Brain abscess as a complication of Salmonella meningitis in an infant: What can we learn from this case?

Novia, Dewi Sutriani Mahalini*, I Gusti Ngurah Made Suwarba¹

INTRODUCTION

Brain abscess is a localized supplicative intracranial infection that accounts for approximately 8% of space-occupying lesions in developing countries.¹ The decline in mortality rates associated with brain abscesses has been attributed to improved hygiene, vaccination, diagnostic imaging allowing for earlier detection, advanced neurosurgical techniques, and broad-spectrum antibiotics covering aerobic and anaerobic organisms.² Despite the decrease in mortality rates, brain abscess remains a life-threatening condition that progresses rapidly, leading to long-lasting and severe neurological complications.³ Focal intracranial infection caused by Salmonella sp. is a rare clinical manifestation of extraintestinal salmonellosis.⁴ It is commonly observed in individuals with predisposing factors such as prior meningitis, trauma, and intracranial hemorrhage. Salmonella meningitis accounts for only 1% of meningitis cases in developed countries; however, in developing countries, it may occur in up to 13%.⁵ Salmonella meningitis predominantly affects neonates and infants and is associated with several complications, high morbidity, and mortality.⁶

CASE PRESENTATION

An eight-month-old male infant was admitted to our hospital with a focal tonic-clonic seizure and decrease of consciousness (GCS E3V2M4). The seizure lasted for approximately an hour before subsiding after the patient received phenytoin and phenobarbital intravenously. One day prior to the seizure, the patient experienced a high fever and projectile vomiting on approximately three occasions. History of traumatic injury or congenital heart disease was denied. The infant is the firstborn child of a mother without a history of seizure disorders in the family. Neither the mother nor the child had any known immunocompromising conditions or risk factors for blood-borne diseases. The infant had an unremarkable prenatal and intranatal history and was breastfed until two months of age before being transitioned to formula milk.

The patient had a history of prior admission to the hospital when he was six months old, diagnosed with bacterial meningitis caused by Salmonella species (sp.). Improvement was observed during the hospital stay; however, the patient developed focal epilepsy, communicating hydrocephalus, and subsequent cerebral palsy as sequelae. The infant had a prior admission to the hospital at 6 months old when he was diagnosed with bacterial meningitis caused by Salmonella sp., treated with intravenous antibiotics for 21 days. Although the last cerebrospinal fluid (CSF) culture evaluation was sterile, slight pleocytosis and low glucose on CSF analysis persisted.

Conclusion: Longer antibiotic administration, up to 4–6 weeks, might be considered for treating Salmonella meningitis. Evaluation of CSF culture, along with CSF analysis and neuroimaging studies, should be carefully considered to determine the appropriate duration of treatment.

Keywords: Salmonella, meningitis, brain abscess, pediatric.


ABSTRACT

Background: Salmonella species (sp.) is a rare yet challenging causative organism of meningitis in the pediatric population. Salmonella meningitis has been reported to present with a more severe clinical course, poorer outcome, and higher degree of complications and relapses.

Case Illustration: An 8-month-old male infant was admitted to our hospital with a history of focal tonic-clonic seizure, fever, projectile vomiting, and a decrease in consciousness. A head CT scan revealed a brain abscess in the frontal-temporoparietal region. The patient was administered a triple combination of intravenous antibiotics as the empirical treatment, followed by craniotomy for abscess evacuation. The abscess specimen culture isolated the growth of Salmonella sp. Improvement was observed during analysis and neuroimaging studies, should be carefully considered to determine the appropriate duration of treatment.

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sp. based on CSF and blood culture results. The antimicrobial susceptibility test showed that the organism was susceptible to Ampicillin, Piperacillin/Tazobactam, Cefixime, Cefoperazone, Ceftriaxone, Cefepime, Meropenem, and Trimethoprim/Sulfamethoxazole but resistant to Gentamicin, Cefuroxime, and Amikacin.

We present the results of CSF on his second admission to the emergency department at eight months old before the diagnosis of brain abscess was established (Table 1) and the previous CSF analysis when he was first diagnosed with bacterial meningitis at six months old (Table 2).

