CASE REPORT

NEUROLOGICAL MANIFESTATIONS OF MELIOIDOSIS IN CHILDREN

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Melioidosis is an infection of birds and mammals caused by the Gram-negative bacterium *Burkholderia pseudomallei*. The organism is a free-living saprophyte found in wet soil, such as rice paddies. The disease is endemic to much of Southeast Asia and northern Australia (Leelarasamee and Bovornkitti, 1989; Ashdown *et al*, 1980; Jayanetra *et al*, 1974; Pit *et al*, 1988). Human melioidosis was first reported from Myanmar in 1912 by Whitmore and Krishnaswami. Occasional imported cases have been reported from the United States, the United Kingdom, France and from Africa (Patamasucon *et al*, 1982). The majority of reported cases are from northeast Thailand. In this area, 70-80% of cases occur during the rainy season months, from June to November (Dance, 1990). The vast majority of infections occur in rice farmers and their families.

Human infection usually occurs by direct inoculation injury but may result from inhalation (Leelarasamee and Bovornkitti 1989, Strauss *et al*, 1969). Clinical manifestations of the disease vary widely and include septicemic melioidosis with or without dissemination, multifocal melioidosis and localized disease; they range from chronic abscess formation to acute fulminant infection. Hematogenous dissemination may result in widespread multiple abscesses, particularly of the liver or spleen, although any organ system may be involved (Kanai and Dejsirilert, 1988). Most reported cases have occurred in adults; there are few reported cases of melioidosis in children. In adults, the lung is the most commonly involved single organ, but in children, the specific syndrome of parotid abscess is a very common presentation. Most children with melioidosis do not have underlying diseases which pre-dispose to infection, whereas in adults, infection occurs predominantly in those with underlying diseases such as diabetes or renal failure (Dance *et al*, 1989; Chaowagul *et al*, 1989). Mortality and morbidity in melioidosis remain high, with an overall mortality in severe disease of approximately 40%, despite the introduction of ceftazidime.

Nervous system involvement in melioidosis is rare (Patamasucon *et al*, 1982). Most of the previously reported cases of neurological involvement have involved brain abscess (Pit *et al*, 1988; Brill and Shoop, 1977; Tremonti and Dart, 1971; Visudhiphan *et al*, 1990). This report describes six children with neurological manifestations of melioidosis admitted to Sappasittiprasong Hospital during the 5 year period 1993-1997. During this period 115 children with melioidosis were admitted to this hospital; thus 5% of pediatric melioidosis cases had significant neurological abnormalities. Datails of the 6 cases are given in Table 1.

There are several reports of direct infection of the central nervous system associated with brain abscess (Pit *et al*, 1988; Brill and Shoop 1977; Tremonti and Dart, 1971; Visudhiphan *et al*, 1990). Culture of CSF or brain abscess fluid yielded *B. pseudomallei* in each case. Two additional reports document encephalitis with sterile mononuclear CSF pleocytosis. The first of these reports described a patient with encephalitis and bilateral third cranial nerve palsies. The CSF contained raised protein and normal glucose levels. A brain CT scan demonstrated enhancement in the interpeduncular fossa. The second report describes an unconscious patient with encephalitis, seizures, sterile CSF with one mononuclear cell, elevated protein and normal glucose level (Singh, 1976; Beck *et al*, 1984).

Another report describes seven adult patients in Australia with a neurological syndrome characterized by peripheral motor weakness, brainstem encephalitis, aseptic meningitis and respiratory failure, without demonstrable foci of infection in the central nervous system (Woods *et al*, 1992).

There is one report from Thailand describing three children with brain abscesses due to melioidosis (Visudhiphan *et al*, 1990). Central nervous

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Table 1

Case summaries.

