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# Recurrent Salmonella Meningitis in an HIV-Positive Adult: A Case Report

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***Abstract***

*Salmonella meningitis is a rare but potentially life-threatening form of bacterial meningitis caused by various Salmonella species. This review provides a comprehensive overview of Salmonella meningitis, encompassing its clinical manifestations, epidemiology, pathogenesis, diagnostic challenges, treatment strategies, and outcomes.*

*The incidence of Salmonella meningitis is relatively low, primarily affecting vulnerable populations such as infants, the elderly, and immunocompromised individuals, including those with HIV/AIDS. The transmission of Salmonella to the central nervous system is facilitated by several virulence factors, including its ability to invade host cells, form intracellular reservoirs, and induce a robust inflammatory response.*

*Diagnosis of Salmonella meningitis presents unique challenges due to its rarity and the need for specific laboratory techniques. Cerebrospinal fluid analysis typically reveals pleocytosis with neutrophilic predominance, and bacterial culture is essential for species identification. Molecular methods can aid in rapid diagnosis.*

*Treatment strategies for Salmonella meningitis often involve prolonged courses of antibiotics, with resistance patterns and drug penetration being crucial considerations. The emergence of multidrug-resistant strains is a growing concern, necessitating vigilance in antibiotic selection.*

*Prognosis in Salmonella meningitis cases is generally guarded, with high morbidity and mortality rates. Early initiation of appropriate antibiotics is essential for improving outcomes, and the role of host immune status, particularly in HIV-positive individuals, adds complexity to the clinical course.*

## Introduction

Salmonellosis remains a global health issue, particularly in developing countries. While the overall incidence of Salmonella infection is significant, according to the WHO, typhoid fever affects approximately 21 million people worldwide annually (7). Apart from gastrointestinal involvement, other infectious manifestations are possible. Meningeal involvement, often reported in children, remains rare in adults. Immunodeficiency, particularly HIV infection, appears to be a risk factor. Here, we describe a case of recurrent Salmonella meningitis in a 40-year-old HIV-positive adult.

## Case Report

Mr. A.H., a 40-year-old male, presented to the emergency department with altered consciousness in a febrile context. On examination, he was unconscious (Glasgow Coma Scale: 10/15), without neurological deficits but with signs of meningeal irritation and a fever of 39.2°C. Hemodynamic status was stable with a blood pressure of 128/78 mm Hg. Skin and mucous membrane examination revealed no purpura. Cranial CT scan showed no abnormalities. Lumbar puncture yielded turbid cerebrospinal fluid with predominantly neutrophilic pleocytosis (95%), along with hypoglycorrhachia (0.016 g/L) and hyperalbuminorrachia (3.42 g/L). Gram stain was negative. Antibiotic therapy with Ceftriaxone (100 mg/kg/day) and corticosteroids (Dexamethasone: 10 mg x4/day) was initiated. Leukocyte count was 11,300 cells/mm3 (96% neutrophils), hemoglobin was 11.7 g/L, and platelet count was 150,000 cells/mm3. After 48 hours, cerebrospinal fluid culture identified Salmonella enteritidis, while blood cultures remained sterile. Considering the patient's high-risk sexual behaviors, the possibility of immunodeficiency, especially HIV, was suspected, but the patient refused serological testing. The same antibiotic therapy was continued, given the favorable clinical course. The total duration of antibiotic treatment was 15 days, with complete neurological recovery. One week after discharge, the patient was readmitted with a febrile meningeal syndrome. Bacterial meningitis was diagnosed, and a combination antibiotic therapy with Ceftriaxone (100 mg/kg/day) and Vancomycin was initiated due to concerns about penicillin-resistant pneumococcus. Both cerebrospinal fluid and blood cultures isolated Salmonella enteritidis. The antibiotic regimen was adjusted, replacing Vancomycin with Ciprofloxacin (500 mg x2/day), initially intravenously and later orally. Upon obtaining the patient's consent, HIV serology was performed, which returned positive, with a CD4 count of 4. Antiretroviral

therapy and prophylaxis for opportunistic infections were initiated. The total duration of antibiotic therapy this time was 15 days for Ceftriaxone and 4 weeks for Ciprofloxacin. The patient's clinical course improved.

