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Pediatric Suppurative Parotitis in Cambodia 2007-2011

Nicole Stoesser, MBBS^{*,1,2,3}, Joanna Pocock, MB BChir^{2,4,5}, Catrin Elisabeth Moore, DPhil^{1,2,3}, Sona Soeng¹, Hor Put Chhat¹, Poda Sar¹, Direk Limmathurotsakul, MD, PhD², Nicholas Day, FRCP, PhD^{2,3}, Vann Thy, MD¹, Vuthy Sar, MD¹, and Christopher M. Parry, FRCPATH, PhD^{1,2,3}

¹Angkor Hospital for Children, Siem Reap, Cambodia ²Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand ³Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford University, Oxford, UK ⁴Department of Medicine, Addenbrooke's Hospital, Cambridge, UK ⁵University of Cambridge, Cambridge, UK

Abstract

The causes of suppurative parotitis in Cambodian children are not known. We describe 39 cases at the Angkor Hospital for Children, Siem Reap between January 2007 and July 2011 (0.07/1000 hospital attendances). The median age was 5.7 years with no neonates affected. *B. pseudomallei* was cultured in 29 (74%) cases. No deaths occurred; one child developed a facial nerve palsy.

Keywords

bacterial parotitis; children; Asia; *Burkholderia*; Melioidosis

BACKGROUND

Pediatric suppurative parotitis (PSP) is uncommon, and details relating to presentation, etiology and management are restricted to a few case series and multiple case reports.^{1,2} Mortality was once substantial but has greatly improved as a result of antimicrobial treatment. Fever, facial swelling, erythema, pain, lymphadenopathy, trismus, purulent aural discharge and facial palsy are all described with PSP, and the presence of pus at the opening of the parotid (Stensen's) duct is considered pathognomonic. Common microbiological pathogens identified include *Staphylococcus aureus*, viridans streptococci and anaerobes in acute cases;² *Streptococcus pneumoniae* and *Haemophilus influenzae* in recurrent parotitis;³ and *Burkholderia pseudomallei* where melioidosis is endemic, such as South-East Asia,⁴ although cases of *B. pseudomallei* parotitis occur rarely in endemic areas of Australia.⁵

Treatment typically involves antimicrobials, with surgical management indicated for abscesses or if there is a poor response to medical therapy. Optimum duration and regimen

*Corresponding author: Dr Nicole Stoesser, Microbiology Laboratory, Angkor Hospital for Children, Vithey Preah Sangreach Tep Vong & Um Chhay St., Sangkat Svay Dangkum Commune, Siem Reap, Cambodia, nicole.stoesser@ndm.ox.ac.uk.

Conflicts of Interest

None of the authors has any conflicts of interest to declare.

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of antimicrobial treatment is unclear, and is likely to vary depending on causative pathogen, particularly with respect to *B. pseudomallei*. Complications include systemic dissemination and septicemia, extension of infection to involve the adjacent bones or para-pharyngeal space and facial nerve palsy or fistula formation.

Descriptions of PSP in Asia are limited to studies investigating melioidosis.^{4,6,7} Melioidosis has been described as a clinical entity in Cambodia in several studies,^{8,9} but there is no study to date investigating PSP in Cambodian children. This study aimed to characterize the clinical presentation, microbiology, management and outcome of cases of PSP at a pediatric hospital in north-western Cambodia, 2007-2011.

METHODS

All potential cases of PSP presenting to the Angkor Hospital for Children (AHC) in Siem Reap, Cambodia from 1st January 2007-31st July 2011 inclusive were identified retrospectively by one of two methods: (i) from the hospital electronic database through the relevant ICD-10 code used by the hospital for encoding parotitis (K11.3), and/or (ii) by reviewing laboratory records for microbiological specimens submitted. Hospital notes for patients with relevant pus specimens were reviewed; if these were consistent with a clinical diagnosis of parotitis, then the case was included.

Details relating to each case were collected on a standardized case report form and included: demographic features, clinical presentation, blood test and microbiology results, radiological investigations, medical and surgical management and clinical outcomes.

Standard operating procedures for laboratory investigations were in place. For microbiology, sample processing, identification and antimicrobial susceptibility testing was undertaken in accordance with CLSI guidelines with some local adaptations as previously described⁸. *B. pseudomallei* was identified on the basis of typical colonial morphology on Ashdown's agar, resistance to gentamicin and colistin, and latex-based antigen detection. Disk diffusion-based susceptibility testing for *B. pseudomallei* was carried out for co-amoxiclav, ceftazidime, imipenem, doxycycline and co-trimoxazole; for co-trimoxazole, isolates that were non-susceptible by disk diffusion (zone diameter < 10mm) had confirmatory MIC-based testing using an Etest (bioMérieux, Marcy-L'Etoile, France). Isolates with a co-trimoxazole MIC of < 2mg/L by Etest were deemed susceptible.

Data were analyzed using Stata 11.1. Ethical approval for the study was obtained from the AHC institutional review board (AHC-IRB) and the Oxford Tropical Research Ethics Committee (OXTREC, UK).