At six months old, the patient underwent an urgent brain computed tomography scan (CT scan) without contrast at the emergency department, which revealed brain edema with subdural hygroma at the left and right frontoparietal regions. A second head CT scan was performed at eight months old, which showed an epidural brain abscess at the right fronto-temporo-parietal region with perifocal edema, subdural hygroma at the left frontal region, active communicating hydrocephalus, and cerebral edema. A comparison was made between the current head CT scan and the previous head CT scan taken at six months old (Figure 1).

When the patient was diagnosed with bacterial meningitis at six months old, he was treated with Ceftriaxone intravenously for 21 days based on the results of the antibiotic susceptibility test. He was discharged in good condition. During his current admission for brain abscess, he received empirical treatment with triple intravenous antibiotics (Ceftriaxone, Metronidazole, and Vancomycin), craniotomy for abscess evacuation, and supportive therapy such as mannitol, dexemethasone, and antiepileptic drugs (phenobarbital and phenytoin). An abscess specimen collected from the abscess evacuation revealed Salmonella sp. as the causative agent. The organism was susceptible to Ampicillin, Cefuroxime, Cefixime, Cefoperazone, Ceftriaxone, Cefepime, Meropenem, Levofloxacin, and Trimethoprim/Sulfamethoxazole but resistant to Amikacin. The result was similar to the previous culture result obtained when he was six months old.

Intravenous antibiotics were administered for six weeks, after which the patient underwent a head CT-scan evaluation that showed improvement of the brain abscess. However, active communicating hydrocephalus and subdural hygroma at the left frontal region persisted (Figure 2a). Oral antibiotics (Cefixime and metronidazole) were prescribed for two weeks. During the remainder of the hospital stay, the patient did not experience any recurrent seizures, fever or vomiting. On a subsequent outpatient visit after discharge, the patient presented with a focal seizure. EEG examination revealed abnormal III, indicating moderate to severe brain hypofunction with multifocal epileptiform waves. The seizures were controlled with medication, and no further seizures were reported. Six months after the completion of treatment, another head CT scan was performed, which revealed persistent communicating hydrocephalus (Figure 2b).

Combination treatment of craniotomy abscess aspiration and intravenous antibiotics resulted in an improvement in the patient’s condition. However, complications were observed as the patient presented with focal epilepsy, communicating hydrocephalus, and subsequent cerebral palsy as sequelae. A Magnetic Resonance Imaging (MRI) assessment conducted one year after completing treatment revealed communicating hydrocephalus (Figure 3). The option of a ventriculoperitoneal

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**Table 1. CSF analysis on current admission to the emergency department**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Current CSF analysis (at 8 months old)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Clear</td>
</tr>
<tr>
<td>Nonne</td>
<td>+2</td>
</tr>
<tr>
<td>Pandy</td>
<td>+2</td>
</tr>
<tr>
<td>Erythrocyte</td>
<td>Negative</td>
</tr>
<tr>
<td>Total cell count</td>
<td>65 cell/µL</td>
</tr>
<tr>
<td>Monomorphonuclear cell (MMN)</td>
<td>100%</td>
</tr>
<tr>
<td>Polymorphonuclear cell (PMN)</td>
<td>0</td>
</tr>
<tr>
<td>Glucose</td>
<td>83 mg/dL</td>
</tr>
<tr>
<td>Total protein</td>
<td>107.8 mg/dL</td>
</tr>
<tr>
<td>CSF culture</td>
<td>No growth</td>
</tr>
</tbody>
</table>

*CSF analysis was obtained in the emergency department when the diagnosis of brain abscess had not been established yet.

