Original Article

Salmonella Meningitis: a Report from National Hue Central Hospital, Vietnam

Dinh Quang Tuan 1, Pham Hoang Hung 1, Phan Xuan Mai 1, Tran Kiem Hao 1, Chau Van Ha 1, Nguyen Dac Luong 1, Nguyen Huu Son 1, Nguyen Thi Nam Lien 2, Junko Yamanaka 3, Noriko Sato 3, and Takeji Matsushita 3 *

1Department of Pediatrics and 2Department of Microbiology, National Hue Central Hospital, Hue, Vietnam; and 3Department of Pediatrics, National Center for Global Health and Medicine, Tokyo, Japan

SUMMARY: Four Vietnamese infants who survived infection with Salmonella meningitis are reported. A female infant who experienced relapse recovered without complications and another had neurological sequelae. The remaining 2 infants survived without complications. The initial treatment was chloramphenicol and ceftriaxone, whereas a change of antibiotics to imipenem and fluoroquinolone was required for 2 infants. Fluoroquinolone may be a treatment option in patients with Salmonella meningitis who experience complications even though the drug is contraindicated for the pediatric age group.

INTRODUCTION

Four cases of Salmonella meningitis, considered to have a poor prognosis in neonates or infants, are reported from National Hue Central Hospital, Vietnam. National Hue Central Hospital treats more than 10,000 children who are admitted annually. The hospital is located in Hue, which is a city in central Vietnam with a population of more than one million people. All 4 infants were Vietnamese and less than 1-year-old. Their ages ranged from 32 days to 6.5 months. The choice of antibiotic used to treat Salmonella meningitis is important because several antibiotics routinely used to treat bacterial meningitis of other causes are reportedly ineffective as the initial treatment. The 2 initial cases were successfully treated with cephalexin and chloramphenicol (CP), whereas the other 2 cases required therapy with imipenem (IPM) and fluoroquinolone. The average duration of antibiotic therapy was 7 weeks. One patient suffered recurrence of meningitis after 4 weeks of treatment, and the second patient experienced neurologic complications with bilateral ventricular dilation and subdural effusion. Although a third generation cephalosporin and CP were the first line treatment for Salmonella meningitis until recently, IPM and fluoroquinolone should also be considered when gram-negative rods are detected in the cerebrospinal fluid (CSF). Although the indication for fluoroquinolone in children is controversial, this drug should be considered as an effective choice for this type of pediatric meningitis.

MATERIALS AND METHODS

A retrospective analysis via chart review was performed for 4 children who were treated for Salmonella meningitis between 2003 and 2008 at National Hue Central Hospital in Hue, Vietnam. Salmonella meningitis was defined as purulent meningitis when Salmonella sp. was cultured from CSF at the onset of the disease. Clinical review included patient history, symptoms, signs, laboratory data, treatment, course, and outcome. Laboratory data included an examination of blood, CSF, and bacterial culture. The isolated bacteria were examined for sensitivity to the following antibiotics: ampicillin (ABPC), cefazolin (CEZ), cefotaxime (CTX), ceftriaxone (CXR), IPM, gentamicin (GM), CP, norfloxacin (NFLX), ofloxacin (OFLX), and ciprofloxacin (CPFX).

RESULTS

Among 187 cases of purulent meningitis treated at Hue Central Hospital from 2003 to 2008, 4 were caused by Salmonella sp. The clinical courses of the 4 cases were as follows.

Case 1: A 3.5-month-old female was admitted to Hue Central Hospital in November 2003 following 1 week of fatigue, fever, and diarrhea. On admission, her appearance was poor because of unconsciousness, convulsions, and a temperature of 40°C. She exhibited a decerebrate posture and weak papillary light reaction without anisocoria. Bulging fontanelle, a stiff neck, and Kernig’s sign were absent. There were no respiratory or circulatory abnormalities. She was born at term after an uncomplicated pregnancy with a weight of 3,100 g, and she had been well until disease onset. Her parents were healthy without gastrointestinal symptoms. Her CSF was turbid because of pleocytosis, and gram-negative bacilli were present. CSF culture yielded Salmonella enterica Claibornei. She was discharged in good health after 4 weeks of treatment with CTRX (100 mg/kg/day) plus CP (100 mg/kg/day), but was readmitted because of recurrence of Salmonella meningitis 2 weeks later. She recovered following an additional 8-week course of treatment with the same antibiotic combination.

