Neonatal Meliodosis: Very Rare But Be Aware

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Summary
Meliodosis is an infectious disease encountered mainly in tropics. It is not an uncommon problem in Malaysia especially in areas with agricultural activities. Although it can occur in all age groups, there have been few reported cases in children. Men are more commonly affected than women due to outdoor activities. Neonatal cases have been reported in Hawaii and Thailand. These infants presented with neonatal sepsis or meningitis. The mode of transmission to these infants has not been elucidated. This is the report of such a case first reported in Hospital Tengku Ampuan Afzan, Kuantan.

Key Words: Meliodosis, Neonatal

Introduction
Meliodosis means "a resemblance to distemper of asses". It is a tropical infectious disease of humans and animals with a protean clinical spectrum ranging from mild inapparent infection to fulminating septicemia. It is caused by the gram negative bacillus Burkholderia pseudomallei (previously known as Pseudomonas pseudo-mallei) which predominantly affects adults who have underlying diseases, such as diabetes, renal or liver failure.

Case Report
This baby girl was born at full term at home with a birth weight of 2.7 kg to a para one divorced Thai immigrant lady whose antenatal history was not known. She was immediately adopted by her foster parents; into a family which had no agricultural background. She was admitted once at day six of life for neonatal jaundice and was put under photo-therapy for a day before being discharged well.

She presented to us again at day thirteen of life with four days history of fever, progressive abdominal distension, vomiting, lethargy and poor feeding. Clinically, she was lethargic, pale and in respiratory distress with tachypnea (respiratory rate of 72 per minute), subcostal and intercostal recession. Her pulses was feeble and fast (182 beats per minute). The peripheral perfusion was poor and she was hypotensive (BP 45/25). Crepitations was detected bilaterally in the lungs. Her abdomen was distended with prominent veins. The bowel sounds were sluggish and the liver was enlarged. Her anterior fontanelle was bulging and tense. She was electively ventilated on admission. Fluid resuscitation and i.v. dopamine infusion (20mcg/kg/min) were needed to maintain the blood pressure. After full septic workout was carried out, she was started on i.v. ceftaxime (50mg/kg/dose Q6H) and piperacillin (50mg/kg/dose Q6H). The initial investigations taken reviewed metabolic acidosis, deranged coagulation profile and markedly raised C reactive protein (>128 mg/L). Although the full blood count and liver function test showed fairly normal results, there was bilateral pneumonic changes on the chest x-ray. Forty-eight hours later, the blood culture and tracheal secretions grew Burkholderia pseudomallei. I.V. ceftazidime (50mg/kg/dose Q12H)
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was subsequently started to replace Cefotaxime. Repeated blood culture 48 hours later documented clearance. However, her condition remained very labile since admission. Persistent hypotension ultimately needed triple inotropic support with I.V. Dopamine (20mcg/kg/min), I.V. Dobutamine (20mcg/kg/min) and I.V. Adrenaline (2mcg/kg/min). In spite of clearance of the bacteraemia, her pneumonia worsened and she developed ARDS which required high ventilatory settings.

Unfortunately she developed nosocomial infection with Stenotrophomonas maltophilia after about two weeks of ventilation and succumbed at the age of thirty days old. The postmortem cultures of the blood, CSF and ascitic fluid did not grow any organism.

Discussion

The acute fulminant form of meliodosis was first reported by Whitmore and Krishnaswami in 1912. It resembles glanders clinically but differ epidemiologically. The organism causing meliodosis is a saprophytic bacterium which is found widely distributed in the soil and water. It can be isolated from soil, stagnant water, rice paddies and market produce. Meliodosis has been recognised as an important cause of morbidity and mortality in South East Asia, particularly in the north-eastern region of Thailand, and Northern Australia.

Although the organism can cause disease in animals such as sheep, goats, swine, horses, seals, cows, rodents and cats, animals are not considered a reservoir for human disease. Arthropod-borne infection does not occur naturally. In endemic areas, humans become infected when they come in contact with soil through an abrasion of the skin, ingestion of the organism, or inhalation. As reported by others, the route of acquisition of the organism is not established. The possible explanation is the contamination of the umbilical cord by non-sterile instruments. Person to person transmission of meliodosis is rare. The development of meliodosis in a two-day old newborn in Hawaii and the demonstration of a significant antibody titre in a nurse who had never been in an endemic area but who worked on wards with meliodosis patients raises the question of spread from person to person within a hospital.

Burkholderia pseudomallei is a small, gram negative, motile, aerobic bacillus. Marked irregularities with a bipolar “safety pin” pattern are observed when it is stained with methylene blue, Wayson’s, or Wright's stain. It grows well on standard bacteriologic media, with a characteristic wrinkling of colony surfaces after 48 to 72 hours of inoculation. Two antigenic types have been distinguished; type I (Asian), found widely, including in Australia, and type II (Australian), found mainly in Australia. Both types are equally pathogenic.

