CASE SERIES

UNCOMMON CLINICAL PRESENTATIONS OF MELIOIDOSIS IN CHILDREN: 2 CASES WITH SORE THROAT AND 1 CASE WITH URTICARIAL RASH

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Abstract. Common clinical presentations of melioidosis in children include suppurative parotitis, lymphadenitis, skin infection and septicemia with pneumonia. Here we describe three cases with uncommon presentations of melioidosis seen among children attending a university hospital in northeastern Thailand. Two patients presented with pharyngitis and subsequently developed cervical lymphadenitis. Another patient presented with high fever and generalized urticarial rash. A pharyngeal culture in each of the first 2 patients and a blood culture and culture of the discharge from the wound of the third patient grew *Burkholderia pseudomallei*. All patients recovered with treatment. Their clinical presentations, initial diagnosis, treatment, clinical course and outcomes are described. Physicians caring for children living in, or returning from, melioidosis endemic areas should be aware of these uncommon presentations.

Keywords: melioidosis, children, pharyngitis, urticaria

INTRODUCTION

Melioidosis, an infection caused by *Burkholderia pseudomallei,* is endemic in Southeast Asia and northern Australia (Cheng and Currie, 2005; Gibney *et al*, 2008; Pagnarith *et al*, 2010). Srinagarind Hospital, Khon Kaen University, is located in Khon Kaen Province in northeastern Thailand, where melioidosis is endemic. Clinical presentations of melioidosis among children includes lymphadenitis, skin infections, suppurative parotitis, septicemia, pneumonia and liver and spleen abscesses (Lumbiganon and Viengnondha, 1995; Edmond *et al*, 1998). Of more than 50 melioidosis cases in children seen from 1994 to 2007, 2 presented with sore throat, and 1 presented with fever and an urticarial rash. The outcomes of treatment in the 2 patients with sore throat were reported previously without clinical details (Lumbiganon *et al*, 2011). Since sore throat and urticarial skin rashes are uncommon in melioidosis, we describe here the clinical presentations, initial diagnosis, management and outcomes of these patients. The microbiological identification of

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B. pseudomallei and the standard disk diffusion test were conducted as described elsewhere (Lumbiganon and Viengnondha, 1995).

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Case 1

A 14-year-old girl from Khon Kaen Province was admitted to our hospital with fever, nasal congestion, headache and sore throat of 1 month duration. She had been treated at a clinic with several oral antibiotics without improvement. One week before admission, she still had sore throat and developed tenderness of both sides of her neck. She had lost 3 kg over the previous 3 weeks. On physical examination she had a temperature of 39.5°C, an injected pharynx, a 2 mm shallow ulcer on the right tonsil, bilateral enlargement of the cervical lymph nodes of 2 x 2 cm and 3 x 4 cm, with mild tenderness.

The initial differential diagnoses in this patient included lymphoma and tuberculosis; nasopharyngeal biopsy was done. Histopathology revealed necrotizing granulomatous inflammation negative for acid-fast bacilli. Fine needle aspiration of right cervical lymph node revealed lymphoid hyperplasia. The nasopharyngeal tissue sent for culture grew *B. pseudomallei*, which was susceptible to Co-trimoxazole (TM/SM), ceftazidime (CTZ) and doxycline (DOX) by the standard disk diffusion test. A throat swab sent for culture on admission also grew *B. pseudomallei*, susceptible to DOX and CTZ, but resistant to TM/SM. Three blood culture specimens were negative, chest radiography was normal, and an indirect hemagglutination antibody (IHA) test for *B. pseudomallei* was >1:5,120.

The patient was initially treated with penicillin G sodium for 3 days. After obtaining the culture results, she was given oral DOX (100 mg, twice a day) and was discharged on the 9th day of hospitalization. At follow-up 10 days after discharge, she still complained of occasional low grade fever and persistent mild sore throat. Physical examination revealed a small area of whitish exudate on the left tonsil and a swab for culture was done. The tonsillar swab still grew *B. pseudomallei,* susceptible to TM/SM and DOX. She was given oral TM/SM (8-10 mg of TM/kg/day) in 2 divided doses in addition to DOX for another 2 weeks. At follow-up 6 months later, she was well and her throat swab culture grew normal flora. The IHA test result for *B. pseudomallei* had reduced to 1:1,280.

Case 2

A 13-year-old boy from Si Sa Ket Province was admitted to our hospital with low grade fever and sore throat for 4 weeks. He had been treated at a clinic with oral amoxicillin and then intramuscular lincomycin without improvement. Two weeks prior to admission, he was admitted to a provincial hospital with fever of 40°C and chills. Physical examination revealed an ulcer on the anterior pillar of left pharynx. He was treated with ceftriaxone, ciprofloxacin and metronidazole sequentially. A culture of the ulcer grew *B. pseudomallei,* the IHA for *B. pseudomallei* was ≥1:640, and the blood culture was negative. He was treated with intravenous TM/SM (8-10 mg/kg/day) in 2 divided doses and CTZ (100 mg/kg/day) in 3 divided doses for 3 days without improvement and was referred to our hospital.

