Case report

A child with melioidosis presenting as septic arthritis

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Melioidosis has various clinical and rheumatological manifestations that may be the first presentation. This disease is less common in children than adults. This study reports the case of a previously healthy 3-year-old boy who presented with high-grade fever and pain in the right hip. He was treated with empirical parenteral antibiotics for septic arthritis and arthrotomy, but his symptoms did not improve. A hemoculture and synovial fluid culture had no bacterial growth. A titer of indirect hemagglutination assay for melioidosis was 1:2048, which is strongly positive. Melioidosis was diagnosed. Intravenous ceftazidime was given for 14 days as intensive treatment before switching to eradication therapy with oral trimethoprim and sulfamethoxazole for 3 months. A 3-phase bone scan also revealed osteomyelitis of the right tibia. The patient gradually improved and was discharged**. Chiang Mai Medical Journal 2016;55(2):75-79.**

keywords: melioidosis, septic arthritis, *Burkholderia pseudomallei*

Introduction

Melioidosis is a tropical disease caused by *Burkholderia pseudomallei*. It is seen predominantly in northern Australia and Southeast Asia, especially northeast Thailand, Malaysia and Singapore[1]. Melioidosis patients commonly present with pulmonary and genitourinary disease, and skin infection[2]. Musculoskeletal involvement including septic arthritis and osteomyelitis is less common, but may be the first presentation[3]. Melioidosis was reported in children aged less than 16 years in 4-15% of all cases[2, 4]. In Thailand, about 9% of melioidosis patients were younger than 15 years and the average incidence rate of this disease in children was 4.8 cases per 100,000 people per year[5]. This study describes the case of a child with septic arthritis from melioidosis.

Case presentation

A previously healthy 3-year-old boy from northeast Thailand presented with a one-week history of low-grade fever and pain in the right hip. He denied any history of recent trauma. He had had pustule on the right foot 2 weeks previously and his grandparent tried to aspirate it. He took acetaminophen, but his symptoms did not improve.

Two days prior to admission, he had high-grade fever and was taken to a private hospital. He had right hip pain with a limping gait. Laboratory studies showed a white-cell count of 17,990 cell/mm^3 with 46% neutrophils, hemoglo-

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bin of 11 gm/dL, platelet count of 295,000/mm^3, erythrocyte sedimentation rate (ESR) of 80 mm/hr, and C-reactive protein (CRP) of 25.9 mg/L. Ultrasound of the hips revealed joint effusion in the right one. He was treated with 200 mg/kg/day of intravenous cefotaxime and 5 mg/kg/day of oral doxycycline on the first day, followed by 2.5 mg/kg/day on the next one. After that, doxycycline was changed to 200 mg/kg/day of intravenous cloxacillin. Arthrotomy of the right hip was performed on the second day of admission. There was minimal synovial fluid with no frank pus or organisms found on a gram stain. After 2 days of hospitalization, he still had high-grade fever and hip pain, and was therefore referred to this hospital.

Examination on admission revealed a boy with a temperature of 40° Celsius, pulse rate of 150/min, blood pressure of 114/70 mmHg, and respiratory rate of 32/min. His right hip demonstrated full range of motion, but with pain throughout all movements. Neither pustule nor a wound was seen. The examination was otherwise normal.

Investigations

Blood tests showed iron deficiency anemia with a hemoglobin concentration of 9.3 gm/dL and transferrin saturation of 8.5%. A complete blood count showed a white-cell count of 10,800 cell/mm^3 with 40% neutrophils, 50% lymphocytes, and a platelet count of 325,000/mm^3. ESR was 66 mm/hr and CRP 81.1 mg/L.

Indirect immunofluorescence assay for scrub typhus and leptospirosis titer was negative. Urinalysis was normal. A plain film of both hips had no bony pathology. Synovial fluid analysis from drainage at the right hip showed a white and red cell count of 722 cell/mm^3 (82% neutrophils, 18% lymphocytes) and 21,370 cell/mm^3, respectively. A chest radiograph showed no infiltration. The hemoculture and synovial fluid culture had no bacterial growth. Melioidosis serology using indirect hemagglutination assay (IHA) was 1:2048.

Differential diagnosis

Initially, the patient was suspected of having septic arthritis. Bacteria were mostly possible pathogen, due to persistent high fever and elevated inflammatory markers. *Staphylococcus aureus*, *Streptococcus pneumonia*, *Streptococcus pyogenes* and *Haemophilus influenzae* are common in this age group[6]. After treatment with appropriate empirical antibiotics, the fever and hip pain persisted. Thus, further investigations were carried out in order to ascertain other sources of infection and complications.

