SALMONELLA SPINAL EPIDURAL ABSCESS IN A CHILD PRESENTING WITH PROLONGED FEVER: CASE REPORT

Ploy Pattanakitsakul[1], Sulak Itsaradisaikul[1, 2], Sophida Boonsathorn[1], Pitak Santanirand[3] and Nopporn Apiwattanakul[1]

[1]Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok; [2]Department of Pediatrics, Uttaradit Hospital, Uttaradit Province; [3]Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Abstract. Prevalence of spinal epidural abscess (SEA) in a pediatric population is rare. Diagnosis is difficult because indicative signs may not be present at initial presentation. Here, we describe the first case of SEA in a child caused by *Salmonella enterica* subsp *houtenae*. The etiologic organism was identified by a 16S rDNA sequencing method. The patient was successfully treated with multilevel laminotomy with abscess draining and a 6-week course of intravenous cefotaxime.

Keywords: *Salmonella enterica* subsp *houtenae*, cefotaxime, immunocompetent, pediatric, spinal epidural abscess

Correspondence: Nopporn Apiwattanakul and Ploy Pattanakitsakul, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, 270 Rama VI Road, Ratchathewi District, Bangkok 10400, Thailand
Tel: +66 (0) 2201 1774; Fax: +66 (0) 2201 1769
E-mail: nopporn.api@mahidol.ac.th; sapp_ploy@hotmail.com

INTRODUCTION

Spinal epidural abscess (SEA) is a rare condition in children. Children affected by this condition present with non-specific symptoms (Tyagi, 2016), making it difficult to diagnose this condition. Clinical presentations of SEA vary from back pain, fever, paraparesis or paraplegia, muscle weakness, incontinence, spinal irritation, local tenderness, and sensory deficit (de Leeuw *et al*, 2018). The classic triad of SEA (fever, back pain and neurological deficit) is uncommon at the first presentation. In nonverbal children, SEA may manifest as non-specific symptoms, such as irritability, abdominal pain, hip

pain, and refusal to bear weight (Tyagi, 2016). The most common etiological agent of SEA is *Staphylococcus aureus* (Zimmerer *et al*, 2011).

Here, we report a case of SEA in a child who initially presented with prolonged fever. The etiologic agent, *Salmonella enterica* subsp *houtenae*, was detected using a 16S rDNA sequencing method.

CASE REPORT

A previously healthy 13-month-old girl was referred to Ramathibodi Hospital, Mahidol University, Bangkok, Thailand owing to fever lasting one month. The patient had initially been admitted to a regional hospital in Sukhothai Province because of an 8-day history of fever with occasional diarrhea. No previous infections, trauma or surgery were noted, and the patient was empirically treated with intravenous cefotaxime for two days then intravenous vancomycin and metronidazole were added owing to persistent fever (temperature >38°C). Complete blood count showed hemoglobin of 10.3 g/dl, total white blood count of 41,290 cells/µl (62% neutrophils, 21% lymphocytes, 8% monocytes, and 6% band forms) and platelet count of 261,000/µl. Erythrocyte sedimentation rate (ESR) was 128 mm/h. Anti-HIV assay was negative and blood culture sterile.

Six days after administration of above antibiotics, antimicrobial treatment was then modified to intravenous ceftazidime, amikacin and metronidazole as fever had not subsided. On the 18th day of fever, abdominal ultrasound, bone marrow study, eye examination, and echocardiography were carried out but results were unremarkable. Twenty-one days after onset of fever, the patient was still unable to walk but could move equally well both lower extremities. This led to a provisional diagnosis of systemic juvenile idiopathic arthritis and was referred to Ramathibodi Hospital for further evaluation.

On admission, the patient was alert and had normal vital signs, including a temperature of 37.1^{o}C. There were no palpable lymph nodes, the chest was clear on auscultation and the abdomen was soft with no tenderness. The patient had weakness of both lower extremities with a motor power of grade III+/V, but no neurological abnormalities were observed. There were no external wounds or obvious joint swelling. Urination and defecation functions were normal. Complete blood count showed hemoglobin of 8.3 g/dl, total white blood count of 6,100/µl (66% neutrophils, 27% lymphocytes and 7% monocytes) and platelet count of 412,000/µl. All antibiotic treatments were discontinued.

On Day 5 post-admission, the patient still could not stand, was unable to walk and had a limited passive range of motion of the right hip. Muscle power was full, except for the lower limbs with motor power remaining at grade III+/V.