Case, age, sex admission date	Presenting symptoms	Physical examination	Investigation	Treatment	Course
1. 4 years Male 17 July 1993	Fever and swelling of left eyelid for 4 days	Drowsy Swelling of left eyelid with purulent discharge Stiff neck	CSF: WBC 800 (N 80 %, L 20 %) Protein 197mg % Sugar 7mg % (BS 77) Culture: *B.pseudomallei* Hemoculture: *B.pseudomallei* Eye discharge: *B.pseudomallei*	Incision and drainage Ceftazidime 120mg/kg/day	Deterioration over 1 week post-admission, discharged against advice. Died 2 days later. Diagnosis: Orbital cellulitis with septicemia and meningitis
2. 5 months Male 20 Oct 1993	Fever 2 days Convulsion 1 day	Febrile Irritable Bulging anterior fontanelle	CSF: WBC 115 (N 66 %, L 34 %) Protein 215 mg % Sugar 51 mg % (BS 112) Culture: *B.pseudomallei* Hemoculture: Coag neg *Staphylococcus* Serum IHA 1:160 Ultrasound cranium: normal	Ceftazidime 120mg/kg/day	Clinically improved after 17 days Rx Continued on Co-amoxiclav 60 mg/kg/day for 2 months Follow up: normal development Diagnosis: Meningitis
3. 14 years Female July 30 1993	Right parotid abscess, 4 months post incision and drainage Right facial palsy 4 days Alteration of consciousness for 1 day	Semi-coma Witnessed convulsion Chemosis both eyes Right facial palsy (LMN)	Pus: *B.pseudomallei* Hemoculture: No growth Serum IHA 1:640 CT brain: multiple areas of white matter edema in both parietal lobes	Supportive treatment Ventilated Treatment of Cerebral edema Co-amoxiclav IV	Clinically improved and discharged Facial palsy resolved at 1 year Diagnosis: parotid abscess with encephalopathy and facial nerve palsy
4. 10 years Female Aug 5 1994	Dysphagia 6 hours Left parotid swelling	Drowsy Left parotid abscess Left cranial nerve 6,7 (LMN) and 9 palsies Right cranial nerve 3 palsy	Pus culture: *B.pseudomallei* Serum IHA 1:320 Ultrasound abdomen: normal CT brain: normal Chest X-Ray: Peri-hilar and right middle lobe infiltration	Ceftazidime 120mg/kg/day. Incision and drainage	One day post-admission developed left cranial nerve 3, 6, 7,9 and 12 paralysis, plus hyperreflexia. CT scan not repeated. 4 days later developed pulmonary edema and ventilated for 5 days. CN palsies resolved. Discharged day 21. Oral Rx: Co-amoxiclav and Co-trimoxazole Diagnosis: Parotid abscess with CN 3, 6, 7, 9 and 12 involvement

5. 6 years Male Aug 26 1995	Left parotid abscess Alteration of consiousness	GCS 10 Stiff neck Right hemiparesis Left facial palsy (LMN) Left CN 9 and 10 palsies (UMN) plus 12th nerve palsy Vertical nystagmus right eye Horizontal nystagmus left eye	CSF: WBC 400 (N 60%, L 40%) Protein 216 mg % Sugar 112 mg% (BS 120) Culture: no growth Hemoculture: *P.aeruginosa* Pus culture: *B.pseudomallei* CT brain: Normal CT brain at 10 days: area of low attenuation left thalamus, external capsule and pons	Ceftazidime 120mg/kg/day plus co-trimoxazole 10mg/kg/day Cloxacillin and Imipenem for hospital-acquired pneumonia	10 days post-admission (2 hours after LP) developed respiratory failure, requiring ventilation. 67 days post-admission died of hospital-acquired pneumonia Diagnosis: parotid abscess with meningo-encephalitis
6. 3 years Male Aug 20 1997	High fever 9 days Focal fits involving left arm 3 days previously Left hemiparesis and inability to walk for 3 days	Pustule left flank Reduced tone left arm and leg Motor power grade 3 on left Sensory exam, normal Left-sided hyporeflexia Right-sided hyperrefleia	CSF: WBC 28 (N 50%, L 50%) Protein 59 mg % Sugar 72 mg% Culture: no growth Pustule culture: *B.pseudomallei* Melioidosis IHA 1:1,280 CT Brain: Enhancing mass in white matter of right parietal lobe, with peri-lesional edema	Craniotomy Ceftazidime 120mg/kg/day Treatment of cerebral edema Physiotherapy	Improvement of left hemiparesis Discharged Follow-up brain CT: normal Diagnosis: Encephalopathy and left hemiparesis

system infection could occur following local spread via venous channels or be secondary to bacteremia (Visudhiphan *et al*, 1990). The majority of pediatric cases with septicemic melioidosis present with rigors and short term fever (median 6 days). Evidence of a primary focus is present in only half of the cases (Dance, 1990).

None of the 6 cases described here had a brain abscess. The first two patients presented with meningitis, which appears to be rare in melioidosis. In the first case this probably resulted from septicemia secondary to orbital cellulitis, while in the second there was primary meningitis.

In the remaining four cases neurological symptoms started after the first week of clinical disease. Three of the patients developed an encephalitis-like picture. The absence of foci of infection in the central nervous system, as demonstrated by brain CT scans and sterility of CSF, are consistent with a previous suggestion that neurological symptoms could result from an exotoxin produced by *B. pseudomallei*. Two exotoxins have been described, a lethal toxin and a dermonecrotic toxin (Heckly 1964, 1978). Studies of animals with melioidosis indicate that central nervous system involvement is unusual. When present it appears to show a prediliction for the brainstem and spinal cord (Omar, 1963; Laws and Hall, 1963; Ladds *et al*, 1981), but toxin studies in animals have not been reported.

Experience in Ubon Ratchathani suggests that in endemic areas, melioidosis should be included in the differential diagnosis in all febrile patients with abnormal neurological signs. If possible, CSF or abscess pus specimens, plus blood, should be sent for culture. CT or MRI of the brain should be performed where possible to exclude brain abscess. Clinicians working in areas where *B. pseudomallei* is endemic should be aware of this form of melioidosis. A high index of suspicion will allow appropriate surgical and medical treatment to be instituted early, and improve the management of this treatable but potentially fatal infection.

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