**Salmonella enteritidis** brain abscess in a sickle cell disease patient: case report and review of the literature

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**Summary**

**Background:** Focal intracranial abscesses due to *Salmonella spp* are rarely reported. They tend to occur in patients who are immunosuppressed and in those with other predisposing factors. We present herein the first reported case of *Salmonella enteritidis* brain abscess in a sickle cell disease (SCD) patient.

**Methods:** We describe the case of a 29-year-old black African female with SCD who presented to her local hospital with a left frontal abscess. She was treated with emergency burr hole aspiration of the abscess and antibiotics. The aspirate grew *S. enteritidis* PT 8 on culture. All investigations into the source of the infection proved negative. The patient made a full recovery. We also present a detailed review of *S. enteritidis* brain abscesses in the medical literature.

**Results and conclusions:** *S. enteritidis* brain abscesses are very rare and are usually associated with immunocompromised conditions. Our patient appears to be the first reported case associated with SCD, the pathogenesis of which is unclear at present. Further clinical research is suggested in countries with a high prevalence of SCD to determine the association of SCD and the development of Salmonella brain abscesses.

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**Introduction**

Intracranial infections are unusual manifestations of salmonellosis in general, and brain abscesses in particular. In the last 117 years, only 22 cases have been described in the world literature. 1–17 Thirteen of the 22 brain abscesses reported were caused by *Salmonella enteritidis*. 6,12,15,17 All reported
Table 1  Summary of 14 patients with *Salmonella enteritidis* brain abscesses reported in the world literature