Hypertonia of both lower extremities and positive Babinski sign were observed. Meningeal signs were absent. Plain radiography and ultrasound of both hips were unremarkable. An urgent magnetic resonance imaging (MRI) examination of both hips and the whole spine showed a rim-enhancing lesion with internal septation at the epidural space extending from T11 to S2 levels with osteomyelitis involving the S1 vertebral body (Fig 1).

Multilevel laminotomy with draining of abscess and irrigation were performed. Immediately after the operation the patient was treated with 200 mg/kg BW/day of intravenous cefazolin. Frank pus from an epidural abscess was subjected to aerobic culture but produced sterile results and so a 16S rDNA sequencing was performed (Fuursted *et al*, 2008), which subsequently (after two weeks) revealed an etiological organism with

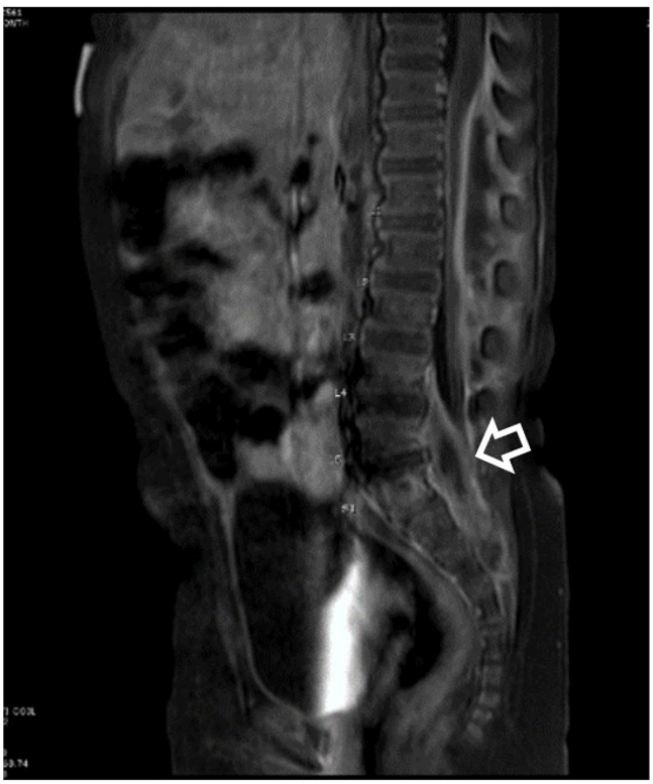

Fig 1 - MRI scan of sagittal fat-suppressed T1W lumbosacral spine of patient

The scan shows a rim-enhancing lesion with internal septation at epidural space extending from T11 to S2 levels (arrow head) with osteomyelitis involving S1 vertebral body causing spinal cord compression with compressive myelopathy.

98.97% identity to *Salmonella enterica* subsp *houtenae* (GenBank accession no. MZ007510). The phylogenetic tree is shown in Fig 2. A diagnosis of *Salmonella* spinal epidural abscess was established and treatment was then changed to 300 mg/kg BW/day of intravenous cefotaxime.

The patient recovered without any sequelae, with normal neurological function 21 days post-surgery and MRI of the spine showing no major change in size and extension of epidural abscess. However, ESR dropped to 15 mm/h. The patient was then transferred to a regional hospital in Sukhothai Province to complete a further 6-week course of intravenous 300 mg/kg BW/day cefotaxime. However, the patient was lost to follow-up, but a telephone inquiry one year later indicated the patient was able to walk and run normally.

DISCUSSION

SEA is uncommon in the pediatric population, with diagnosis frequently delayed until appearance of neurological deficits (Rubin *et al*, 1993), as described in the current case. Thus, deep-seated infection should be extensively sought in young children presenting with prolonged fever and marked leukocytosis without appearance of an etiologic agent. A careful physical examination and appropriate imaging study are necessary for early diagnosis of SEA.

SEA caused by *Salmonella* spp is not common and predominantly occurs in the elderly or immunocompromised subject, such as those with malignancy, diabetes mellitus, human immunodeficiency virus (HIV) infection, or those receiving immunosuppressive agents (El-Herte *et al*, 2011). In the current case, we were not able to identify any source of infection, except for occasional diarrhea, which could be an associated symptom in non-typhoidal *Salmonella* infection (Aoki *et al*, 2017). We surmised the patient might have had a preceding *Salmonella* colonization or *Salmonella* gastroenteritis with subsequent transient bacteremia and focal seeding in the epidural space. The patient tested negative for HIV infection and had been healthy without any recurrent infections, suggesting an underlying primary immune deficiency. The only risk factor for extra-intestinal *Salmonella* infection was the young age; children <6 years of age and adults >60 years of age are at risk for deep infections caused by non-typhoidal *Salmonella* (Lee *et al*, 2005). However, an earlier study reported infants <6 months of age constitute a high-risk group of extra-intestinal non-typhoidal *Salmonella* infection (Sirinavin *et al*, 1988).

