



Typhoid Encephalopathy: When Fever Takes Over The Mind – A Compelling Case Study and Insightful Review

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Citation this Article: Dr Rohan M S, Dr Anandan, Dr Saketh Ramineni, “Typhoid Encephalopathy: When Fever Takes Over The Mind – A Compelling Case Study and Insightful Review”, IJMSIR - September - 2024, Vol – 9, Issue - 5, P. No. 75 – 80.

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Typhoid fever, caused by *Salmonella enterica* serotype Typhi, remains a significant health concern in many developing countries. While the disease predominantly affects the gastrointestinal tract, it can also involve multiple organ systems, including the central nervous system, leading to a rare but serious complication known as typhoid encephalopathy. This neuropsychiatric manifestation is characterized by altered mental status, ranging from confusion and delirium to deep coma. The pathophysiology of typhoid encephalopathy is not entirely understood, but it is believed to be associated with the systemic inflammatory response and cytokine release rather than direct bacterial invasion of the brain. The diagnosis is primarily clinical, supported by the presence of typhoid fever, and the exclusion of other causes of encephalopathy. Management includes prompt antibiotic therapy, supportive care, and the management of complications. This case report discusses a patient with typhoid encephalopathy, detailing the clinical presentation, diagnostic workup, treatment, and outcomes. Through this case, we aim to highlight the importance of early recognition and treatment of this rare complication to prevent adverse outcomes. Additionally,

we review the current literature on the pathophysiology, clinical features, differential diagnosis, and management strategies for typhoid encephalopathy. Despite advances in public health measures and vaccination, typhoid fever and its complications remain prevalent in endemic areas. This underscores the need for ongoing efforts to improve diagnosis, treatment, and prevention strategies.

Keywords: Typhoid fever, *Salmonella* Typhi, encephalopathy, neuropsychiatric complications, central nervous system, cytokine release, altered mental status.

Introduction

Typhoid fever, caused by *Salmonella enterica* serotype Typhi, is a systemic infectious disease that primarily affects the gastrointestinal tract. Despite significant advances in public health and the availability of effective antibiotics, typhoid fever remains endemic in many parts of the world, particularly in South Asia, Africa, and Latin America. The global burden of the disease is substantial, with an estimated 11–21 million cases and approximately 128,000–161,000 deaths annually.

The clinical presentation of typhoid fever typically includes prolonged fever, abdominal pain, diarrhea or constipation, and a range of nonspecific symptoms such as headache, malaise, and anorexia. However, in some

cases, typhoid fever can lead to severe complications, including intestinal perforation, hemorrhage, and systemic involvement of organs such as the liver, spleen, and bone marrow. One of the less common but serious complications is typhoid encephalopathy, a neuropsychiatric condition characterized by altered mental status, seizures, and other neurological deficits.

Typhoid encephalopathy is a diagnostic challenge due to its nonspecific symptoms and the need to rule out other causes of encephalopathy. The condition is associated with a high mortality rate if not promptly recognized and treated. Early initiation of appropriate antibiotic therapy and supportive care is crucial for a favorable outcome. This article presents a detailed case discussion of a patient with typhoid encephalopathy and reviews the literature on its pathophysiology, clinical features, differential diagnosis, and management strategies.

Case Discussion

A 34-year-old male from a rural area of South Asia presented to the emergency department with a 10-day history of high-grade fever, severe headache, and generalized weakness. The patient also reported episodes of confusion and disorientation over the past two days. He had no significant past medical history and no known allergies. The patient's family noted a recent history of unfiltered water consumption and poor sanitation in their community, which is known for frequent typhoid outbreaks.

Upon arrival at the hospital, the patient was febrile, with a temperature of 39.5°C, and appeared acutely ill. He was disoriented to time and place, with a Glasgow Coma Scale (GCS) score of 10/15. Physical examination revealed a toxic appearance, mild hepatosplenomegaly, and generalized abdominal tenderness. Neurological examination showed no focal deficits, but the patient exhibited signs of meningeal irritation, including neck

stiffness and a positive Brudzinski's sign. There were no signs of rash or petechiae.

Initial laboratory investigations showed leukopenia (white blood cell count: 3,000/ μ L), anemia (hemoglobin: 9.5 g/dL), and thrombocytopenia (platelet count: 85,000/ μ L). Liver function tests revealed mild transaminitis (AST: 120 U/L, ALT: 105 U/L), while renal function tests were within normal limits. Blood cultures were obtained, and empirical antibiotic therapy with intravenous ceftriaxone was initiated.

