CASE REPORT

SALMONELLA ENTERITIDIS VENTRICULITIS

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Abstract. *Salmonella* sp are important causes of meningitis among neonates and young children in Malaysia. We present a case of *Salmonella enteritidis* meningitis in a six week old female who presented with a one week history of fever, diarrhea and seizures which was unsuccessfully treated with a third generation cephalosporin. She had a relapse of meningitis complicated with ventriculitis and hydrocephalus, requiring an eleven week course of meropenem. She improved clinically, but did not have improvement in the cerebrospinal fluid (CSF) glucose level despite prolonged antibiotic use. This case illustrates the dilemma in determining the duration of antibiotic needed to successfully treat *Salmonella enteritidis* ventriculitis.

Keywords: *Salmonella enteritidis*, meningitis, ventriculitis, cerebrospinal fluid glucose, Malaysia

INTRODUCTION

Salmonella infection among children usually presents as gastroenteritis and only requires symptomatic treatment. Rarely, extra-intestinal infections occur especially in the younger age groups (Pickering *et al, 2006*). Central nervous system salmonella infection can include meningitis, hydrocephalus, subdural effusion, empyema and ventriculitis (Lee *et al,* 2000). Ventriculitis presents a treatment dilemma as there are no clear cut guidelines on the duration of antibiotic required. We present a six weeks old infant with *Salmonella enteritidis* meningitis complicated with ventriculitis.

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CASE REPORT

A six week old female was admitted to our hospital with a four day history of fever, seizures and loose stool at home. She had no vomiting, cough, runny nose, rashes or eye or ear discharge. She had been born at full term, via a normal vertex delivery and was discharged home in a well condition of age twenty-four hours of life.

Upon presentation to the hospital her temperature was 39ºC. She was irritable and had inconsolable crying. Her anterior fontanelle was full and bulging. Hemodynamically, she was stable. Her peripheral limb tone was increased with brisk reflexes. She had marked hepatosplenomegaly. Her other systems were unremarkable.

She was diagnosed as having meningitis. Three attempts to abtain cerebrospinal fluid (CSF) were unsuccessful. Her initial leukocyte count was 2.2 x 10^9/l, her platelet count was 169 x 10^9 /l and her hemoglobin was 8.0 g%. She was initially treated with ceftriaxone and the fever abated rapidly. Blood cultures grew *Salmonella* sp which was sensitive to ceftriaxone, tetracycline, trimethoprim-sulphmethoxazole, ciprofloxacin and chloramphenicol but was resistant to ampicillin. An ultrasound of the head revealed a possible sub-arachnoid hemorrhage which was confirmed with a computed tomographic scan. Her initial coagulation profile also showed normal prothrombin time of 14.3 seconds with prolonged activated partial thromboplastin time of 71.6 seconds. Intravenous vitamin K was given for three days and her coagulation profile normalized.

Her final diagnosis was Salmonella meningitis. She had seizures in the ward which responded well with phenytoin. She showed improvement with resolution of fever. Her head circumference was monitored closely and showed no sudden enlargement. Repeat blood cultures were negative and the inflamatory marker c-reactive protein levels normalized. No surgical drainage was required for the sub-arachnoid hemorrhage which resolved by two weeks; this was confirmed with magnetic resonance imaging (MRI) of the brain. However, MRI revealed presence of mild bilateral hydrocephalus, also treated conservatively. She completed four weeks of ceftriaxone and was subsequently discharged home well, with follow-up appointment to monitor her head circumference and neurodevelopment.

However, she was readmitted after three weeks with a one week history of fever and recurrent seizures at home. Her head circumference had rapidly increased by three cm within three weeks. An urgent CT scan revealed enlarging hydrocephalus. Urgent external ventricular drainage (EVD) was performed to relieve hydrocephalus. The CSF collected had a greenish tinge and grew *Salmonella enteritidis*. The initial CSF white bllod cell count was more than 1,000 cells/ml with protein of 1.2 g/l and glucose of 1.2. She was treated for *Salmonella enteritidis* ventriculitis with meropenem. Clinically, her temperature gradually improved and the anterior fontanelle became flat. Her CSF was monitored on a weekly basis using an Omaya reservoir inserted after three weeks in the hospital. Her CSF white blood cell count reduced gradually and subsequent CSF cultures were negative. However, her CSF glucose levels remained consistently low; ranging between 15-20% of the serum glucose. She completed eleven weeks of meropenem with normalization of all blood markers. A ventriculoperitoneal shunt was inserted during the stay. She was discharged well at the completion of three months of treatment. Hearing assessment revealed right unilateral mild hearing loss. Her human immunodeficiency virus screen was negative and her serum immunoglobulin levels, T and B cells counts and phagocytic function were all found to be normal.

