Short report

Children with melioidosis in Far North Queensland are commonly bacteraemic and have a high case fatality rate

Simon Smith, James D. Stewart, Catherine Tacon, Neil Archer and Josh Hanson

Abstract:

Paediatric melioidosis is uncommon in Northern Australia. In the Northern Territory, children with melioidosis often report an inoculation event and localised skin and soft tissue infections predominate. However, in Far North Queensland, children with melioidosis are frequently bacteraemic and have a high case fatality rate. To confirm this observation, all culture-confirmed cases of *Burkholderia pseudomallei* processed at Cairns Hospital between 1998 and March 2017 were reviewed. During the study period, *B. pseudomallei* was isolated from 223 people; ten (4%) were children (aged from three days to 14 years). Bacteraemia occurred in 6/10 (60%) children compared with 161/213 (76%) adults (p=0.24). The primary diagnosis was localised, cutaneous disease in three children, meningoencephalitis in two and pneumonia in two. Three had bacteraemia with no primary source evident. No child had a parotid abscess or liver abscess. Five children (50%) died, and all of whom were bacteraemic.

Keywords: Tropical medicine, melioidosis, paediatrics

Background and methods

Melioidosis, a disease caused by the environmental bacterium *Burkholderia pseudomallei*, has a diverse range of clinical presentations. Some patients have skin and soft tissue infections (SSTI) that resolve without antibacterial therapy, while others present in septic shock and have a high case fatality rate, even with optimal supportive care. In adults, clinical presentation is strongly linked to the presence of comorbidities, particularly diabetes mellitus, renal disease, chronic lung disease and hazardous alcohol use. Indeed, the disease is uncommon in adults without these conditions.[1] Conversely, children with melioidosis usually lack comorbidities[2] and uncommonly develop symptomatic melioidosis.[3] The reason that only some children develop symptomatic infection may relate to the route of transmission, the size of the inoculum, the presence of bacterial virulence factors or host susceptibility.[4]

Adults have similar presentations in different countries, but in children, the clinical phenotype varies significantly by geographic location. In Southeast Asia, children with melioidosis commonly have suppurative parotitis and liver abscesses, possibly due to the ingestion of *B. pseudomallei* contaminated water.[5, 6] Bacteraemia is reported in over a third of hospitalised cases in Thailand.[7] In contrast, in the Northern Territory (NT) of Australia, bacteraemia occurs in only 16%, much less frequently than in adults. Children with melioidosis usually report an inoculation event; SSTIs predominate while parotid involvement is unusual.[2]

The paediatric case fatality rate is over 20% in Asia compared to 7% in the NT. [2, 5, 7] This is at least partly explained by access to healthcare;[2] however, the higher rate of bacteraemia in Asian case series also contributes. [5, 7] High case fatality rates are also seen with neonatal melioidosis and neurological melioidosis.[8, 9]

In Australia, adults with melioidosis have a similar prognosis wherever they are managed,[1, 10] however, anecdotally, children with melioidosis in Far North Queensland (FNQ) have a less benign clinical course than that reported in the NT. To confirm this observation, all culture-confirmed cases of *B. pseudomallei* processed at Cairns Hospital between 1998 and March 2017 were reviewed. Cairns Hospital provides microbiological laboratory services for the Cairns region, Cape York Peninsula (CYP) and Torres Strait Islands (TSI). The study was approved by the Far North Queensland Human Research Ethics Committee.

Results

During the study period, *B. pseudomallei* was isolated from 223 people; ten (4%) were children (aged from three days to 14 years); six (60%) of whom were male (Table 1). Four children identified as Aboriginal or Torres Strait Islanders, three were Caucasian and three were from Papua New Guinea (PNG). Three children acquired their infection in PNG, three in the Cairns region, two in the Torres Strait and two on the CYP. Only two children recorded an inoculation event; one child injuring his head swimming in a flooded river in Cairns and one child from PNG having mud applied to an open head wound by a traditional healer. Only two children had classical risk factors for melioidosis – one with diabetes mellitus and another receiving high dose corticosteroids for systemic lupus erythematosus (SLE). Both cases survived. There was one neonate in our case series who died within two days of hospitalisation.