On the second day of hospitalization, the patient's mental status deteriorated, and he became increasingly drowsy, with a GCS score dropping to 8/15. A lumbar puncture was performed, revealing a slightly elevated cerebrospinal fluid (CSF) protein level (75 mg/dL) and normal glucose levels, with no pleocytosis. CSF cultures were negative for bacterial growth. Magnetic resonance imaging (MRI) of the brain was performed, showing no significant abnormalities, ruling out abscesses, infarcts, or encephalitis. An electroencephalogram (EEG) was also conducted, which showed diffuse slowing, consistent with an encephalopathic process.

Given the patient's clinical presentation and epidemiological history, a diagnosis of typhoid encephalopathy was strongly considered. The blood cultures later confirmed the presence of *Salmonella enterica* serotype Typhi, which was sensitive to ceftriaxone. The patient's antibiotic regimen was continued, and supportive care, including intravenous fluids, electrolyte correction, and antipyretics, was provided.

Over the next few days, the patient's condition remained critical, with persistent high fever and fluctuating levels of consciousness. He required close monitoring in the intensive care unit (ICU) and was managed with intravenous fluids to maintain adequate hydration and

blood pressure. Broad-spectrum antibiotics were continued, and adjunctive therapies such as

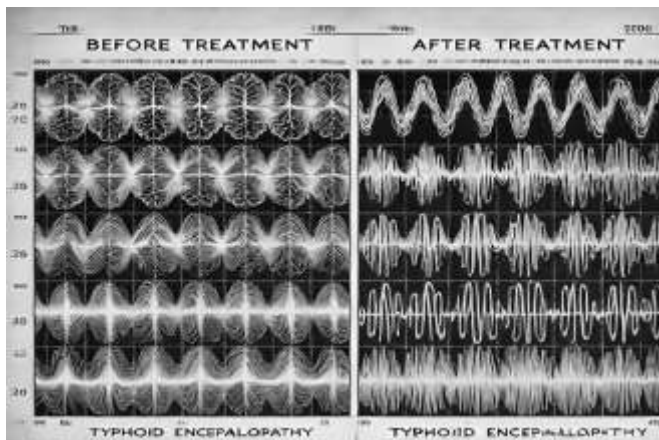


Figure 1: EEG

Corticosteroids were considered to reduce the inflammatory response, although there is limited evidence supporting their efficacy in typhoid encephalopathy.

On day five of hospitalization, the patient's neurological status began to improve gradually. He became more responsive, with a GCS score improving to 12/15, and his fever started to subside. However, the patient continued to experience intermittent episodes of confusion and agitation, which were managed with low-dose sedatives. Repeat blood cultures were negative, and inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), showed a downward trend.

As the patient's condition stabilized, he was transferred out of the ICU to a general medical ward. His mental status continued to improve, and by day ten, he was fully alert and oriented. The patient's liver enzymes normalized, and his blood counts gradually returned to baseline. A follow-up MRI of the brain showed no new abnormalities, and the EEG findings improved, correlating with the clinical recovery (Fig.1)

The patient was discharged on day fourteen of hospitalization with oral antibiotics to complete a 14-day

course. At the time of discharge, he was neurologically intact, with no residual cognitive deficits. The patient was advised on the importance of clean water consumption and proper sanitation to prevent future infections. Follow-up after one month showed no recurrence of symptoms, and the patient had returned to his usual activities.

Discussion

Typhoid encephalopathy is a rare but severe complication of typhoid fever, manifesting as an altered mental status, seizures, and other neuropsychiatric symptoms. The exact incidence of typhoid encephalopathy is difficult to determine, but it is reported to occur in 5–35% of cases, depending on the population and the severity of the disease. The pathophysiology of typhoid encephalopathy is not fully understood, but several mechanisms have been proposed, including cytokine-induced inflammation, microvascular thrombosis, and metabolic derangements.

The role of cytokines, particularly tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6), has been implicated in the development of typhoid encephalopathy. These pro-inflammatory cytokines are elevated in patients with severe typhoid fever and are thought to contribute to the systemic inflammatory response that can affect the central nervous system. This systemic response may lead to increased permeability of the blood-brain barrier, allowing for the entry of cytokines and other inflammatory mediators into the brain, resulting in encephalopathy.

Another proposed mechanism involves the microvascular changes seen in severe typhoid fever. The inflammation and endothelial dysfunction may lead to micro thrombi formation in the cerebral vasculature, causing ischemic injury and contributing to the neurological manifestations of typhoid encephalopathy. Additionally, metabolic

abnormalities, such as hyponatremia and hypoglycemia, may exacerbate the encephalopathy.