Physical examination on admission revealed a temperature of 38.5°C. The pharynx and tonsils were not injected and no ulcer was seen. The cervical lymph nodes were enlarged bilaterally, 4 cm

and 2 cm and were mildly tender. The liver was palpable 2 cm below the right costal margin with mild tenderness. CTZ and TM/SM were continued. On the fifth day of hospitalization, the patient still had high fever and developed a maculopapular rash. On the seventh day of hospitalization, the antibiotic was changed to imipenem under the suspicion of drug allergy. Three days later, the rash disappeared but he persisted with high fever, tenderness of the left cervical lymph node and fluctuation. The enlarged left cervical lymph node was incised and about 5 ml of frank pus was drained. A Gram stain of the pus revealed numerous neutrophils but no obvious organisms. However, a pus culture grew *B. pseudomallei*, susceptible to TM/SM, DOX and CTZ. Three sets of blood cultures were negative. Abdominal ultrasonography revealed microabscesses in the liver. An IHA for *B. pseudomallei* performed 2 weeks after the first test was 1:5,120. His fever resolved after drainage of the pus, and the antibiotics were changed to oral TM/SM and DOX. He was discharged after 18 days of hospitalization. At follow-up, the parent reported the TM/SM was stopped 4 days after discharge because the patient developed a rash. DOX alone was continued for another 2 months. The patient was well during the next 2 years of follow-up.

Case 3

A 14-year-old boy living in Khon Kaen Province was admitted to our hospital with fever and an urticarial rash. Five days prior to admission, he developed a dull, aching pain in his epigastrium and an urticarial rash over his trunk and legs. The rash subsided after symptomatic treatment. The next day he had another episode of dull, aching abdominal pain, nausea, vomiting, high fever without chills and a generalized urticarial rash over his entire body and face. He was treated at a local hospital with intravenous ampicillin and dexamethasone (4 mg intravenously every 6 hours for 4 doses). By 3 days of hospitalization, his high fever and urticarial rash still persisted, so he was referred to our hospital.

Initial physical examination revealed a generalized urticarial rash over the body, face and extremities. His temperature was 40.3ºC. He had a 2 cm ulcer on his left thigh with minimal serum oozing but no pus. The patient could not recall how he got the wound but stated a small amount of pus drained from it one month previously. Staphylococcal sepsis and *Mycoplasma* infection was suspected; he was treated with intravenous cloxacillin and oral roxithromycin. Both the blood and wound culture grew *B. pseudomallei*. His antibiotics were changed to CTZ and TM/SM. The urticarial rash and itching disappeared the next day. His fever gradually decreased and resolved by the seventh day. An IHA for *B. pseudomallei* was 1:320, but, 7 days later, it rose to 1:5,120. A repeat blood culture was negative. Abdominal ultrasonography and radiography of right foot were unremarkable. Intravenous antibiotics were administered for 15 days before switching to oral TM/SM for another 4 months. He was doing well at a follow-up visit 2 weeks after the TM/SM was stopped.

DISCUSSION

Pharyngocervical melioidosis is rare. The symptoms of pharyngitis in our two patients persisted for several weeks despite treatment with common antibiotics used for pharyngitis and they subsequently developed cervical lymphadenitis. A case of pharyngeal melioidosis

in a 14-year-old girl was reported from Singapore (Tan and Sethi, 1997). The patient had severe sore throat for 2 weeks before receiving appropriate treatment, but she did not have cervical lymphadenitis. A culture of the pharyngeal ulcer helped make the diagnosis. In Thailand, 4,535 subjects were screened for *B. pseudomallei* by throat culture using a selective medium, but no asymptomatic carriers were found (Wuthiekanun *et al*, 2001). In their study, the throat cultures were positive for *B. pseudomallei* only in subjects with symptoms of melioidosis but there was no information on what symptoms they had.

In the present study, the clinical course of the third patient suggested *B. pseudomallei* can be a direct cause of generalized urticarial rash because the rash and severe itching persisted despite symptomatic treatment but disappeared one day after CTZ and TM/SM administration. The history in this patient supports the most likely route of acquisition of *B. pseudomallei* was skin inoculation of the left thigh during his daily activities (Gibney *et al*, 2008). There has been only 1 case report of pulmonary melioidosis associated with urticaria in an adult patient (Steck and Byrd, 1969). *B. pseudomallei* may produce a toxin (Haase *et al*, 1997) that induces an urticarial rash. Treatment with appropriate antibiotics kills the organisms stopping toxin production.

Sore throat and urticarial rashes may be associated with melioidosis in children. Physicians caring for children who live in, or are returning from melioidosis endemic areas should be aware of these uncommon presentations.

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