NEONATAL MELIOIDOSIS PRESENTING WITH SUPPURATIVE CERVICAL LYMPHADENITIS: A CASE REPORT

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Abstract. We present the first reported case of neonatal melioidosis presenting with late neonatal sepsis and suppurative cervical lymphadenitis. The late preterm infant aged 23 days born from a gestational diabetic mother presented with fever, mild respiratory tract symptoms without any other significant foci of infection. He was empirically treated with cloxacillin and gentamicin but he subsequently developed suppurative cervical lymphadenitis. His blood culture eventually grew *Burkholderia pseudomallei*. Pulmonary, intra-abdominal organ and CNS involvement were absent in this case. Although the infant had not had appropriate antibiotics for 96 hours after admission, he was successfully treated with intravenous ceftazidime and subsequent oral trimethoprim-sulfamethoxazole. Recurrence has not been observed in this case. This is the first case of neonatal melioidosis presenting with bacteremia and suppurative cervical lymphadenitis and having a favorable outcome.

Keywords: neonatal melioidosis, cervical lymphadenitis, late neonatal sepsis

INTRODUCTION

Melioidosis is endemic in many parts of Southeast Asia, the Indian subcontinent, and northern Australia (Cheng and Currie, 2005). Patients can present with disseminated infection with severe septic shock, localized infection or asymptomatic infection (Lumbiganon and Viengnondha, 1995). The mode of transmission is primarily via direct contact with contaminated water or soil or via inhalation of contaminated dust particles (Howe *et al*, 1971; Currie *et al*, 2000). Infants under one month of age are not usually engaged in outdoor activity; therefore, they are at low risk of acquiring this disease. However, the number of reported cases of neonatal melioidosis is increasing (Lumbiganon *et al*, 1988; Thatrimontrichai and Maneenil, 2012). The modes of transmission to neonates have been speculated to be vertical transmission (Lumbiganon *et al*, 1988), breastfeeding (Ralph *et al*, 2004), household contacts (Fang *et al*, 2016) and health care-associated infection (Lumbiganon *et al*, 1988). Thatrimontrichai and Maneenil (2012) conducted a systematic review of the literature regarding neonatal melioidosis in 2012 that included 22 cases. The

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crude mortality rate in that review was 73%. Four additional cases were reported later (Fong *et al*, 2015; Fang *et al*, 2016; Nivedhana and Rajendran, 2016). We report here a case of neonatal *B. pseudomallei* bacteremia with suppurative cervical lymphadenitis.

CASE REPORT

A 23-day-old male infant born at 34 weeks gestation to a diabetic mother (gestational diabetes mellitus A1) presented to the hospital with a 1-day history of low-grade fever and mild rhinorrhea. The infant lived with his family in Chon Buri, on the east coast of Thailand. On examination, the child had a temperature of 37.7°C, and was active. A complete blood count revealed a hemoglobin level of 14.2 g/dl, total white blood cell count of 16,370 cells/μl (N55% L35% M9%) and a platelet count of 433,300 cells/μl. The results of the cerebrospinal fluid analysis were within normal limits. The neonate was provisionally diagnosed with late neonatal sepsis, admitted and empirically treated with cloxacillin and gentamicin after a blood culture had been performed. Forty-eight hours after admission, the patient's temperature rose to 39°C and he began to have apneic episodes. The total white blood cell count rose to 39,000 cells/μl (N59% L23% M18%), and the CRP was 182 mg/l. Chest radiography was normal. At this time, the initial blood culture was reported to be positive for gram-negative rods. The antibiotics were subsequently changed to cefotaxime and amikacin. The patient's clinical status remained unchanged, although the patient's temperature remained at 38-38.5°C. Approximately 48 hours after the change in antibiotics (96 hours after admission), the infant developed a warm, tender and swollen upper cervical lymph node 1.5 cm in diameter. The initial blood culture was finally identified to be *B. pseudomallei*. The antibiotics were then switched to ceftazidime. The patient's fever gradually declined but the swollen lymph node became increasingly fluctuant. Incision and drainage was performed, and culture of the pus grew *B. pseudomallei*. The organisms isolated from the blood culture and cervical lymph node were susceptible to cefotaxime, ceftazidime, and trimethoprim-sulfamethoxazole. Abdominal ultrasound revealed no hepatosplenic abscesses. The infant was treated with intravenous ceftazidime for 21 days and subsequently with oral trimethoprim-sulfamethoxazole for 20 weeks. The swollen node eventually resolved prior to discontinuation of the intravenous ceftazidime. The patient's melioid titer measured 5 days after admission was undetectable. The patient has been doing well and has not had any recurrence of the infection for 8 months after discontinuation of the antibiotics.

Further history revealed all of the patient's family members had been healthy except for the maternal gestational diabetes mellitus. The patient's older brother had been very active outdoors and liked to play with soil. The brother frequently played with and kissed the patient.