Clinically, typhoid encephalopathy is characterized by a spectrum of neuropsychiatric symptoms ranging from mild confusion and delirium to seizures and deep coma. The presence of altered mental status in a patient with typhoid fever should raise suspicion for encephalopathy, particularly in the absence of other identifiable causes. Diagnosis is primarily clinical, supported by laboratory findings consistent with typhoid fever, such as positive blood cultures for *Salmonella Typhi* and characteristic laboratory abnormalities like leukopenia, anemia, and thrombocytopenia. Neuroimaging is typically unremarkable, but it is essential to rule out other causes of encephalopathy, such as cerebral abscesses, infarcts, or meningitis.

The management of typhoid encephalopathy involves prompt initiation of appropriate antibiotic therapy to target the underlying infection. Ceftriaxone and azithromycin are commonly used antibiotics due to their efficacy against multidrug-resistant *Salmonella* strains. The choice of antibiotic should be guided by local resistance patterns, and treatment duration is typically 10-14 days, depending on the severity of the disease and the patient's clinical response.

In addition to antibiotic therapy, supportive care is crucial in managing typhoid encephalopathy. Patients with altered mental status require close monitoring in an intensive care setting, particularly if they are at risk of complications such as aspiration pneumonia, seizures, or hemodynamic instability. Intravenous fluids are essential to maintain adequate hydration and electrolyte balance, especially in patients with significant gastrointestinal losses due to diarrhea or vomiting.

The role of corticosteroids in the treatment of typhoid encephalopathy is controversial. While corticosteroids

have been used in other forms of encephalopathy to reduce inflammation and cerebral edema, there is limited evidence supporting their use in typhoid encephalopathy. Some studies suggest that corticosteroids may help mitigate the inflammatory response and improve outcomes in severe cases, but their use should be considered on a case-by-case basis, weighing the potential benefits against the risks of immunosuppression and other side effects.

Outcomes in typhoid encephalopathy vary depending on the severity of the condition and the timeliness of treatment. The mortality rate has been reported to range from 10% to 50%, with higher rates observed in patients with delayed diagnosis or inadequate treatment. Neurological recovery is possible in survivors, but some patients may experience persistent cognitive deficits, particularly if the encephalopathy was severe or prolonged. Early recognition and treatment are critical in improving the prognosis for these patients.

Preventing typhoid fever and its complications, including typhoid encephalopathy, requires a multifaceted approach. Vaccination remains one of the most effective measures, particularly in endemic regions. The World Health Organization (WHO) recommends typhoid vaccination for individuals living in or traveling to areas with high transmission rates. Improved sanitation, access to clean water, and public health education are also essential in reducing the incidence of typhoid fever and preventing outbreaks.

In endemic regions, public health efforts should focus on improving infrastructure to ensure access to clean water and proper sewage disposal. Additionally, educating communities about the importance of hand hygiene, safe food practices, and vaccination can help reduce the transmission of *Salmonella Typhi*. In non-endemic regions, clinicians should maintain a high index of

suspicion for typhoid fever in travelers returning from endemic areas, particularly if they present with febrile illness and gastrointestinal symptoms.

The case presented in this article underscores the importance of considering typhoid encephalopathy in patients with typhoid fever who develop neurological symptoms. Despite the availability of effective treatment, the condition remains a significant cause of morbidity and mortality in endemic areas. Early diagnosis, appropriate antibiotic therapy, and supportive care are essential in managing typhoid encephalopathy and improving patient outcomes.

Conclusion

Typhoid encephalopathy is a rare but life-threatening complication of typhoid fever, characterized by altered mental status and a range of neuropsychiatric symptoms. The pathophysiology involves complex mechanisms, including cytokine-induced inflammation, microvascular thrombosis, and metabolic disturbances. Early recognition and prompt initiation of appropriate antibiotic therapy are crucial in managing the condition and improving patient outcomes. Supportive care, including fluid and electrolyte management, is essential, and the potential role of corticosteroids remains an area for further research.

The case discussed in this article highlights the challenges in diagnosing and managing typhoid encephalopathy, particularly in resource-limited settings. Despite advances in public health and vaccination, typhoid fever continues to pose a significant health burden in endemic regions, underscoring the need for ongoing efforts in prevention, early diagnosis, and treatment.

In conclusion, typhoid encephalopathy should be considered in any patient with typhoid fever who presents with neurological symptoms. Clinicians must

maintain a high index of suspicion, particularly in endemic areas, to ensure timely treatment and reduce the risk of adverse outcomes.

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