Gadolinium-enhanced MRI is considered to be the gold standard for diagnosing SEA (Pradilla *et al*, 2010) and pus culture facilitates specific treatment. In the current case, prolonged use of

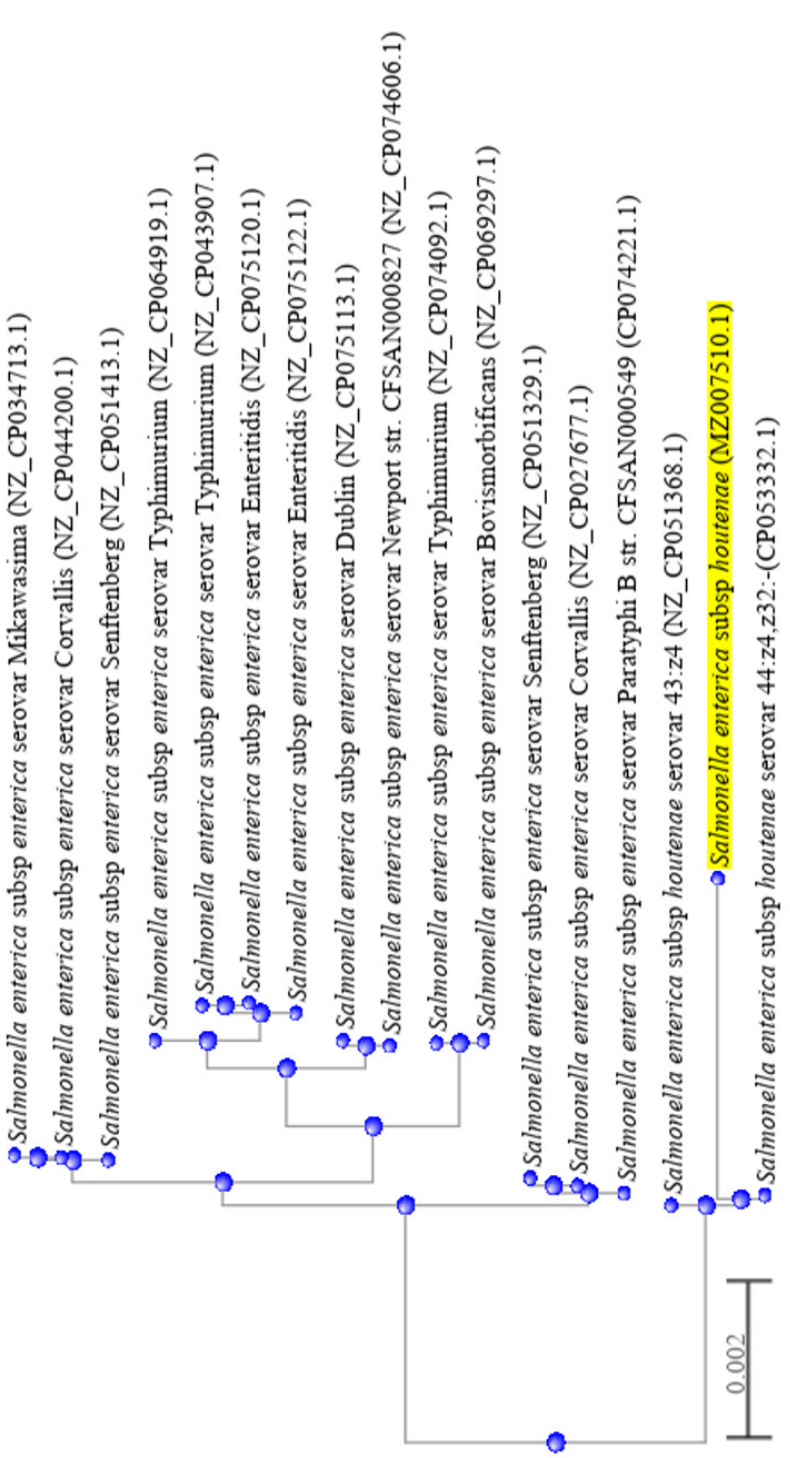

Fig 2 - Phylogenetic tree of *Salmonella enterica* serovars

The tree was constructed from 486-bp amplicon of 16SrDNA using BLAST analysis (https://blast.ncbi.nlm.nih.gov/Blast.cgi). GenBank accession number is shown in parenthesis. Scale bar represents number of nucleotide substitutions per site.