At follow-up she was found to be normal and attaining developmental milestones. There was a satisfactory growth of her head with no seizures since discharge. At one year of age, there were not any obvious residual neurological sequelae.

DISCUSSION

Salmonella enteritidis constitutes about 14% of all *Salmonella* sp infections in humans (CDC, 2008). Extra-intestinal manifestations of *Salmonella enteritidis* are uncommon, but include septic arthritis, endocarditis, urinary tract infections, pneu-

monia and meningitis. Salmonella meningitis is uncommon in developed countries but is an emerging cause of gram-negative bacterial meningitis in developing nations especially in infants and young children (Miller *et al*, 2008). It is associated with high mortality, neurological sequelae in survivors and a high relapse rate (Kavaliotis *et al*, 1994). Complications of Salmonella meningitis include subdural effusions, hydrocephalus, cerebral infarctions, subdural empyema, brain abscess, encephalitis and ventriculitis (Baraff *et al*, 1993). In Malaysia, only 5% of culture confirmed bacterial meningitis cases are caused by *Salmonella* sp (Lee *et al*, 1999). Other notable findings are a mortality rate of 18% with 35% relapse rate (Lee *et al*, 1999). Mortality rates in most series, range from 0 to 31% (Mishu *et al*, 1994; Angulo and Swerdlow, 1999). Most previous reports are limited in sample size with only a few case series having more than five cases.

Antibiotic treatment for non-typhoidal *Salmonella* meningitis includes ampicillin, amoxicillin, cefotaxime, ceftriaxone, chloramphenicol, trimethoprim-sulphamethoxazole and fluoroquinolones (Agrawal *et al*, 2008). Third generation cephalosporins have a high degree of cerebrospinal fluid (CSF) penetration with rapid clearance of organisms (Saez-Llorens *et al*, 1995). Huang *et al* (1997) noted 18% mortality with no relapses with cefotaxime usage in his series. Lee *et al* (1999) found no treatment failures with third generation cephalosporins. However in our patient, clinical relapse occurred despite four weeks of treatment with ceftriaxone. This raises the question of inadequacy of treatment duration in our patient. A prolonged course of antibiotics may be necessary to prevent frequent relapses and mortality associated with *Salmonella* sp meningitis. Other possible causes for this failure could be resistance of the organism to ceftriaxone despite *in-vivo* sensitivity shown initially. Resistance of *Salmonella* sp to cephalosporins has been documented before; in a recent study from the United States, data from the National Antimicrobial Resistance Monitoring System showed 58% of *Salmonella* spp were resistance to at least one antibiotic and 3 multidrug-resistant strains accounted for 74% of isolates (Rodrigue *et al*, 1992).

Our patient developed Salmonella ventriculitis, which was confirmed with a positive CSF culture obtained from external ventricular drainage. Lyke *et al* (2001) defined ventriculitis as the culture of a recognized pathogen from the CSF either at the time or within 2 days of intraventricular catheter insertion. Other criteria are progressively declining CSF glucose and increasing CSF protein accompanied by CSF pleocytosis with clinical sign of meningitis (Lozier *et al*, 2002). Ventriculitis might be a cause of persistent infection and therapeutic failure in the management of meningitis. Carbapenem use has been studied in patients with bacterial meningitis. Meropenem has broad *in vitro* coverage and less seizure proclivity than imipenem, making it a preferred choice in patients with cephalosporin resistant strain (Odio *et al*, 1999).

Most of the literature we reviewed agreed a minimum duration of antibiotics is four weeks (Mahapatra *et al*, 2002; Pickering *et al*, 2006). Our patient was treated with a prolonged course of meropenem since her CSF glucose failed to show improvement. However, the CSF pleocytosis resolved and the CSF protein normalized. There were no further positive CSF cultures after the initial positive culture. She also had clinical improvement and was able to be discharged well. She did

not demonstrate any obvious neurological sequelae at 1 year of age but will require further neurodevelopmental follow-up.

Our case report poses a question of the optimum duration of antibiotic treatment for treating *Salmonella enteritidis* meningitis complicated with ventriculitis. Further studies are needed to look at the role of CSF glucose as a parameter to gauge clinical and biochemical improvement.

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