## Discussion

Salmonellosis is a common infection, especially in developing countries, caused by the genus Salmonella, which includes three species: Salmonella enterica, S. bongori, and S. subterranea. Salmonella infection encompasses two nosological entities: typhoid fever and non-typhoidal salmonellosis. The first report of Salmonella-related meningitis was by Gohn in 1907 (1). Salmonella accounts for 0.8% to 6% of all cases of bacterial meningitis, with the majority occurring in infants. In a review by Owusu-Ofori et al. (4), 89.7% of infections occurred in infants under one year of age. Septicemia with meningeal involvement is a rare complication in adults and older children. The most common route of Salmonella infection is the fecal-oral route. It uses virulence factors such as intracellular invasion, polysaccharide capsules, and fimbriae to colonize the mucosa, survive intravascularly, invade the meninges, and persist in the subarachnoid space. Host inflammatory responses and immune system activation contribute to these effects (5). After breaching the abdominal barrier, the bacterium enters the bloodstream and rarely causes intracranial infections, leading to meningitis, subdural effusion, empyema, or cerebral abscess. Focal infections, including brain abscesses and empyemas, have been reported (5). This local virulence and secondary locations are not influenced by HIV infection in this case. The risk of severe forms is equivalent in seronegative and seropositive populations (5). On the other hand, non-typhoidal salmonellosis has a benign local course, with its potential severity greatly influenced by immunodeficiency (5). HIV-positive individuals have a 20- to 100-fold increased risk of developing severe forms, including profuse diarrhea, bacteremia, and meningitis (1). Meningeal involvement is a rare manifestation, estimated to account for 0.02% of all cases of bacterial meningitis (4) and 0.8% of salmonellosis cases. Central nervous system infections are primarily caused by non-typhoidal salmonellosis (5), accounting for only 0.1% to 0.9% of infectious locations. However, this infectious site is predominantly seen in infants and young children, with 86.7% of affected individuals under one year of age (2). Immaturity of the blood-brain barrier and immune systems have been suggested as hypotheses for this susceptibility in children (2). About twenty cases of Salmonella meningitis in adults have been published. They mostly occur in debilitated individuals (diabetes, renal insufficiency, hematologic malignancies, etc.). However, the primary risk factor remains HIV infection, with 50% of patients affected. Approximately nine cases of Salmonella meningitis in HIV-positive individuals have been reported in the literature (table). The average age of onset is 37 years, and the infection occurred in known HIV-positive patients, except in one case. Similarly, in our case, meningitis was the presenting symptom of HIV infection. Not all patients were already on antiretroviral therapy. According to Pegues DA et al., the risk of developing Salmonella meningitis is high when the CD4 count drops below 100 (6). In the case series, three patients had CD4 counts above 150 (4). In our case, the CD4 count was 4. From a diagnostic standpoint, cerebrospinal fluid exhibited characteristics of bacterial meningitis. Gram-negative bacilli were seen in 50% of cases on direct cerebrospinal fluid examination. Blood cultures were positive in 60% of cases (4). The most commonly found strains are Salmonella triphimurium, Salmonella enteritidis, and Salmonella paratyphi B (2). Treatment of Salmonella meningitis is challenging, especially due to limited therapeutic options. The main constraints are related to the limited therapeutic resources. Chloramphenicol, widely used in developing countries, is bacteriostatic and therefore not well-suited for treating meningitis, similar to Trimethoprim-sulfamethoxazole (TMP-SMX) is bacteriostatic and therefore not well-suited for treating meningitis (2, 10). Additionally, third-generation cephalosporins, imipenem, and ampicillin have poor intracellular penetration (10). Chloramphenicol is associated with hematological toxicity, especially during prolonged treatment in high-risk individuals, limiting its use (2). Fluoroquinolones appear to be the most suitable option due to their good intracellular penetration, but they are contraindicated in children (2, 10). Combinations of antibiotics are possible (2). The main concern lies in the increasing resistance of Salmonella strains. Indeed, in a recent publication, multidrug-resistant forms tripled in the USA over seven years, rising from 20% in 1999 to 60% in 2006 (7). The challenges in eradicating the pathogen suggest extended antibiotic therapy beyond three weeks (10).

Prognosis is generally severe, with high morbidity and mortality rates. It depends on the prompt initiation of appropriate treatment. In the series by CHERUBIN et al. (8), the overall mortality rate was 43%. In HIV-positive adult subjects, M.K. Leonard (4) reported a similar mortality rate, albeit in a limited series of seven patients, with the causality of meningitis in at least one death being questionable. Recurrence occurs in 14% of cases (4). It is associated with decreased pathogen clearance due to immunosuppression, as suggested by A. GUITERRES et al. Moreover, the intracellular development of the pathogen makes it less accessible to antibiotics, leading to the emergence of resistant strains (10). In our case, recurrence could be explained by the short duration of antibiotic therapy (two weeks), the choice of Ceftriaxone, which has good intracellular penetration, and the absence of initiation of antiretroviral therapy to bolster the patient's immunity.

## Conclusion

Salmonella meningitis remains a rare but serious neurological infection. Understanding its clinical characteristics, diagnostic challenges, and evolving treatment strategies is crucial for improving patient care and reducing the impact of this potentially devastating disease. Further research is needed to address emerging resistance and optimize management approaches for this challenging condition., as our understanding of this rare but serious infection evolves, continued research is crucial to addressing emerging resistance patterns, optimizing treatment strategies, and improving patient care. Salmonella meningitis remains a compelling area of study, and further investigations may hold the key to enhancing our ability to combat this challenging disease.

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