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>Predisposing factors</th>
<th>Clinical features</th>
<th>Abscess location</th>
<th>S. enteritidis isolated from</th>
<th>Antibiotics used</th>
<th>Surgical drainage</th>
<th>Outcome/ follow-up</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 months/F</td>
<td>Gastroenteritis</td>
<td>Fever, restlessness, bulging fontanelles, tremors</td>
<td>Single/left</td>
<td>Stool</td>
<td>Penicillin, streptomycin, chloramphenicol</td>
<td>Yes</td>
<td>Recovered/2 years</td>
<td>6 (1969)</td>
</tr>
<tr>
<td>28 years/M</td>
<td>Excision metastatic brain tumor, bacteremia</td>
<td>Fever, headache, decreased LOC</td>
<td>Single/occipital</td>
<td>Brain, blood</td>
<td>Chloramphenicol, TMP–SMX</td>
<td>Yes</td>
<td>Recovered/NS</td>
<td>1 (1986)</td>
</tr>
<tr>
<td>78 years/M</td>
<td>GBM, steroid therapy, bacteremia, meningitis</td>
<td>Septic shock, seizures, decreased LOC</td>
<td>Multiple/occipital, biventricular, blood</td>
<td>CSF</td>
<td>Cefotaxime, amikacin, ampicillin, chloramphenicol</td>
<td>No</td>
<td>Died</td>
<td>7 (1987)</td>
</tr>
<tr>
<td>47 years/M</td>
<td>AIDS, IVDA, meningitis, gastroenteritis, bacteremia</td>
<td>Fever, headache, decreased LOC</td>
<td>Single/frontal</td>
<td>Brain, CSF, blood</td>
<td>Amoxicillin, TMP–SMX, chloramphenicol, cefotaxime, ceftriaxone, ceftazidime</td>
<td>Yes</td>
<td>Died 7 weeks later</td>
<td>8 (1990)</td>
</tr>
<tr>
<td>3 weeks/M</td>
<td>SAH, gastroenteritis, bacteremia, meningitis</td>
<td>Fever, seizures, jaundice</td>
<td>Multiple/bifrontal and occipital</td>
<td>Brain, blood, nasal swab</td>
<td>Cefotaxime, chloramphenicol, ciprofloxacin</td>
<td>Yes</td>
<td>Recovered, delayed development/2 years</td>
<td>9 (1993)</td>
</tr>
<tr>
<td>24 years/M</td>
<td>GBM, steroid therapy, bacteremia, meningitis</td>
<td>Fever, VI CN palsy, decreased LOC</td>
<td>Single/temporal</td>
<td>Brain, CSF, blood</td>
<td>Ofloxacin, cefotaxime, ceftriaxone, amikacin, ciprofloxacin</td>
<td>Yes</td>
<td>Recovered/NS</td>
<td>10 (1993)</td>
</tr>
<tr>
<td>49 years/F</td>
<td>Excision brain astrocytoma, steroid therapy, bacteremia, meningitis</td>
<td>Sepsis, decreased LOC</td>
<td>Single/parietal</td>
<td>Brain, CSF, blood</td>
<td>Cefotaxime, gentamicin, ceftazidime</td>
<td>Yes</td>
<td>Residual hemiparesis/NS</td>
<td>11 (1995)</td>
</tr>
<tr>
<td>59 years/M</td>
<td>DM, gallbladder adenocarcinoma, choledochocholithiasis, gastroenteritis</td>
<td>Fever, neck mass</td>
<td>Multiple/frontal temporal</td>
<td>Stool</td>
<td>Cefotaxime, metronidazole</td>
<td>No</td>
<td>Recovered after excision of concurrent mycotic carotid aneurysm/6 months</td>
<td>12 (1996)</td>
</tr>
<tr>
<td>43 years/M</td>
<td>Bacteremia, meningitis, IgA and IgG1 deficiency, bacteremia, meningitis</td>
<td>Fever, confusion, headache, fever, irritability, signs of increased ICP, hydrocephalus</td>
<td>Single/parietal</td>
<td>CSF, blood</td>
<td>Cefotaxime, ciprofloxacin</td>
<td>No</td>
<td>Recovered/6 months</td>
<td>13 (1998)</td>
</tr>
<tr>
<td>4 weeks/F</td>
<td>Bacteremia, meningitis, IgA and IgG1 deficiency, bacteremia, meningitis</td>
<td>Fever, confusion, headache, fever, irritability, signs of increased ICP, hydrocephalus</td>
<td>Multiple/bifrontal</td>
<td>Brain, CSF, blood</td>
<td>Cefotaxime, ciprofloxacin</td>
<td>No</td>
<td>Recovered/2 years</td>
<td>14 (1999)</td>
</tr>
<tr>
<td>58 years/F</td>
<td>GBM</td>
<td>Fever, hemiparesis, decreased LOC, III CN palsy</td>
<td>Single/frontal</td>
<td>Brain</td>
<td>Ceftazidime</td>
<td>Yes</td>
<td>Died</td>
<td>15 (2000)</td>
</tr>
<tr>
<td>55 years/F</td>
<td>SAH, coiling and clipping of multiple cerebral aneurysms</td>
<td>Fever, headache, vomiting, malaise, meningism</td>
<td>Single/frontal</td>
<td>Blood, CSF</td>
<td>Ceftriaxone, cephalaxin</td>
<td>No</td>
<td>Recovered/18 months</td>
<td>16 (2002)</td>
</tr>
<tr>
<td>46 years/F</td>
<td>Craniohypophyseal excision, steroid therapy</td>
<td>Headache, painful left hip, decreased LOC</td>
<td>Single/frontal</td>
<td>Brain, stool</td>
<td>Ciprofloxacin, chloramphenicol</td>
<td>Yes</td>
<td>Recovered, left hip needed further surgery</td>
<td>17 (2003)</td>
</tr>
<tr>
<td>29 years/F</td>
<td>(present case) Sickle cell disease</td>
<td>Headache, fever, rigors</td>
<td>Single/frontal</td>
<td>Brain</td>
<td>Ceftriaxone</td>
<td>Yes</td>
<td>Recovered/21 months</td>
<td>2006</td>
</tr>
</tbody>
</table>

LOC, level of consciousness; TMP–SMX, trimethoprim–sulfamethoxazole; NS, not stated; GBM, glioblastoma multiforme; CSF, cerebrospinal fluid; AIDS, acquired immunodeficiency syndrome; IVDA, intravenous drug abuse; SAH, subarachnoid hemorrhage; CN, cranial nerve; DM, diabetes mellitus; ICP, intracranial pressure.
cases had significant predisposing conditions including brain tumors, diabetes mellitus, subarachnoid hemorrhage, etc. (Table 1). However the association between Salmonella brain abscesses and sickle cell disease (SCD) has not been described. We present herein the first reported case of a primary Salmonella brain abscess caused by \textit{S. enteritidis}, in a 29-year-old black African woman with SCD.

