophils 74% (55-75%), lymphocytes 17% (20-40%), platelets 61000/cu mm (140000-450000/cu mm), serum aspartate transferase 375 U/L (5-35 U/L), lactate dehydrogenase 536U/L (90-200U/L), creatinine kinase 29 U/L (25-175 U/L), blood urea nitrogen 6 mg/dl (5-22 mg/dl), creatinine 0.7 mg/dl (0.5-1.3 mg/dl), albumin 2.6 gm/dl (3.5-5.0 gm/dl), triglycerides 286 mg/dl (35-165 mg/dl), sodium 135 meq/L (135-147 meq/L), and potassium 3.9 meq/L (3.5-5.3 meq/L). The chest x-ray was normal, as were abdominal and renal sonography. She was initially treated with ceftriaxone and gentamicin, but the fever persisted for 3 days with increasing headache and myalgia. A throat swab for SARS-associated-coronavirus PCR was negative. A Widal test, and Mycoplasma pneumoniae antibodies were negative. At this point, a rickettsial infection was considered. Blood was drawn for serology and parenteral minocycline was added to her other antibiotics on hospital day 3. Because of the persistent severe headache, a lumbar puncture was recommended but the patient refused. Computerized tomography of the brain was normal. A Gallium 67 inflammatory scan revealed mild splenomegaly. On the fifth hospital day, she experienced severe shortness of breath and precordial chest pain. Other than showing sinus tachycardia, an EKG was normal, as were cardiac enzymes. A chest x-ray showed cardiomegaly, a right lower lung field infiltrate, and bilateral pleural effusions [Fig.1]. A minimal pericardial effusion was present on echocardiography [Fig.2]. One day later, the fever subsided but the chest discomfort persisted. No microorganisms were isolated from her urine and blood cultures. A repeat EKG again showed sinus tachycardia. Thyroid function tests were within normal limits. On day 12 of hospital stay, followed up chest x-ray revealed resolving of pleural effusion [Fig.3]. The initial serology test was negative, and second time was performed on day 14. At that time, the indirect immunofluorescence assay (IFA) for murine

typhus antibody was reported with an IgM titer of 1:80 and a four-fold rise in IgG titer. She was discharged after 16 days of hospitalization, still with some chest discomfort and palpitation after discharge.

Discussion

Murine typhus is an febrile illness that should be considered in the differential diagnosis of obscure fever \geq 1 week⁴. It is endemic in many parts of the world, including North and South America, Southeast Asia, Africa, Australia, and some southern European countries^{5,6}. Murine typhus is endemic in Taiwan, and increasingly recognized. It has been a reportable disease since 1983⁷.

In 2002, 7 cases of murine typhus were reported in patients residing in southern Taiwan. Animal contact history was a significant factor⁷. The patient we have described lived in a suburban area of southern Taiwan and had known exposure to rats. She also had the most common clinical symptoms of fever, chills, headache, and myalgia. Her laboratory abnormalities of pancytopenia, deranged aminotransferase, elevated lactate dehydrogenase, and hypoalbuminemia also matched those of other reports^{5,8,9}. The peripheral blood pancytopenia with hypertriglyceridemia may be a result of hemophagocytosis, which also occurs in Q fever^{7,10}. The important diagnostic clue of a skin rash was not present in this case^{4,5}. Relative bradycardia was noted in previous study⁷, but our patient had sustained sinus tachycardia even after her fever subsided.

The clinical course of murine typhus is usually uncomplicated². In our patient, her course was complicated by the development of interstitial pneumonitis, pleuritis, and pericarditis, which are rarely found in murine typhus. Wittel et al reported 104 cases of murine typhus over 17 years, 9 patients (8.6%) developed organ complications. There were 6 cases of pneumonitis, with pleuropericarditis and pulmonary embolism in one⁵. Lee et al reported 7 cases of murine typhus, and one patient with old age, underlying valvular heart disease complicated with acute renal failure, hepatitis, disseminated intravascular coagulation, pneumonitis, and respiratory failure⁷. In fatal cases, interstitial pneumonitis, interstitial nephritis, interstitial myocarditis, meningitis, or portal triaditis may be present¹¹. There are few accurate descriptions of histopathology of murine typhus. Lymphohistiocytic vasculitis may be seen in any organ. As vascular injuries accumulate, there is substantial loss of intravascular volume, albumin, and electrolytes. If hypoperfusion ensues, the result may be adult respiratory distress syndrome, respiratory or renal failure, central nervous system abnormalities, or multiorgan failure¹¹. Increasing age, prolonged interval before specific therapy, indexes of renal function abnormalities, and hypoalbuminemia correlated with severe disease¹². Some deaths are reported, and the case fatality rate ranges between 1 and 4%¹³.

The diagnostic test for *R. typhi* is IFA to typhus group antigens. Confirmation of the diagnosis is seen with a fourfold antibody titer rise between acute and convalescent serum samples to a titer of $\geq 1:64$. A probable diagnosis can be made within the first week of illness if a single IgM or IgG titre is $\geq 1:128$. The IFA test cannot, however, differentiate between *R. typhi* and *R. felis*. Polymerase chain reaction is necessary to do that 9,11-16.