Treatment

The patient was treated with 200 mg/kg/day of intravenous cloxacillin, 30 mg/kg/day of intravenous clindamycin and 15 mg/kg/day of intravenous amikacin for 6, 9 and 3 days, respectively, and the drainage was removed. As the patient did not respond to the therapy on the fourth day of hospitalization, and melioidosis serology was positive with a titer of more than 1:128, his antibiotic treatment was changed to 150 mg/kg/day of intravenous ceftazidime. A 3-phase bone scan showed a lobulated focus of increased radiotracer uptake along the proximal half of the right tibia, with suspected osteomyelitis (Figure 1). An abdominal ultrasound was performed with no abscess.

Outcome and follow-up

The fever went down and the hip pain decreased after changing the antibiotics. The patient received a total of 2 weeks intravenous ceftazidime treatment and switched to 10 mg of oral trimethoprim/kg/day with sulfamethoxazole (TMP-SMX). At 1-month follow-up, he had no fever or pain, and a full range of motion in the right hip, and his repeated melioidosis serology was 1:2048. He continued on eradication therapy (oral TMP-SMX) for 3 months.

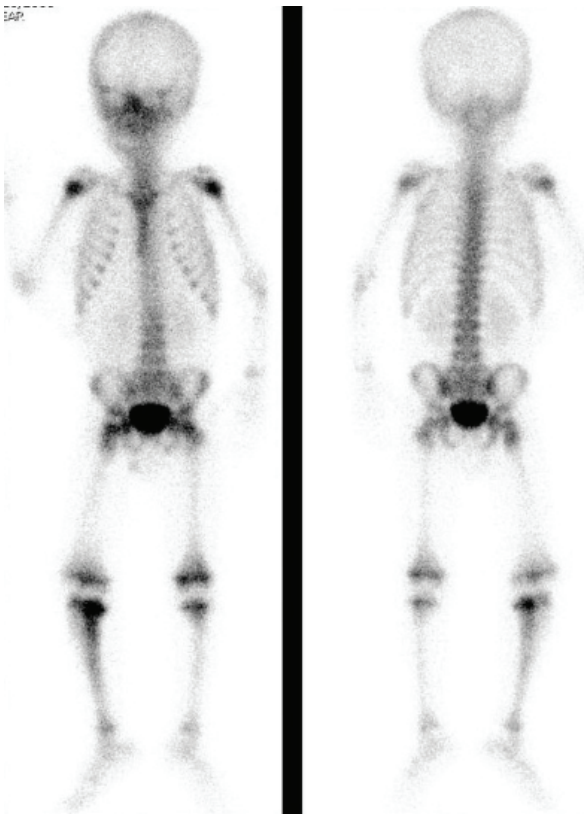

Figure 1. Anterior (left) and posterior (right) whole body scintigrams demonstrating a lobulated focus of increased radiotracer uptake along the proximal half of the right tibia with suspected osteomyelitis.

Discussion

As *Burkholderia pseudomallei* can be isolated from soil and water in regions of Southeast Asia and other parts of the world, including northern Australia, Africa, and North and South America[1], fever in travellers returning from these endemic areas should raise suspicion of melioidosis. The patient in this study came from northeast Thailand, where melioidosis is endemic[7], and history of the pustule on his right foot indicates that percutaneous inoculation may be the mode of transmission. Therefore, melioidosis should be in differential diagnosis. Rheumatological involvement is found in 4-14.4% of melioidosis patients[2,3,8]. The frequency reported previously in Thailand was higher than that in Australia.

The majority of melioidosis patients with septic arthritis have monoarthritis[8] and the lower extremities are affected more often than the upper ones. Arthritis of the hip joint is affected commonly[8]. Predisposing conditions in adults with melioidosis are diabetes mellitus, excessive alcohol consumption, chronic liver disease, chronic renal failure, and chronic lung disease[2,9]. Melioidosis patients with diabetes mellitus or thalassemia are more likely to have rheumatological involvement[8]. Interestingly, infections often occur in paediatric patients with no underlying disease[4].

Positive bacterial culture for *Burkholderia pseudomallei* from any clinical specimen represents the current diagnostic gold standard for melioidosis. However, it is an imperfect gold standard because of its low sensitivity (60.2%) [10]. A negative culture does not rule out melioidosis. Another reason why the patient had a negative culture was his doxycycline medication, which is an antimicrobial agent for melioidosis treatment.