**Case report**

A 29-year-old black African woman with SCD presented to her local hospital in September 2003 with a nine-day history of fever, rigors, and left-sided pounding headaches. Clinical assessment and evaluation suggested a clinical diagnosis of cerebral abscess. Computed tomography (CT, Figure 1) and magnetic resonance imaging (MRI, Figure 2) of the brain revealed a left frontal thick walled lesion with surrounding edema consistent with a diagnosis of brain abscess.

Blood cultures were obtained and the patient was immediately transferred to the regional neurosciences center for further management. On admission she was pyrexial with a
temperature of 38.7 °C and had a Glasgow Coma Score of 15/15; no neurological deficits were detected. Hematological and biochemical investigations revealed hemoglobin 7.2 g/dl, white cell count 5.8 × 10^9/l, platelet count 134 × 10^9/l, C-reactive protein (CRP) 115 mg/l, erythrocyte sedimentation rate (ESR) 3 mm/1st hour, mean corpuscular volume (MCV) 78.4 fl, reticulocyte count 5.2%, and hemoglobin electrophoresis showing HbA2 3%, HbF 14%, HbS 45%. Electrolytes and renal and liver function tests were within normal limits.

Blood and urine samples were obtained for culture, but the patient refused to provide a fecal specimen for investigations. Thin and thick blood films showed no malarial parasites. Serology for toxoplasmosis, hepatitis A, B, C, HIV, and cytomegalovirus (CMV) was negative. Serology for Epstein–Barr virus (EBV) was positive for both nuclear antigens (EBNA) and capsid antigen (VCA). IgM was negative, but IgGs were detected suggesting evidence of EBV infection of more than two months.

An echocardiogram and ultrasound scan of the liver and gall bladder were normal. Prior to surgery the patient was given six units of exchange blood transfusion to correct the anemia and minimize sickling. Burr hole aspiration of the frontal abscess was done under general anesthesia, and 15 ml of frank pus was aspirated.

Microscopic examination of the pus showed moderate amounts of pus cells, but no organisms were seen. The pus inoculated on blood (aerobic and anaerobic), chocolate, and MacConkey agars grew pure cultures on all plates. The isolate was an oxidase-negative, non-lactose fermenting coliform, eventually identified as Salmonella enteritidis using the API-20 E® bacterial identification kit (bioMérieux, Inc.) and confirmed by the reference laboratory at the Health Protection Agency, Colindale, London as Salmonella enteritidis PT 8. The isolate was sensitive to amoxicillin, trimethoprim, cefuroxime, ceftriaxone, and ciprofloxacin. The treatment was changed from ceftriaxone (2 g once daily IV) and metronidazole (500 mg tds IV) to ceftriaxone 2 g given intravenously twice daily for three weeks.

Within two days following aspiration of the abscess and antibiotic administration, her symptoms subsided, and CRP reduced to <5 mg/l. The blood and urine cultures gave no growth at five days of incubation. The antibiotics were continued for a period of six weeks. A repeat MRI scan done at six months (Figure 3) showed a small area of mature brain damage at the area of the previous brain abscess. She remained clinically very well and was discharged from follow-up.

Discussion

Brain abscesses remain potentially fatal central nervous system (CNS) infections. Yang et al., in their largest study of 400 cases of brain abscesses, found that 21% (82/400) of the infections were caused by Gram-negative bacilli, with Proteus spp, Enterobacter spp, and Alcaligenes spp, the three most prevalent Gram-negative pathogens. The other organisms frequently involved included Klebsiella pneumoniae, Pseudomonas aeruginosa, and Escherichia coli. Salmonella spp were uncommon.