Bacteraemia occurred in 6/10 (60%) children compared with 161/213 (76%) adults (p=0.24). The primary diagnosis was localised, cutaneous disease in three children, meningoencephalitis in two and pneumonia in two. Three had bacteraemia with no primary source evident. No child had a parotid abscess or liver abscess. Five children (50%) died compared with 26/213 (12%) adults (p=0.001). Every child that died was bacteraemic. Three children died within two days of hospitalisation, none of whom received antibacterial therapy with *B. pseudomallei* cover. Two children died despite appropriate antimicrobial therapy and intensive care unit (ICU) support; one child with hydrocephalus requiring an external ventricular drain died 14 days after admission and one child with multi-organ failure requiring extracorporeal membrane oxygenation, died four days after hospitalisation.

Table 1. Demographics, risk factors, clinical presentation and outcomes of paediatric melioidosis cases in Far North Queensland (n=10)

Age(yrs) /Sex	Location	Inoculation event	Comorbidities	Weight in kg/ (Percentile)	Primary site of infection	Bacteraemic	ICU Admission	Died
0M	TSI	No	Neonate	3 (21)	Bacteraemia	Yes	Yes	Yes
4M	PNG	No	Malnourished	13 (<3)	CNS	Yes	No*	Yes
6F	PNG	No	Malnourished	14 (<3)	Pneumonia	Yes	No†	Yes
6M	CYP	No	Nil	19 (15)	Pneumonia	Yes	Yes	Yes
10M	PNG	Yes	Nil	30 (35)	Bacteraemia	Yes	Yes	Yes
11M	Cairns	No	Diabetes mellitus	35 (42)	SSTI	No	No	No
11F	TSI	No	Nil	N/A	SSTI	No	No	No
12F	Cairns	No	Nil	50 (79)	CNS	No	Yes	No
13M	Cairns	Yes	Nil	58 (76)	SSTI	No	No	No
14F	CYP	No	SLE, immunosuppressed	75 (95)	Bacteraemia	Yes	No	No

TSI = Torres Strait Islands; PNG = Papua New Guinea; CNS = Central nervous system; CYP = Cape York Peninsula; SSTI = Skin and soft tissue infection; N/A = Not available; SLE = Systemic lupus erythematosus
* Intubated and awaiting ICU bed, however died in Emergency Department
† Intubated in remote hospital and awaiting ICU bed in Cairns, however died prior to transfer

Discussion

There were only 10 cases over the study period, demonstrating that paediatric melioidosis is uncommon in FNQ. Nonetheless, the high case fatality rate and common finding of bacteraemia contrasts starkly with NT findings. This may be partly due to the small sample and reporting bias. Three of the children that died were PNG nationals, all were bacteraemic and two had significant comorbidity. Delayed ICU admission and poor physiological reserve resulting from socioeconomic disadvantage almost certainly contributed to their poor outcomes.

The higher proportion of bacteraemic cases might result from less aggressive case finding of SSTI, which was much less common than in the NT. In remote communities, patients commonly receive co-trimoxazole for mild SSTI (to treat community-acquired methicillin-resistant *Staphylococcus aureus*) without collection of samples for culture. Furthermore, *B. pseudomallei* infection may resolve in the absence of antimicrobial therapy.[11]

However, acknowledging these potentially confounding factors, the rate of bacteraemic melioidosis in adults and children in FNQ continues to be amongst the highest ever reported.[1] This is particularly relevant in the paediatric population given their extremely poor prognosis if bacteraemic. The case fatality rate of bacteraemic children in a Thai case series[7] was 60% and was even higher in a Cambodian case series (72%).[5] In our case series all but one (83%) of the bacteraemic children died. In the NT, there were only three children that died over the 24 years of one study however, two of the three cases were bacteraemic, while the third did not have blood cultures collected.

B. pseudomallei has multiple potential virulence factors and a highly variable genome, which partly explain the disease's protean clinical manifestations. It is possible that this might result in a greater propensity for patients to develop bacteraemia and its associated complications when infected with particular strains. Notably, non-bacteraemic skin infections have been associated with strains that lack the virulence factor filamentous hemagglutinin gene, fhaB3 – a gene that may be absent in FNQ.[12] In our study, a minority of patients had comorbidities or reported inoculation events which would support the hypothesis that patients were infected with more virulent strains, however this contention is limited by the retrospective nature of the study.

These findings are provocative, but they require prospective validation. It should also be noted that paediatric melioidosis remains uncommon in FNQ. Clinicians should only prescribe empirical regimens covering *B. pseudomallei* in children if they have a high clinical suspicion.

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