Early and specific antirickettsial therapy is indicated to avoid severe or potentially fatal disease, so treatment should not be withheld while awaiting laboratory confirmation. The preferred treatment is a tetracycline, such as doxycycline.

Tetracycline, doxycycline, minocycline, and chloramphenicol are all considered effective. Our patient became afebrile after 3 days of treatment with minocycline. In other series, defervescence has been noted within 3 to 7 days of treatment 7,14.

Antimicrobial therapy should be continued until 2 to 3 days after defervescence.

Recently, fluoroquinolones have been tested as alternative treatment 2,9,17,18.

Prevention is mainly directed toward the control of flea vectors and potential flea hosts 2.

In conclusion, murine typhus, a disease endemic in Taiwan, presents with nonspecific clinical features and laboratory findings. A high index of suspicion is required if it is to be diagnosed with appropriate serology and treated with effective antibiotics.

Control of vectors and their hosts is also important.

References

1. Azad AF. Epidemiology of murine typhus. *Annu Rev Entomol* 1990; 35: 553-69.
2. Dumler JS, Walker DH. *Rickettsia typhi* (Murine typhus). In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases*. Philadelphia: Churchill Livingstone; 2000: 2053-5.
3. Boostrom A, Beier MS. Geographic association of *Rickettsia felis*-infected opossums with human murine typhus, Texas. *Emerging Infect Dis* 2002; 8: 549-54.
4. Silpapojakul K, Chupuppakarn S, Yuthasompob S. Scrub and murine typhus in children with obscure fever in the tropics. *Pediatr Infect Dis J* 1991; 10: 200-3.
5. Wittel MB, Pachon J, Alarcon A. Murine typhus as a common cause of fever of intermediate duration. A 17-year study in the south of Spain. *Arch Intern Med* 1999; 159: 872-6.
6. Fergie JE, Purcell K. Murine typhus in south Texas children. *Pediatr Infect Dis J* 2000; 19: 535-8.
7. Lee HC, Ko WC, Lee HL. Clinical manifestations and complications of rickettsiosis in southern Taiwan. *J Formos Med Assoc* 2002; 101: 383-92.
8. Whiteford SF, Taylor JP, Dumler JS. Clinical, laboratory, and epidemiologic features of murine typhus in 97 Texas children. *Arch Pediatr Adolesc Med* 2001; 155;

396-400.

9. Gikas A, Doukakis S, Pediaditis J. Murine typhus in Greece: epidemiological, clinical, and therapeutic data from 83 cases. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2002; 96: 250-3.
10. Hufnagel M, Niemeyer C. Hemophagocytosis: a complication of acute Q fever in a child. *CID* 1995; 21: 1029-31.
11. Miller ES, Beeson PB. Murine typhus fever. *Medicine* 1946; 25: 1-15.
12. Dumler JS, Taylor JP, Walker DH. Clinical and laboratory features of murine typhus in south Texas, 1980 through 1987. *JAMA* 1991; 266: 1365-70.
13. Manea SJ, Sasaki DM, Ikeda JK. Clinical and epidemiological observations regarding the 1998 Kauai murine typhus outbreak. *Hawaii Med J* 2001; 60: 7-11.
14. Ng CP, Lo CB, Wong KK. A returned traveler with persistent fever due to murine typhus. *Hong Kong Med J* 2002; 8: 457-9.
15. Ong AKY, Tambyah PA, Ooi S. Endemic typhus in Singapore - a re-emerging infectious disease? *Singapore Med J* 2001; 42: 549-52.
16. Wong SY, Lam MS. Rickettsioses: the new and old diseases. *Singapore Med J* 2001; 42: 546-8.
17. Raoult D, Drancourt M. Antimicrobial therapy of rickettsial diseases. *Antimicrobial Agents Chemother* 1991; 35: 2457-62.
18. Strand O, Stronberg A. Ciprofloxacin treatment of murine typhus. *Scand J Infect Dis* 1990; 22: 503-4.

Fig.1. Chest x-ray film on day 5 of hospitalization showing cardiomegaly, right lower lung field infiltration and bilateral pleural effusions.

Fig.2. Echocardiography showing minimal pericardial effusion (arrow).

Fig.3. Followed up chest x-ray film on day 12 of hospitalization showing resolution of right lower lung field infiltration and pleural effusions.

地方性斑疹傷寒合併有肺炎，
胸膜炎及心包炎：一病例報告

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摘 要

地方性斑疹傷寒分布在世界各地，是一種人畜共通的傳染病。我們報告的這個個案是一位中年女性，她所表現出來的症狀有持續性的發燒和寒顫，嚴重頭痛，和肌肉痛。之後合併有肺炎、胸膜炎及心包炎，是罕見的併發症。地方性斑疹傷寒的診斷是根據臨床的懷疑和血清學上的確認。這個報告的主要目的是要探討此疾病在台灣的流行病學及臨床特徵。