**Table 2. CSF analysis at previous admission when the patient was diagnosed with bacterial meningitis at 6 months old**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Previous CSF analysis (at 6 months old)</th>
<th>1st CSF evaluation (antibiotic day 7)</th>
<th>2nd CSF evaluation (antibiotic day 14)</th>
<th>3rd CSF evaluation (antibiotic day 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
</tr>
<tr>
<td>Nonne</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
</tr>
<tr>
<td>Pandy</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
</tr>
<tr>
<td>Erythrocyte</td>
<td>Negative</td>
<td>0-1 cell/µL</td>
<td>0-1 cell/µL</td>
<td>Negative</td>
</tr>
<tr>
<td>Total cell count</td>
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<td>165 cell/µL</td>
<td>111 cell/µL</td>
<td>66 cell/µL</td>
</tr>
<tr>
<td>MMN</td>
<td>40%</td>
<td>53%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>PMN</td>
<td>60%</td>
<td>47%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Glucose</td>
<td>25 mg/dL</td>
<td>16 mg/dL</td>
<td>18 mg/dL</td>
<td>18 mg/dL</td>
</tr>
<tr>
<td>Total protein</td>
<td>143.9 mg/dL</td>
<td>82.3 mg/dL</td>
<td>66.8 mg/dL</td>
<td>71.7 mg/dL</td>
</tr>
<tr>
<td>CSF culture</td>
<td>Salmonella sp.</td>
<td>Salmonella sp.</td>
<td>Salmonella sp.</td>
<td>No growth</td>
</tr>
</tbody>
</table>

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A brain abscess is a suppurative infection that develops within the cerebral parenchyma as a complication of other conditions such as meningitis, otitis media, mastoiditis, sinusitis, dental infection, bacterial endocarditis, or congenital heart defects. Pediatric brain abscess is a life-threatening condition that can result in mortality rates of up to 10-12% and long-term morbidity rates of 30-50%. Infants and toddlers are especially vulnerable to brain abscesses as a complication of bacterial meningitis.  

Salmonella is a motile gram-negative bacillus that produces Hydrogen Sulfide (H$_2$S), a non-spore-forming, facultative anaerobic bacterium. Its natural habitat is the intestinal tract of humans and animals. There are over 2500 designated Salmonella serotypes based on the immunoreactivity of the O and H antigens. Salmonella organisms are classified as either Salmonella associated with enteric fever (Salmonella typhi or Salmonella paratyphi) or nontyphoidal Salmonella (NTS) based on the clinical disease. The main transmission mode is fecal-oral, and contaminated foods or carriers are common sources of infection. Although bacteremia, sepsis, and meningitis are relatively common in infants, intracranial infection caused by Salmonella sp. is considered a relatively rare clinical entity, accounting for less than 1% of confirmed cases in neonatal and infantile age groups.  

Brain abscess may be asymptomatic in the early stages, and the clinical presentation depends on various factors such as the location of the lesion, the pathogenic organism, and the host immune status. The clinical presentation of brain abscess vary widely among patients. Commonly reported symptoms include altered level of consciousness, headache, fever, and vomiting, each occurring in 60-70% of cases. Seizures and focal neurologic signs occur in 25-50% of cases. The "classic triad" of fever, headache, and meningitis is only present in 20% of pediatric patients with brain abscess.  

The combination of signs indicating increasing intracranial pressure, with or without focal neurologic dysfunction,
suggests the possibility of a mass lesion and warrants neuroimaging. Neuroimaging techniques such as CT-scan or MRI can confirm the diagnosis of brain abscess, determine the location and number of lesions. Most abscesses appear as an area of decreased density surrounded by a rim of intense enhancement, which is referred to as a ring lesion on CT-scan. No specific features are found in the symptoms or signs and in routine and biochemical tests for intracranial infection caused by *Salmonella* sp. The clinical manifestation in younger children tends to be more atypical. Therefore, diagnosing *Salmonella* infection mainly relies on CSF culture, while cultures of blood, stool, bone marrow, and other specimens can be valuable for facilitating its diagnosis.

The basic principle of treating brain abscess is appropriate antibiotics with or without aspiration, treating sequelae, and eradicating the primary source. The choice between conservative versus operative treatment is influenced by age, neurological status, location, number, size, and stage of abscess formation. Each case must be individualized and treated based on its own merits. Combination therapy with broad-spectrum or organism-specific antimicrobial therapy and surgical drainage is the preferred treatment for most cases of brain abscess. For small-sized lesions (<2.5 cm), multiple abscesses, and deep-seated lesions, antimicrobial therapy alone may be used.