Case 2: A 32-day-old female was admitted in September 2004. The child displayed refusal to feed with lethargy and a weak cry beginning 1 day before admission. She had high-grade persisting fever, bulging anterior fontanelle, and convulsions. A motor system ex-
Table 1. Clinical and laboratory features of 4 cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age (Mo)</th>
<th>Admission date</th>
<th>Admission</th>
<th>Continuous fever (≥38.5°C)</th>
<th>Vomiting</th>
<th>Blood Examination</th>
<th>CSF Examination</th>
<th>Antiibiogram</th>
<th>Stool Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>female</td>
<td>3.5</td>
<td>10/Nov/2003</td>
<td>7 days</td>
<td>+</td>
<td>—</td>
<td>Hb (g/dl): 8.6</td>
<td>WBC/mm³: 2,500</td>
<td>Salmonella</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>female</td>
<td>32 days</td>
<td>12/Sept/2004</td>
<td>1 day</td>
<td>+</td>
<td>—</td>
<td>Leukocytes: 12.5</td>
<td>WBC/mm³: 2,160</td>
<td>Claibornei</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>female</td>
<td>6.5</td>
<td>08/Aug/2008</td>
<td>1 day</td>
<td>+</td>
<td>+</td>
<td>Neutrophils: 56</td>
<td>WBC/mm³: 620</td>
<td>arizonae</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>female</td>
<td>5</td>
<td>08/Aug/2008</td>
<td>1 day</td>
<td>+</td>
<td>+</td>
<td>CRP (mg/l): 51.4</td>
<td>WBC/mm³: 1,440</td>
<td>Salmonella</td>
<td>—</td>
</tr>
</tbody>
</table>

Blood examination:
- Hb (g/dl): 8.6 - 8.6
- Leukocytes (×10⁹/l): 12.5 - 6.2
- Neutrophils (%): 56 - 6.2
- CRP (mg/l): 51.4 - 176.2
- Glucose (mmol/l): 6.2 - 7.7
- Na⁺ (mmol/l): 130 - 131

Blood culture:
- —

CSF examination:
- WBC/mm³: 2,500 - 620
- Neutrophils (%): 90 - 95
- Gram stain: GNR - GNR
- Glucose (mmol/l): 0.2 - 0.8
- Protein (g/l): 1.71 - 1.56

Culture:
- Salmonella Claibornei
- Salmonella arizonae
- Salmonella sp.
- Salmonella Paratyphi B

Antibiogram:
- Sensitive to all antibiotics

Stool examination:
- —

Table 2. Clinical courses

<table>
<thead>
<tr>
<th>Case</th>
<th>Initial antibiotics</th>
<th>2nd antibiotics</th>
<th>Stable general state</th>
<th>1st treatment duration</th>
<th>Time of relapse after treatment</th>
<th>2nd treatment duration</th>
<th>Post-treatment fontanel echography</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CTRX + CP</td>
<td>CTRX + CP</td>
<td>13 days</td>
<td>4 weeks</td>
<td>2 weeks</td>
<td>8 weeks</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>CTRX + CP</td>
<td>CTRX + CP</td>
<td>11 days</td>
<td>7 weeks</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>CTRX + CP</td>
<td>IPM + CPFX</td>
<td>13 days</td>
<td>8 weeks</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>CTRX + CP</td>
<td>IPM + CPFX</td>
<td>13 days</td>
<td>6 weeks</td>
<td>—</td>
<td>—</td>
<td>Dilated lateral ventricles, subdural fluid collection</td>
</tr>
</tbody>
</table>

1): disease day after onset.
2): Sensitivity was tested for ABPC, CEZ, CTX, CTRX, IPM, GM, CP, NFLX, OFLX, and CPFX.

Mo, months; GNR, gram-negative rods; ABPC, ampicillin; CEZ, cefazolin; CTX, cefotaxime; CTRX, ceftriaxone; IPM, imipenem; GM, gentamicin; CP, chloramphenicol; NFLX, ofloxacin; OFLX, ofloxacin; CPFX, ciprofloxacin.

amination revealed increased tone in the extremities and hyperreflexia with clonus. She was delivered normally near term weighing 2,200 g, and she cried immediately after birth. No abnormalities were observed during the neonatal period. Her parents were healthy without infectious symptoms. CSF was turbid because of pleocytosis, displaying gram-negative bacilli, and Salmonella enterica subsp. arizonae was cultured. She was administered CTRX (100 mg/kg/day) and CP (100 mg/kg/day) and discharged in good health after 7 weeks of treatment.

Case 3: A 6.5-month-old female was admitted in August 2008 due to high fever and convulsions with loss of consciousness. Her medical history was unremarkable. She was delivered at term weighing 3,300 g. She had been febrile, with vomiting and diarrhea, for 4 days before admission. On physical examination, she was febrile, lethargic, and mildly dehydrated with brisk lower limb reflexes. CSF was turbid because of pleocytosis, displaying gram-negative bacilli, and Salmonella sp. She was discharged in good health after an 8-week course of treatment with IPM (50 mg/kg/day) and CPFX (30 mg/kg/day) following the initial treatment with CTRX and CP. Subdural effusion and hydrocephalus during her clinical course resulted in mild-to-moderate neurological deterioration.