DISCUSSION

To our knowledge, this is the first reported case of neonatal melioidosis presenting with late neonatal sepsis and suppurative cervical lymphadenitis. The case is classified as non-disseminated septicemia, since one organ (cervical lymph node) was involved. Lymphadenitis caused by *B. pseudomallei* is not uncommon in children; the prevalence of lymphadenitis was reported to be 18% among all cases of melioidosis in one case

series with favorable outcomes (Foong *et al*, 2015). Our infant had *B. pseudomallei* bacteremia on presentation and subsequently developed cervical lymphadenitis. This suggests the lymphadenitis could be a consequence of bacterial seeding from the preceding bacteremia. The patient survived, although effective antibiotic treatment with ceftazidime was delayed for 96 hours. The mode of transmission in this case was not clear. The most likely sequence of events is that the patient contacted the organism from his older brother, who often played with soil and kissed the patient. The patient may have acquired the pathogen from his older brother through skin, ingestion or inhalation. Another possibility is that the patient may have acquired the organism at birth in the hospital and then subsequently developed an invasive infection 3 weeks later. Hospital-acquired neonatal melioidosis has been well reported (Thatrimontrichai and Maneenil, 2012). It is less likely the patient acquired the organism from his mother since the child's melioid titer was negative. If the mother were infected, she would have had melioid antibodies which she would have passed to the patient.

Melioidosis in children is less common than in adults. Neonatal melioidosis is even rarer. Only 27 total cases have ever been reported in the literature (including this case) (Lumbiganon *et al*, 1988; Thatrimontrichai and Maneenil, 2012; Fong *et al*, 2015; Fang *et al*, 2016; Nivedhana and Rajendran, 2016). The crude mortality rate for neonatal melioidosis has been reported to be 74% (20/27), and the overall mortality rate of this disease in Thailand is approximately 40% (Limmathurotsakul *et al*, 2010). Since our case had a favorable outcome, even though appropriate antibiotics were delayed, we tried to identify factors associated with mortality in the 27 reported cases. Pulmonary involvement was strongly associated with death (odds ratio: 14.67). Patients with central nervous system (CNS) involvement had a slightly higher death rate but this did not reach statistical significance (Table 1). The association between poorer outcomes and pulmonary (and possibly CNS) involvement may reflect infection with more virulent strains. Molecular study reveals some virulent factors may be associated with CNS involvement, pneumonia or positive blood cultures (Sarovich *et al*, 2014). It is possible our patient may acquire a less virulent strain, since the infant had no pulmonary or CNS involvement, resulting in a favorable outcome.

Among the 27 reported cases, receiving appropriate antibiotics (ceftazidime or carbapenem) within 48 hours resulted in a slightly better outcome but this did not reach statistical significance (odds ratio: 0.25). The lack of reaching statistical significance for CNS involvement and early use of appropriate antibiotics may be due to the small sample size or differences in virulence among the infecting strains. Preterm birth was also associated with a good outcome, although the reason for this association is unclear.

The presence of neonatal melioidosis in endemic area poses difficulty in selecting appropriate empirical antibiotics to treat infants presenting with late neonatal sepsis. Empiric antibiotics in late neonatal sepsis are selected to target *Escherichia coli*, group B *Streptococcus* and *Staphylococcus aureus* in common clinical practice. Cefotaxime or cloxacillin plus aminoglycoside are now recommended (Sivanandan *et al*, 2011). These antibiotics have very poor activity against *B. pseudomallei*. Cefotaxime has been reported to exhibit some *in vitro* activity against this organism, although the MIC is high (Thibault

Table 1
Factors associated with mortality in neonatal melioidosis.

Factors	Percent mortality (*n*)	Odds ratio (95% CI)
Sex		
Male	76.9 (3/13)	6.67 (0.79-56.22)[a]
Female	33.3 (2/6)	
Received ceftazidime/meropenem within 48 hours		
Yes	42.9 (3/7)	0.25 (0.03-1.82)
No	75.0 (9/12)	
Age of onset > 7 days		
Yes	60.0 (6/10)	0.75 (0.12-4.90)
No	66.7 (6/9)	
History of preterm birth		
Yes	33.3 (3/9)	0.07 (0.01-0.88)
No	87.5 (7/8)	
Chronological age of onset before term[b]		
Yes	37.5 (3/8)	0.17 (0.02-1.44)
No	77.8 (7/9)	
Pulmonary involvement		
Yes	78.6 (11/14)	14.67 (1.16-185.24)
No	20.0 (1/5)	
CNS involvement		
Yes	83.3 (5/6)	12.5 (0.84-186.23)
No	28.6 (2/7)	

[a]Female as a reference, "no" as a reference in other parameters; [b]Chronological age of disease onset was less than GA 37 weeks.

et al, 2004); successful treatment with this antibiotic might be possible (Lumbiganon *et al*, 1988). Because pulmonary involvement is associated with a poor outcome, empiric antibiotics with activity against *B. pseudomallei* should be considered in neonates in melioid endemic areas who present with sepsis and pulmonary involvement until final cultures return. Earlier identification of the organism may also be facilitated by increased awareness among microbiologists performing Gram stains from blood cultures positive for gram-negative bacilli. *B. pseudomallei* exhibits a characteristic bipolar staining pattern (safety pin appearance on Gram stain). Reporting such suspicious results to clinicians can help clinicians consider more appropriate antibiotics.

In conclusion, neonatal melioidosis can present with late neonatal sepsis and suppurative lymphadenitis. The present case was successfully treated with ceftazidime and subsequent oral trimethoprim-sulfamethoxazole without evidence of relapse. A literature review suggests pulmonary involvement is associated with a poorer outcome.

ACKNOWLEDGEMENTS

We would like to thank the Department of Microbiology, Queen Sawang Wadhana Memorial Hospital for facilitat-

ing the organism identification.

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