Therapy should be narrowed when a specific organism or multiple organisms are identified. Parenteral antibiotics are required for 4 to 6 weeks in surgically treated abscesses, and 6 to 8 weeks for those with medical treatment only. *Salmonella* intracranial infection management has not been well-defined. Recent studies show that *Salmonella* strains are resistant to ampicillin, while their sensitivity to Ceftriaxone is still relatively high, and almost all of them are sensitive to carbapenems. Third-generation cephalosporins (such as Ceftriaxone) are recommended as initial empiric therapy for intracranial infection caused by *Salmonella*, and carbapenems may be considered for those with poor efficacy. Combining cephalosporins with other antibiotics appears to have produced promising results. However, *Salmonella* meningitis has a high relapse rate.

In our case, the patient presented with a brain abscess caused by *Salmonella* sp., obtained from the abscess specimen culture’s result following previous bacterial meningitis caused by the same organism, *Salmonella* sp., revealed from the CSF and blood culture’s results. The patient had been treated with an appropriate antibiotic based on the organism susceptibility (Ceftriaxone) for the previous *Salmonella meningitis*. Before the antibiotic was decided to be stopped after the duration of administration of 21 days, the CSF revealed no organism growth from the culture result, yet it was still presented with slight pleocytosis (total cell count 66 cell/µL) and low CSF glucose (18 mg/dL). Studies have shown that non-typhoid salmonella (NTS) persists in CSF for at least 3 to 4 weeks. The documented relapse rate of NTS meningitis is up to 60%. The rate of relapse declined with increasing length of antibiotic therapy. Duration of treatment with appropriate antibiotic for more than 4 weeks seems reasonable, with the optimal duration probably being 6 weeks. The American Academy of Pediatrics (AAP) recommends that treatment for *Salmonella* meningitis with Cefotaxime or Ceftriaxone should continue often for 4 weeks or more and suggests that localized invasive *Salmonella* disease should be treated for at least 6 weeks to prevent relapse.

Moon et al. (2022) reported a similar case where the duration of antibiotic (Ceftriaxone) administration was 4 weeks from the first sterile CSF culture, and the patient was discharged home without any complications. The patient remained healthy without any neurologic sequelae at the five-month follow-up. Other case series by Zhao et al. (2021) consisting of 3 cases of *Salmonella* meningitis showed a duration of antibiotic (Meropenem) administration for 3-5 weeks. One patient died, and subdural effusion occurred in one of the two survivors. Previous studies have reported a duration of antibiotic administration in *Salmonella* meningitis ranging from 3 to 8 weeks.

It is crucial to continually assess the clinical course and follow-up laboratory and imaging examinations to establish the appropriate duration of antimicrobial therapy. In cases of bacterial meningitis with a complicated course, such as persistent positive CSF; a neuroimaging evaluation should be performed before discontinuing therapy, especially in neonates or older infants. Neuroimaging studies are recommended for every case of *Salmonella* meningitis even if the patient has presented an apparent clinical resolution and optimal response to antibiotics due to risk of relapse.
Based on our experience with this case, we suggest that a longer duration of antibiotics up to 4-6 weeks may be considered for treating Salmonella meningitis. A shorter duration of treatment was associated with a higher risk of relapse. Therefore, the evaluation of therapy should aim to achieve sterile CSF culture and normal CSF analysis and neuroimaging. Considering these parameters might give us a better estimation in determining the appropriate duration of antibiotic administration for Salmonella meningitis in each patient.

Intracranial infection caused by Salmonella sp. is associated with a higher degree of complications, significant neurological sequelae, relapse rate and mortality compared to meningitis caused by other gram-negative pathogens. Children with NTS meningitis are frequently complicated by seizures, abscesses, hydrocephalus and subdural empyema, and may have severe developmental delay and motor disabilities.19

In this case, the patient was diagnosed with a brain abscess two months after the previous Salmonella meningitis. Combination treatment with craniotomy abscess aspiration and antibiotics with a total therapy duration of 8 weeks resulted in an improvement of the patient’s condition. At one-year follow-up, the patient did not experience any relapse but presented with neurological sequelae, including hydrocepha lus, epilepsy, and cerebral palsy.

CONCLUSION

Salmonella sp. can lead to a complication of brain abscess despite prior antibiotic administration. Longer antibiotic administration up to 4-6 weeks might be considered for the treatment of Salmonella meningitis. Sterile CSF culture along with normal CSF analysis at evaluation and results of repeat neuroimaging studies should be carefully considered to determine the appropriate duration of treatment.

REFERENCES


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