RESULTS

Thirty-nine cases were identified, equating to a crude incidence of 0.07 cases/1000 hospital attendances or 9.9/1000 surgical ward admissions. Twenty-two (56%) patients were male. The median age of children with parotitis was 5.7 years (inter-quartile range [IQR] 3.7-9.6 years; range 0.7-14.6 years), and no neonatal cases were observed. The median duration of symptoms before admission was 7 days (IQR 7-10 days; range 4-30 days), and most (n=38; 97%) patients presented with fever, facial swelling and localized pain/tenderness of the parotid region. Presenting symptoms occurring in more than five percent of cases are listed in the Table; other symptoms included aural pain/discharge, cough/coryza, seizures, gastrointestinal symptoms, rigors, and one case presented with widespread erythema (later confirmed as a disseminated staphylococcal infection).

Pre-hospital treatment was common. At least 6 cases had taken antimicrobials (one or more of amoxicillin, ceftriaxone, gentamicin, amoxicillin-clavulanate, erythromycin, cephalexin), 5 had visited a “Krou Khmer” (traditional healer), and 14 had been given an unknown medication, typically from the market, pharmacy or a private practitioner. Nineteen percent of children had been seen in a private healthcare clinic and two had had prior incision and drainage procedures.

Mean admission temperature was 38.1°C; there was a significant difference in mean admission temperature for *B. pseudomallei* culture-positive cases and non- *B. pseudomallei* cases (38.5 versus 37.1; t-test; p=0.006). Of 24 patients who had blood tests taken, all but 2 had a leucocytosis (91%); all of these cases presented with neutrophilia (mean % neutrophils 76%; range 37-92%) except the child with the disseminated staphylococcal infection, who had lymphocytosis. 25 (64%) children had an ultrasound scan at presentation; of the 24 who had results reported, all had parotid enlargement and 13 (54%) had a visible collection of fluid.

Culture from parotid specimens was positive in 34 (87%) cases: 29 (85% of culture-positive cases; 74% of all cases) with *B. pseudomallei*, 4 (12% of culture-positives; 10% of all cases) with *S. aureus* and one with coagulase negative staphylococci, which may have been a contaminant. No MRSA infections were detected. Susceptibility testing was variably recorded on *B. pseudomallei* isolates, but 5/28 (18%) were resistant to co-trimoxazole, 1/23 (4%) to ceftazidime and 0/21 to doxycycline; 1/29 (3%) isolates showed intermediate susceptibility to amoxicillin-clavulanate. Six patients had a blood culture taken; all were negative.

All patients were treated with antimicrobials, but for cases where clear pathogens were cultured (*S. aureus* or *B. pseudomallei*), only 16/33 (48%) were initially treated with antimicrobials that provided appropriate activity for the subsequently isolated organism (all *B. pseudomallei* cases). All patients received at least one surgical incision and drainage procedure; requirement for more than one surgical intervention was significantly associated with a culture positive for *B. pseudomallei* (Fisher’s Exact Test p<0.001).

No deaths were observed in any of the PSP cases in this series. A lower motor neuron facial palsy was observed in one child, and weight loss at follow-up in another. Median duration of follow-up post-discharge was 33 days (IQR 1-81 days; range 0-1577 days).

DISCUSSION

Localized melioidosis was by far the commonest cause of PSP at our institution, followed by *S. aureus*. We may have missed cases of anaerobic/mixed-anaerobic parotitis, given the lack of anaerobic culture. No deaths and a low rate of complications were observed, which concurs with other published cases of non-septicemic PSP caused by *B. pseudomallei*.^{4,6} This was despite initial inappropriate antimicrobial cover in 52% of cases, a phenomenon also described in Thailand.⁴

The optimum antimicrobial regimen and duration for localized pediatric melioidosis has not been defined, although recommendations support the use of either ceftazidime or co-amoxiclav as acute parenteral therapy, and co-trimoxazole or co-amoxiclav as consolidation/eradication therapy in children.⁴ In our setting, 18% of *B. pseudomallei* isolates were resistant to co-trimoxazole (compared with 13-16% in Thailand and 2.5% in Australia) and so this should not be used without confirmation of susceptibilities. Co-amoxiclav was used for consolidation/eradication therapy in 24 of the melioid PSP cases, although in 16 the dose was insufficient according to the recommendation to use 20/5 mg/kg of amoxicillin-

clavulanate.¹⁰ There was no evidence of relapse in this group, although it did include both cases with sequelae at follow-up.

One limitation of this study is the variable nature of documented follow-up, with a median of only 33 days, which impacts on the ability to measure outcomes and comment on appropriate treatment strategies. However, many patients in our setting return to the hospital if there are significant problems post-discharge, given that free care and follow-up are provided. In addition, 56% (19/34) of culture-positive cases were reviewed by the hospital on at least one further occasion more than 30 days after discharge for the initial acute illness.