Str: strain

multiple antibiotics, including third-generation cephalosporins to which *Salmonella* might be susceptible, resulted in sterile pus culture. Fortunately, 16S rDNA sequencing revealed the presence of *S. enterica* subsp *houtenae*. This technique has proven useful for identification of etiological organisms of an epidural abscess caused by slow-growing or uncultivable bacteria (Sanmillan *et al*, 2013; Hammer *et al*, 2017), and, as in this case report, this technique was also useful in situations where antimicrobial therapy has been initiated before acquiring pus for culture. In most cases of SEA, empirical antibiotics are usually administered before surgical intervention, which may render standard microbiological techniques for identification of etiologic organisms ineffective. On the other hand, drawbacks of 16S rDNA sequencing technique for organism identification include high cost and inability to test for antibiotic susceptibility.

Surgical intervention and antibiotic therapy remain the standard treatment of SEA (Hawkins and Bolton, 2013). The optimum duration of antibiotics treatment remains unclear and depends on the patient's immune status and response to treatment, clinical improvement, decline in inflammatory markers, and improvement of MRI findings. The majority of SEA patients receive prolonged antimicrobial treatment ranging 4-8 weeks (Vergori *et al*, 2015).

To the best of our knowledge, this is the first pediatric case of *Salmonella* SEA and the first case caused by *S. enterica* subsp *houtenae*, a rare subspecies of *Salmonella*, comprising less than 1% of *Salmonella* spp (Tavechio *et al*, 2002). *S. enterica* subsp *houtanae* usually cohabitates with reptiles, but the origin of this infectious agent in the current case remained unknown. Case reports of infection caused by this organism are summarized in Table 1. Notably, all cases had underlying diseases or extreme age. Interestingly, this organism tends to cause deep-seated abscesses, such as subdural empyema, empyema thoracis and epidural abscess. The outcome of treatment of the infection is excellent in all patients with follow-up data. This supports the notion this subspecies is a non-virulent strain, in contrast to other strains, such as *S. enterica* subsp *typhimurium* (Sirinavin *et al*, 1988), and *S. enterica* subsp *cholerasuis* (Chiu *et al*, 2004). The indolent course of the illness in the current case also supported this subspecies is a non-virulent strain.

In summary, we report a child who first presented with prolonged fever without localizing signs with subsequent inability to bear body weight. *Salmonella* epidural abscess was diagnosed using 16S rDNA sequencing. Because SEA is a rare in children and presents with nonspecific clinical signs and symptoms, this may lead to delayed diagnosis and treatment. A high index of suspicion of SEA should be considered in children with fever and inability in bearing body

Table 1

Case reports of *Salmonella enterica* subsp *houtenae* infections in humans

Reference	Age	Gender	Underlying disease	Sites of infection	Antibiotic treatment	Other treatment	Recurrence	Outcome
Ma *et al* (2003)	44 months	Male	Chronic granulomatous disease	Skin and brain abscess	Ceftriaxone for 84 days	IFN-γ for 53 days	Yes	Full recovery
Wybo *et al* (2004)	2.5 months	Male	None	Meningitis	Ceftriaxone for 10 weeks, and when relapsed, additional ceftriaxone for 6 weeks	None	Yes	Not available
Lourenco *et al* (2004)	33 years	Male	HIV infection	Bacteremia	Not available	None	No	Full recovery
Tabarani *et al* (2010)	5 months	Female	Chronic subdural hemorrhage	Subdural empyema	Ceftriaxone for 6 weeks	Pus drainage	No	Full recovery
Nimir *et al* (2011)	6 weeks	Female	None	Meningitis and empyema	Ceftriaxone and ciprofloxacin for 21 days	Pus drainage	Not available	Full recovery
Mukai *et al* (2018)	76 years	Male	Chronic tuberculous empyema	Empyema thoracis with pneumonia	Ciprofloxacin followed by levofloxacin for 6 weeks	None	No	Full recovery
This report	13 months	Female	None	Spinal epidural abscess	Cefotaxime for 6 weeks	Pus drainage	No	Full recovery

HIV: Human immunodeficiency virus; IFN-γ: Interferon gamma

weight, and immediate MRI allows SEA diagnosis. In addition, 16S rDNA sequencing technique should be considered for bacterial identification of uncultivable bacteria or when antibiotics have been administered prior to pus collection. Prompt surgical drainage and appropriate duration of antibiotics provided excellent therapeutic outcome in the current case.

ACKNOWLEDGEMENTS

The authors thank the parents of the patient for providing prior written consent to report the findings and Edanz Group (https://en-author-services.edanzgroup.com/) for assistance in editing the manuscript.

CONFLICTS OF INTEREST DISCLOSURE

All authors declare no conflicts of interest.

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