The mortality of severe meliodosis remains high, up to 40%, and most patients have died during the 1st 48 hours of admission. In adults, approximately two thirds of the patients are septicemic. The delay in diagnosis, due to lack of awareness of this organism as a possible cause of community acquired septicemia, may result in a delay of appropriate treatment and a high mortality.

The clinical manifestations of meliodosis are variable. It can present as an acute, subacute, or chronic process. The incubation period has not been defined; it may be as short as 2 days or clinically inapparent infections may remain latent for a number of years after an individual leaves an endemic area, with an interval of 26 years reported in one patient. Chronic cases are more prevalent in whites than in Asians. Early serosurveys conducted by Strauss et al detected antibodies in 1.9-15.8% the Malaysian population indicating previous exposure.

Meliodosis involves primarily the skin and lungs. In adults, the most common clinical manifestation is rapidly progressive pneumonia and septicemia. Similar manifestations have been believed to occur in the pediatric patients as in the case reported here. Infections of the skin and lymph node were common in childhood meliodosis; however, localized infection of the lung was less common than in adults. Dance et al reported that parotitis was present in 38% of 126 children with meliodosis in Thailand. While in adults, it is considered to be a rare manifestation.

To diagnose meliodosis 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 any clinical specimen. There is no evidence for a carrier state. Burkholderia pseudomallei is easily isolated from blood, pus, urine or other sterile body fluids. It will grow on most laboratory media but with the use of selective pre-enrichment broth culture and Ashdown’s selective agar has considerably
improved the diagnostic yields. However, the use of culture is time consuming, usually taking at least 48 hours to obtain the result. Many severely ill patients are dead before the diagnosis can be established by this method. The serological tests are more useful in establishing the diagnosis of meliodosis in latent or asymptomatic patients.

The available tests are haemagglutination, indirect haemagglutination and complement fixation tests. Indirect haemagglutination (IHA) using crude whole cell extract is the serological test that is most widely used. But this has recently been found to be unhelpful in endemic areas where the majority of people have been exposed to this organism since childhood. A positive IHA test may be of some use in very young children, and a negative test may be useful in excluding the disease in adults.

Various antigen detection tests have been recently developed, and these show considerable promise for the early detection of the organism. These include latex agglutination test, which detects polyclonal antigen (lipopolysaccharides) of *Burkholderia pseudomallei*. The direct immunofluorescence technique using the same antibody to detect the *Burkholderia pseudomallei* antigen from clinical specimen such as sputum, urine or pus had been reported to be 73% sensitive and 99% specific. It is the only antigen detection test that has been tested in field conditions, and therefore should be used when the fluorescence microscope is available.

*Burkholderia pseudomallei* has unusual antimicrobial susceptibility patterns. It is resistant to aminoglycosides except kanamycin, and sensitive to the third generation cephalosporins, amoxycillin/clavulanate, piperacillin, chloramphenicol, doxycycline, cotrimoxazole, and imipenem. Ceftazidime is the antimicrobial of choice in severe meliodosis. The mortality rate was reduced by 50% in severe cases of meliodosis treated with ceftazidime in a recent study. In an open randomised controlled study, parenteral amoxycillin/clavulanate has proven to be as effective as ceftazidime in severe meliodosis. The mortality rate was similar with either ceftazidime or amoxycillin/clavulanate treatment in that study but treatment failure is higher with amoxycillin/clavulanate.

Patients with meliodosis should be treated with parenteral therapy until they have clinically improved and afebrile for at least 72 hours before switching to an oral maintenance treatment. At least 14 days of parenteral antibiotic therapy is required by most patients. Long term oral therapy and follow up should be provided to patients who survive the initial infection. A total of 12 to 20 weeks of combined oral and parenteral treatment is recommended. If patients were given only 8 weeks or less of therapy, the relapse rate was 23%. The relapse may present as severe as the initial infection and the reported mortality rate may be 30%. Relapse is common and more likely to occur in those with severe initial infections e.g. disseminated or multiple foci infection.

The oral maintenance treatment can be provided by a combination of oral chloramphenicol, doxycycline and cotrimoxazole or amoxycillin/clavulanate for children or pregnant women. Levamisole (150mg twice per week) has been used as an adjunct to antibiotic therapy in several patients with results that suggest it may be beneficial in the treatment of relapses.

**Conclusion**

Prior to antimicrobial, meliodosis was nearly always fatal. Even with vigorous appropriate therapy, the mortality rate in patients with meliodosis septifcemia is greater than 50%. So, a high index of suspicion and awareness of meliodosis is necessary especially in endemic areas for obtaining specimens for culture or serology and for initiating appropriate empirical antibiotic therapy. It remains a difficult disease to manage.

Prevention is difficult in endemic areas, as the lack of a vaccine and the ubiquitous nature of the organism. However, vigorous cleansing of abrasions and lacerations is recommended. As the compliance is problem, a search for a more effective oral drugs given for a shorter course are required.
References