The treatment regimens used in our cases also varied widely so that recommendations cannot be drawn solely from our data. Advantages of treating with amoxicillin-clavulanate include anaerobic and more consistent staphylococcal activity than co-trimoxazole if mixed infections are present. A pragmatic suggestion is that children who require admission be treated empirically with ceftazidime and cloxacillin (intravenous preparations of amoxicillin-clavulanate are very expensive locally) pending culture results, as this would treat both *B. pseudomallei* and *S. aureus*. For confirmed parotid melioidosis, amoxicillin-clavulanate 500/125mg three times/day for those >12kg and 20/5 mg/kg for those <12kg could be used as consolidation/eradication therapy for 12 weeks when clinical improvement is observed and no further surgical intervention is anticipated. Children managed as out-patients could be treated with oral amoxicillin-clavulanate dosed as above from the outset.⁴ The difficulties of undertaking a trial to characterize the optimum dose and duration of therapy relate to the limited numbers of cases reviewed at any one institution, especially those with the capacity to undertake diagnostic microbiology. High rates of surgical intervention were seen in our series and just over a quarter of patients required multiple surgical procedures – all of these cases had culture-confirmed parotid melioidosis.

Suppurative parotitis is typically thought to be attributable to the ascending colonization of the parotid duct with oral bacteria. The ingestion of *B. pseudomallei* in water is therefore the most likely explanation for the parotid form of melioidosis, given that for the rural Cambodian population the drinking water supply is often taken from boreholes, surface water, rainwater and other unprotected water sources. The observation that parotid melioidosis appears to be mostly a disease of childhood may relate either to types of exposure, or perhaps to the impact of changing oral microbiota and mucosal immunity with increasing age.

No neonatal cases of suppurative parotitis were seen, although this may be due to ascertainment bias. Siem Reap has a second pediatric hospital which also provides maternity services, and more neonates are seen there. In a recent survey of febrile illness requiring admission at AHC, only 2.6% of admissions were less than 28 days old (Emary K, unpublished data).

PSP in Cambodia (excluding neonates) is predominantly caused by *B. pseudomallei*, and generally has a favorable prognosis, although it requires high rates of surgical intervention. A pragmatic antimicrobial treatment strategy has been proposed for our setting, given local antimicrobial availability and difficulty of ensuring adequate follow-up.

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REFERENCES

1. Strong BC, Sipp JA, Sobol SE. Pediatric parotitis: A 5-year review at a tertiary care pediatric institution. *Int J Pediatr Otorhinolaryngol.* Mar; 2006 70(3):541–4. [PubMed: 16154645]
2. Brook I. Suppurative parotitis caused by anaerobic bacteria in newborns. *Pediatr Infect Dis J.* Jan; 2002 21(1):81–2. [PubMed: 11791111]
3. Giglio MS, Landaeta M, Pinto ME. Microbiology of recurrent parotitis. *Pediatr Infect Dis J.* Apr; 1997 16(4):386–90. [PubMed: 9109141]
4. Lumbiganon P, Chotechuangnirun N, Kosalaraksa P, Teeratakulpisarn J. Localized melioidosis in children in Thailand: treatment and long-term outcome. *J Trop Pediatr.* Jun; 2011 57(3):185–91. [PubMed: 20819799]
5. Cheng AC, Currie BJ. Melioidosis: epidemiology, pathophysiology, and management. *Clin Microbiol Rev.* Apr; 2005 18(2):383–416. [PubMed: 15831829]
6. Dance DA, Davis TM, Wattanagoon Y, et al. Acute suppurative parotitis caused by *Pseudomonas pseudomallei* in children. *J Infect Dis.* Apr; 1989 159(4):654–60. [PubMed: 2926159]
7. How HS, Ng KH, Yeo HB, Tee HP, Shah A. Pediatric melioidosis in Pahang, Malaysia. *J Microbiol Immunol Infect.* Oct; 2005 38(5):314–9. [PubMed: 16211138]
8. Pagnarith Y, Kumar V, Thaipadungpanit J, et al. Emergence of pediatric melioidosis in Siem Reap, Cambodia. *Am J Trop Med Hyg.* Jun; 2010 82(6):1106–12. [PubMed: 20519608]
9. Rammaert B, Beauté J, Borand L, et al. Pulmonary melioidosis in Cambodia: a prospective study. *BMC Infect Dis.* May 14.2011 11:126. [PubMed: 21569563]
10. Cheng AC, Chierakul W, Chaowagul W, et al. Consensus guidelines for dosing of amoxicillin-clavulanate in melioidosis. *Am J Trop Med Hyg.* Feb; 2008 78(2):208–9. [PubMed: 18256414]

Table
Prevalence of symptoms in cases of PSP presenting to the Angkor Hospital for Children, Siem Reap, Cambodia, 2007-2011

Symptom	Number of cases presenting with symptom (%)
Fever	39 (100)
Facial swelling	39 (100)
Left	22 (56)
Right	15 (39)
Bilateral	2 (5)
Pain	38 (97)
Erythema	31 (79)
Decreased appetite	12 (31)
Warmth over gland	5 (13)
Lymphadenopathy	4 (10)
Purulent discharge from the parotid duct	3 (8)
Trismus	3 (8)
Dental problems	3 (8)
Palpable fluctuance over parotid gland	3 (8)