

# การติดเชื้อmelioidosisในทารกแรกเกิด: รายงานผู้ป่วย และทบทวนวรรณกรรม

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## Neonatal Melioidosis: A Case Report and Literature Review.

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### บทคัดย่อ:

ทารกเพศชายอายุ 21 วัน มีอาการไข้ ชัก อาเจียนเป็นเลือด และความดันโลหิตต่ำ ผลการเพาะเชื้อจากเลือดพบเชื้อ *Burkholderia pseudomallei* และผู้ป่วยเสียชีวิตภายใน 24 ชั่วโมงหลังส่งเลือดเพาะเชื้อ

คำสำคัญ: จุลชีววิทยา, ทารกแรกเกิด, melioidosis, *Burkholderia pseudomallei*

### Abstract:

A 21-day-old term male baby had a fever, seizure, hematemesis and hypotension. *Burkholderia pseudomallei* was isolated from aseptically collected blood culture of the neonate. The neonate died within 24 hours after blood cultures were taken.

**Key words:** *Burkholderia pseudomallei*, melioidosis, microbiology, newborn

## Introduction

Melioidosis is a tropical infectious disease caused by a Gram-negative, motile, aerobic bacillus with bipolar staining. It is vacuolated and slender and has rounded ends; it is often described as having a “safety pin” appearance, *Burkholderia pseudomallei*. It is endemic to South-east Asia and northern Australia, and cases are increasingly being reported in countries elsewhere in Asia, the Pacific, the Americas, the Caribbean, Africa, the Middle East, and Brazil, and in travelers returning from tropical countries.<sup>1,2</sup> To diagnose melioidosis clinically is difficult as the symptoms and signs are non-specific. It is known as ‘the great imitator’ to many other diseases. Definite diagnosis is made when *Burkholderia pseudomallei* is isolated from blood, pus, urine or other sterile body fluids. Almost neonatal melioidosis is bacteremia. However, the use of cultures is time consuming, usually taking at least 48 hours to obtain the result. Many severely ill patients died before the diagnosis can be established.

This article reported and reviewed neonatal melioidosis literature, caused by *Burkholderia pseudomallei*, from 1971 to the present, to address the mode of transmission, clinical presentation, laboratory diagnosis, treatment and outcome.

## Case report

A term male baby, appropriate for gestational age, was born spontaneous vaginal delivery attended by an unqualified midwife. He weighed 2.5 kg at birth and did not receive vitamin K. He received exclusive breast feeding. He presented with hematemesis, melena and lethargy on the 21<sup>st</sup> day of life. He developed high grade fever

and seizure on right extremities and was brought to the hospital. On examination he was drowsy and had tense anterior fontanel. The pupils were 3 mm in diameter both sides and react to light. There was no sign of menigism. His completed blood count revealed hematocrit 31%, white blood cell 8,700 cells/mm<sup>3</sup> and platelet 257,000 cells/mm<sup>3</sup>. The coagulogram was not performed. The serum electrolyte revealed hyponatremia with sodium of 118 mEq/l and within normal limit of other electrolyte and glucose level. The lumbar puncture found bloody cerebrospinal fluid without clotting. The child was provisionally diagnosed as gastrointestinal and intraventricular hemorrhage from acquired prothrombin complex deficiency (APCD). He received vitamin K injection, fresh frozen plasma 10 ml/kg and packed red cell 10 ml/kg transfusion, cefotaxime 200 mg/kg/day, cloxacillin 200 mg/kg/day, phenobarbital 10 mg/kg/day, and intravenous fluid to correct hyponatremia. Ten hour later, he developed apnea and fixed unequal pupils, 1 and 3 mm on right and left side, respectively. He was intubated and put on dexamethasone. He was then referred to our hospital on the 23<sup>rd</sup> day of life.