Apart from bacterial culture, some serological methods, such as indirect hemagglutination antibody (IHA), have been utilized in order to provide presumptive evidence of infection. Many studies in northeast Thailand demonstrated that healthy children in endemic areas developed seropositivity, due to exposure to *Burkholderia pseudomallei* in contaminated soil and water[11, 12]. An antibody response occurred early in 2,214 children aged between birth and 14 years in northeast Thailand, with a sharp increase in the first 4 years of life, before the titer was static[11]. However, less than 10% of healthy children had IHA titer of 1:160 or more[11]. This result was similar to the findings of Charoenwong *et al*[12], who found that mean titer was higher in the older age group, and only 1 from 124 children aged 1 to 4 years had a titer of 1:640. Thus, age should be considered when interpreting IHA titer. The 3-year-old patient in this study had IHA titer of 1:2048, which was strongly positive and less likely to have had spontaneous environmental exposure. Paired sera could be tested at least 2 weeks apart to demonstrate rising antibody titer.

Septic arthritis often occurs following disease dissemination from infection elsewhere. Hepatic and splenic abscesses were reported

in a quarter of melioidosis patients in Thailand, but in only 6% of patients in Australia[2, 13]. More than half of the patients with hepatosplenic abscess formation were without abdominal pain or tenderness[1]. Nevertheless, septic arthritis can be a primary infection[3]. In addition, patients with signs and symptoms of more than 2 weeks septic arthritis have a high risk of adjacent bone infection[8]. Thus, abdominal ultrasound and a bone scan should be performed in order to seek internal organ abscesses and osteomyelitis.

Initial parenteral antibiotic therapy remains the initial treatment for patients diagnosed as melioidosis, followed by oral eradication therapy. Administration of intravenous ceftazidime or carbapenem is recommended for a minimum 10 to 14 days. Ceftazidime is used as first-line treatment in Thailand unless the patient has severe melioidosis, allergy to the drug or treatment failure, in which case meropenem is used. In addition to 2 weeks initial therapy of ceftazidime, the patient in this study was given subsequent eradication therapy with 3 months oral TMP-SMX. TMP-SMX monotherapy is as effective as and tolerated better than a combination of TMP-SMX and doxycycline[14].

Learning points

- Septic arthritis may be the first presentation of melioidosis.
- Melioidosis should be suspected as part of differential diagnosis in patients coming from endemic areas, especially from northeast Thailand, with fever or septic arthritis.
- Even if environmental exposure causes seropositivity in healthy children, melioidosis can be diagnosed in patients with a strong positive titer of IHA, and clinical features consistent with melioidosis.
- Further investigations, such as abdominal ultrasound or imaging, chest radiograph and bone scan should be performed in order to evaluate extensive infection.

Conflicts of interest

The authors declare no conflicts of interest.

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รายงานผู้ป่วยเด็กโรคเมลิออยโดสิสที่มาด้วยข้ออักเสบติดเชื้อ

วัชรีวรรณ สนธิชัย และ เพณณินาท์ โอเบอร์ดอร์เฟอร์
ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ โรคเมลิออยโดสิสมีอาการแสดงที่หลากหลายและอาการทางระบบกล้ามเนื้อและกระดูกอาจเป็นอาการแสดงแรก โรคนี้พบน้อยในเด็ก ผู้นิพนธ์รายงานผู้ป่วยเด็กอายุ 3 ปีมาด้วยไข้สูงและปวดสะโพกขวา ได้รับการรักษาแบบข้ออักเสบติดเชื้อด้วยยาปฏิชีวนะเข้าทางหลอดเลือดดำ และระบายหนองด้วยการผ่าตัด แต่อาการไม่ดีขึ้น ไม่พบเชื้อแบคทีเรียจากการเพาะเชื้อในเลือดและน้ำไขข้อ ตรวจพบแอนติบอดีต่อเชื้อ *Burkholderia pseudomallei* ด้วยวิธี indirect hemagglutination assay ได้ค่า 1:2048 ได้รับการวินิจฉัยโรคเมลิออยโดสิส ได้รับยา ceftazidime เข้าทางหลอดเลือดดำเป็นเวลา 14 วันเพื่อ intensive treatment และทานยา trimethoprim/sulfamethoxazole ต่ออีก 3 เดือนเพื่อ eradication การตรวจสแกนกระดูกพบกระดูกแข้งด้านขวาอักเสบ ผู้ป่วยอาการดีขึ้นหลังรักษา **เชียงใหม่เวชสาร 2559;55(2):75-79.**

คำสำคัญ: โรคเมลิออยโดสิส ข้ออักเสบติดเชื้อ *Burkholderia pseudomallei*