Case 4: A 5 month-old female was admitted in September 2008 due to high fever, restlessness, convulsions, nausea, and coughing. Her medical history included hospitalization 2 weeks earlier for acute gastroenteritis. Stool culture had yielded no Salmonella sp. on that occasion. She was delivered vaginally at term, after an uncomplicated pregnancy, weighing 2,600 g. Her parents and elder sister were healthy without gastrointestinal symptoms. Her CSF was turbid because of pleocytosis, exhibiting gram-negative bacilli, and culture yielded Salmonella Paratyphi B. She was discharged in good health after 6 weeks of treatment with IPM and CPFX.
following treatment with CTRX and CP. Laboratory examinations revealed leukocytosis and pleocytosis of CSF in all cases. Widal reactions were all negative. Bacterial culture isolated Salmonella spp. from CSF but not from stool samples.

**DISCUSSION**

Bacterial meningitis is an important pediatric disease because it generally has a poor prognosis in infants and young children, but intact survival without neurological sequel can be expected if the illness is diagnosed early and treated promptly. Salmonella infection as a cause of bacterial meningitis is reported primarily in tropical areas (1,2), but also occasionally in industrialized countries (3–5). Most cases of Salmonella meningitis involve children less than 1 year of age, primarily less than 3 months old (3,4). Underlying disorders, such as human immunodeficiency virus infection, malaria, or malnutrition, may act as causative factors. The poor prognosis of Salmonella meningitis has been emphasized to reflect that of bacterial meningitis in general (6). The mortality rate and incidence of neurological complications because of Salmonella meningitis are high, especially in Africa (6,7).

The 4 patients described here had typical clinical features of Salmonella meningitis, and they recovered following repeated administration or a change of antibiotics. Salmonellosis is recognized as a food borne infection, and the route is believed to be the same in infants. Gastrointestinal symptoms are rare in mothers and other family members even though most cases occur in neonates or infants.

Reports on Salmonella surveillance in asymptomatic family members of patients are rare. However, Salmonella infection is suspected when there might be a carrier of Salmonella among family members. As the mother has the most contact with an infant, the pathogen may readily be transmitted from mother to child. There are case reports of Salmonella meningitis that have described the isolation of Salmonella from maternal breast milk (4,8). Breast milk is known to be protective against many infectious diseases. It has thus been emphasized that breastfeeding should not be stopped or reduced because of the risk of transmitting the Salmonella meningitis pathogen, considering that breast milk itself reduces Salmonella infection rates in children (9).

Gram-negative rods were identified in CSF by microscopic examination, and Salmonella spp. were cultured in the 4 cases described. Laboratory findings for this organism were the same as those for other causes of bacterial meningitis. Blood examination revealed leukocytosis and positive inflammatory reactions. CSF exhibited pleocytosis, decreased glucose levels, and increased protein content. Blood cultures were negative in all 4 cases.

The initial treatment was CTRX plus CP. Case 1 experienced recurrence of meningitis despite the apparent success of the initial treatment. She was retreated with the same antibiotic combination. Antibiotics were changed due to slow clinical responses in cases 3 and 4. Subdural abscess and dilated ventricle resulted in neurological delay in case 3. Salmonella meningitis should be considered when gram-negative rods are identified in CSF. Gram-negative rods that cause meningitis include Escherichia coli, and Salmonella spp. Until recently, disease recurrence was occasionally reported for Salmonella meningitis, even when patients received ABPC and CP for sufficient periods (10). CP has limited efficacy because of the increasing prevalence of resistance and undesirable side effects (7). It is necessary to administer the most appropriate treatment based on laboratory test findings.

Clinical improvement is achieved with IPM and fluoroquinolone. The use of fluoroquinolone is sometimes advocated (2,3,10), although its use is discouraged in young children because of possible adverse effects. The drug should be considered an effective choice for treating meningitis in special clinical settings.

In conclusion, Salmonella meningitis occurs mainly in tropical countries in infants, and it is considered to have a poor prognosis compared to other forms of bacterial meningitis. The selection of initial antibiotics is important for sequelae-free survival. Combining IPM and fluoroquinolone may improve survival and neurological outcomes in complicated cases. The use of fluoroquinolone in children is controversial, but it should be considered as an effective treatment against bacterial meningitis caused by gram-negative rods.

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**Conflict of interest** None to declare.

**REFERENCES**