The septic workups on arrival revealed hematocrit 28%, white blood cell 8,000 (band 12%), platelet 308,000. The coagulogram was within normal limit. The emergency computed tomography (CT) scan of the brain revealed intracerebral hemorrhage at left temporal area and left subdural hemorrhage with shifted midline. The craniotomy was performed for clot removal immediately. He was put on 200 mg/kg/day of cloxacillin injection. The initial blood culture obtained on the 23<sup>rd</sup> day of life revealed methi-

cillin-susceptible *Staphylococcus aureus*. Two days later, he developed hypotension and deterioration of consciousness with a Glasgow Coma Scale score decrease from 6T to 2T. The repeated CT scan of the brain revealed cerebral infarction in the area supplied by middle cerebral artery and brain edema. He died after the 4<sup>th</sup> day of admission or 26<sup>th</sup> day of life. The hemoculture on the 25<sup>th</sup> day of life grew *Burkholderia pseudomallei* susceptible to augmentin, cefotaxime, ceftazidime, chloramphenicol, imipenem, tetracycline and sulperazon, but resistant to amikacin, ampicillin, cotrimoxazole and gentamicin. The source of infection was not found.

## Discussion

There were a total of 22 cases reported of neonatal melioidosis identified in the original search but the detailed clinical data were available in only 14 cases. The earliest case was reported in 1971, and the latest case reported in 2011. Table 1 summarizes the main features of the 22 reported cases.

In Pahang state of Malaysia, the average annual incidence rate of melioidosis in children was found to be 1.6 cases per 100,000 populations.<sup>3</sup> The incidence of neonatal melioidosis was more predominant in male than in female, similar to pediatric melioidosis.<sup>4,5</sup> The presence of specific risk factors for *B. pseudomallei* infection may be operating by impairing neutrophil function, defined virulence factors (including a type III secretion system)<sup>1</sup> and produces a glycocalyx polysaccharide capsule (biofilm or slime) that is probably an important virulence determinant.<sup>6</sup> In adults the most common clinical

manifestation are rapidly progressive pneumonia and septicemia.<sup>7</sup> In children, on the other hand, parotitis and infections of the skin and lymph node were more common.<sup>8</sup> In this case, we speculated that the late-onset *B. pseudomallei* infection might have acquired from environmental source either by inhalation or by direct or indirect contact.

Neurological melioidosis appeared to be more significant in children (3/8, 37.5%) compared to adults (6/145, 4.1%).<sup>9</sup> Two cases of neonatal melioidosis reported had intracranial hemorrhage diagnosed by autopsy.<sup>10</sup> Our case had intracranial hemorrhage caused by acquired prothrombin complex deficiency, diagnosed by no history of vitamin K injection prophylaxis and exclusive breast feeding, but not clear that intracranial hemorrhage in this case is related to melioidosis.

In literature review (Table 1), all cases in neonatal period presented with bacteremia and/or meningitis. The clinical presentations of neonatal melioidosis were nonspecifically neonatal sepsis. The common signs and symptoms were fever (15/22, 68.2%), and respiratory distress (tachypnea, grunting, apnea and respiratory failure, 10/14, 71%). Of the 22 reported cases, 10 reported the mode of transmission. Two cases were investigated and identified mother to child transmission, one case was from vertical transmission (placental microabscess, case 10) and the other case was from breastfeeding (case 11). The other eight cases were probably health care-associated infection and probably community acquired infection equally. Mortality rate of neonatal melioidosis was extremely high (16/22, 72.7%),<sup>10-12</sup> whereas death in pediatric melioidosis had only 0.37-37.5%.<sup>9,13</sup> Mortality in

Table 1 Demographic and clinical characteristics of 22 documented cases of neonatal melioidosis sorted by year of publication