Salmonellosis is usually a self-limited disease, generally restricted to the gastrointestinal tract and acquired following food poisoning. Salmonella bacteremia is known to occur in 5–45% of all cases of salmonellosis and may remain unrecognized because of lack of pyrexia and gastroenteritis. Salmonella brain abscesses are a rare condition complicating salmonellosis, even in endemic areas. In a review of cases of focal intracranial Salmonella infections in the world literature between 1884 and 2001, Mahapatra et al. reviewed 80 reported cases of focal intracranial Salmonella infections in the literature, of which 22 were brain abscesses, 40 subdural empyemas, and 18 were combinations of abscesses, empyemas, and epidural abscesses. They noted that brain abscesses were common in adults and subdural empyemas more frequent in children. Mortality rates of 21–60% were reported for patients with intracranial infections caused by Salmonella spp, and a significant number of survivors developed permanent neurological sequelae.

Sarria et al., in their study of 11 cases of Salmonella enteritidis brain abscesses, found only four had antecedent gastroenteritis, eight had bacteremia, and seven had meningitis. Nine patients survived and six recovered without neurological deficits.

Our case illustrates a serious complication with presumed hematogenous spread of the infection from a pre-existing asymptomatic and unknown colon infection. In the immunocompetent population, the majority of Salmonella intracranial empyemas occur in those under three years of age. In the pathogenesis of brain abscesses, hematogenous seeding of the organism either from transient or current bacteremia is one of the major mechanisms by which they occur. Our patient did not have current bacteremia or a febrile illness before developing the abscess. No evidence of gastroenteritis was noted in the history. Therefore it is difficult to establish the source of infection in this case. The blood cultures taken on admission remained negative indicating no bacteremia at that point. The occurrence of S. enteritidis in the gastrointestinal tract could not be eliminated, as the stool cultures were not performed. Therefore the possibility of transient bacteremia leading to hematogenous spread still remains.

Figure 3  Enhanced T1–weighted magnetic resonance image revealing a small area of mature brain damage in the area of previous abscess.
Salmonella has a tendency to infect diseased tissue, and a variety of predisposing factors have been described. These include patients with primary or metastatic brain tumors, subarachnoid hemorrhage, corticosteroid use, diabetes mellitus, immunoglobulin deficiencies, HIV infection, and meningitis. Meningitis is the most important predisposing factor to focal intracranial infection by Salmonella.1  

Brain abscesses due to Salmonella spp, including S. enteritidis, have previously been reported and are usually assumed following bacteremia in the presence of some compromise of the reticulo-endothelial system (RES) immunity. Beta-thalassemia and SCD are known to lead to RES compromise due to iron overload from repeated transfusions and functional asplenism due to the erythrocyte lesion itself. This predisposes individuals to serious systemic infections due to Gram-negative bacteria. Although Gram-negative bacillus brain abscesses in many patients with hemoglobinopathies have been reported, none of the bacilli isolated were Salmonella spp. The explanation for this observation has yet to be given, and hence further studies are warranted. We were not able to offer a causal relationship between SCD in our patient and development of the S. enteritidis brain abscess. In general it appears that these hemoglobinopathies are protective in preventing such individuals from developing Salmonella brain abscesses, which was not the case here.  

Management of Salmonella brain abscesses requires a combination of antimicrobial agents, surgical drainage/excision as appropriate, and eradication of primary foci. Third-generation cephalosporins are the most consistently used agents to treat Salmonella CNS infections because they achieve high brain tissue concentrations. Chloramphenicol could be used as an alternative drug if there is a contraindication to the use of cephalosporins. The recommended duration of antibiotic treatment is 4–6 weeks or longer, with radiological and biochemical monitoring of the inflammatory markers.  

**Conclusions**

Salmonella enteritidis brain abscesses are very rare and usually associated with immunocompromised conditions. Our patient appears to be the first reported case associated with SCD, the pathogenesis of which is unclear at present. Further clinical research is suggested in countries with a high prevalence of SCD to explain the association of SCD and the development of Salmonella brain abscesses. Early diagnosis and treatment with surgical drainage and third-generation cephalosporins is vital in this potentially fatal condition.

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**References**