Case	Country, year	Sex	Age at onset (days)	PROM	Mode of delivery	GA (weeks)	BW (g)	Mode of transmission	Clinical features	Investigation	Diagnosis	Treatment and duration of antibiotics therapy	Outcome
1	USA, 1971 <sup>16</sup>	M	2 (37 h)	No	Forceps extraction	Term	2,977	NA <sup>†</sup>	Poor sucking, lethargy, fever, jaundice, grunting	NA	- <i>B. pseudomallei</i> sepsis and meningitis -Depressed right frontal skull fracture -Pneumonia	-Surgery at 3 h after birth -Polymyxin B (parenterally and intrathecally), 9 h	Died (119 h after birth)
2	Thailand, 1988 <sup>10</sup>	M	14	No	Forceps extraction	33	1,230	Probably HCAI	Asymptomatic	WBC6,750 (PMN40%, Band11%)	- <i>B. pseudomallei</i> and <i>Klebsiella</i> sepsis -Twin B, sterile CSF	-Cefotaxime and gentamicin, 14 d	Recovered
3	Thailand, 1988 <sup>10</sup>	F	14	No	C/S due to placental previa totalis	32	1,370	Probably HCAI	Respiratory distress, apnea, lethargy	WBC1,980 (PMN70%, Band17%)	- <i>B. pseudomallei</i> sepsis, sterile CSF - Omphalitis	-Ceftazidime, 20 d	Recovered
4	Thailand, 1988 <sup>10</sup>	F	IAB	NA, but chorioamnionitis	SVD (criminal abortion 5 days before delivery)	32	1,340	NA	Asymptomatic	NA	- <i>B. pseudomallei</i> sepsis	-Penicillin and gentamicin, 10 d	Recovered
5	Thailand, 1988 <sup>10</sup>	M	IAB	Yes (1 week)	SVD	Preterm	1,330	NA	Severe respiratory distress	NA	- <i>B. pseudomallei</i> sepsis -Respiratory distress syndrome	-Penicillin and gentamicin, 20 h	Died (20 h after birth)

Table 1 (Continued)

Case	Country, year	Sex	Age at onset (days)	PROM	Mode of delivery	GA (weeks)	BW (g)	Mode of transmission	Clinical features	Investigation	Diagnosis	Treatment and duration of antibiotics therapy	Outcome
6	Thailand, 1988 <sup>10</sup>	M	5	Yes (1 week)	SVD, birth in a car	Preterm	1,600	Probably HCAI	Apnea	NA	- <i>B. pseudomallei</i> meningitis and <i>Candida albicans</i> sepsis -Pneumonia	-Cefotaxime, 4 h	Died (9 <sup>th</sup> date of life)
7	Malaysia, 1993 <sup>17</sup>	M	2 (30 h)	NA	SVD	Term	3,400	Probably HCAI	Respiratory distress, lethargy, poor feeding and diffuse macular rash	WBC6,300 (PMN47%, Band7%)	- <i>B. pseudomallei</i> and <i>Acinetobacter</i> sepsis -Septic shock and respiratory failure from broncho-pneumonia	-Penicillin and gentamicin, 1 d then -Ticarcillin, 2 d	Died (5 <sup>th</sup> date of life)
8	Malaysia, 1998 <sup>18</sup>	M	10	No	SVD, birth in an ambulance	Term	3,200	Probably community-acquired	Respiratory distress, fever, cough, lethargy, poor feeding	WBC1,400 Plt.124,000 (CRP>9.6 mg/dl)	- <i>B. pseudomallei</i> sepsis -Septic shock, bronchopneumonia	-Clotaxillin and gentamicin	Died (20 h after admission)
9	Malaysia, 1998 <sup>18</sup>	M	8	No	SVD	Term	3,600	Probably community-acquired	Fever, irritability, tachypnea, convulsion	WBC 32,800 (PMN83%) Plt.336,000 (CRP>9.6 mg/dl)	- <i>B. pseudomallei</i> sepsis and meningitis -Pneumonia and omphalitis	-Cefotaxime and gentamicillin, then -Ceftazidime, 3 weeks	Recovered
10	Netherlands, 2001 <sup>19</sup>	F	2	NA	C/S due to severe vaginal bleeding	32	1,850	Transmitted from mother-to-child (probably placental infection) <sup>‡</sup>	Respiratory distress, sepsis	NA	- <i>B. pseudomallei</i> sepsis and pneumonia -Right lung abscess -Placental microabscesses	-Ceftazidime, 8 weeks then -Amoxicillin-clavulanate, 6 weeks	Recovered

Table 1 (Continued)

Case	Country, year	Sex	Age at onset (days)	PROM	Mode of delivery	GA (weeks)	BW (g)	Mode of transmission	Clinical features	Investigation	Diagnosis	Treatment and duration of antibiotics therapy	Outcome
11	Australia, 2004 <sup>20</sup>	M	2	NA (mastitis at 2 <sup>nd</sup> date before delivery)	SVD	37	3,020	Transmitted from mother-to-child <sup>s</sup>	Fever, tachypnea, bradycardia, hypotension	WBC1,900 Plt.18,000	- <i>B. pseudomallei</i> sepsis -Septic shock and respiratory failure	-Ampicillin and gentamicin	Died (5 <sup>th</sup> date of life)
12-19	Thailand, 2004 <sup>12</sup>	NA	NA	NA	NA	NA	NA	NA	Fever (100%), peritonitis (2/8)	NA	- <i>B. pseudomallei</i> sepsis	NA	All died (1 <sup>st</sup> -3 <sup>rd</sup> date after admission)
20	Malaysia, 2005 <sup>21</sup>	F	8	NA	SVD, birth at home	Term	2,700	Probably community-acquired	Fever, progressive abdominal distension, vomiting, lethargy, poor feeding, pale, respiratory distress, hypotension	NA (normal LFT, CRP>12.8 mg/dl)	- <i>B. pseudomallei</i> sepsis and pneumonia -Acute respiratory distress syndrome	-Cefotaxime (200 mg/kg/day) and piperacillin (200 mg/kg/day), 2 d then -Ceftazidime 50 mg/kg/dose q 12 h	Died (30 <sup>th</sup> date of life)
21	India, 2009 <sup>11</sup>	F	IAB	Yes	SVD	35	1,900	NA*	Fever, grunting, tachypnea, lethargy, poor peripheral perfusion	WBC4,500 (normal LFT)	- <i>B. pseudomallei</i> sepsis -Bronchopneumonia	-Ceftriaxone and gentamicin, 1 d then -Ceftazidime and vancomycin, 10 d then -Amoxicillin-clavulanate, 2 weeks	Recovered

Table 1 (Continued)

Case	Country, year	Sex	Age at onset (days)	PROM	Mode of delivery	GA (weeks)	BW (g)	Mode of transmission	Clinical features	Investigation	Diagnosis	Treatment and duration of antibiotics therapy	Outcome
22	Thailand (present case)	M	21	NA	SVD, by unqualified midwife	Term	2,500	Probably community-acquired	Fever, hematemesis, melena, lethargy, seizure	WBC8,700 (PMN51% Band12%) Plt257,000, normal LFT	- <i>B. pseudomallei</i> and methicillin-susceptible <i>Staphylococcus aureus</i> sepsis -Septic shock -Gastrointestinal and intracerebral hemorrhage from acquired prothrombin complex deficiency -Brain herniation	-Cloxacillin (200 mg/kg/day)	Died (26-date of life)

† = Cultures of the mother's urogenital tract were negative for *B. pseudomallei*. The father had recent military service in Vietnam, but he had no contact with the infant. The maternal grandmother had diabetes mellitus.

‡ = On prednisone due to ulcerative colitis and had vacation to Thailand. Cervical culture showed *B. pseudomallei* with both IgG and IgM enzyme immunoassay were reactive

§ = *B. pseudomallei* total antibody titer of 1/160 by indirect hemagglutination inhibition with both IgG and IgM enzyme immunoassay were reactive

\* = Vaginal swab of the mother or environmental samples from the NICU were not recovered *B. pseudomallei*.

C/S = Cesarean section, CSF = cerebrospinal fluid, F = Female, HCAI = Health care-associated infection, IAB = immediately after birth, M = Male, NA = not available, PROM = polynuclear neutrophil, Plt = platelet, PROM = premature rupture of membrane, SVD = Spontaneous vaginal delivery, USA = United States of America, WBC = white blood cell

pediatric melioidosis who were bacteremia was reported to be between 25–80%.<sup>4,14,15</sup> There was no mortality reported in localized infection<sup>4,14</sup> There was no report of relapsed infection in survived newborns and some patients were not elucidated.

*Burkholderia pseudomallei* has unusual antimicrobial susceptibility patterns. It is resistant to aminoglycosides except kanamycin, and sensitive to the cefazidime, amoxicillin/clavulanate, and carbapenems. There have been no guidelines of types of antibiotic and duration of therapy available for neonatal melioidosis.

## Conclusion

**Melioidosis is a rare bacterial infection in neonates and should be considered in the cases of sepsis. We hope this report alerts general pediatricians and neonatologists, especially in endemic areas, to consider melioidosis as a possible cause of sepsis in neonates.**

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