

Case Report

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Typhoid fever presenting as neuropsychiatric oddities: A case report

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ABSTRACT

Rationale: *Salmonella* is a common etiological agent behind the tropical fever syndrome in the Indian subcontinent. Its prevalence in India remains high due to a lack of proper sanitation services in large parts of the country. Its neuropsychiatric manifestations is rare and the understanding on their pathophysiology is still poor.

Patient concerns: A 19-year-old male, presented with a 10-day history of altered mental status, high-grade fever and violent behaviour. 2 Days prior to admission, he developed decreased responsiveness and a muttering delirium with self-talking.

Diagnosis: Coma vigil secondary to salmonellosis.

Interventions: Intravenous ceftriaxone and dexamethasone.

Outcomes: The resolution of the coma vigil and the associated *Salmonella* infection were observed; however, the patient developed residual mutism.

Lessons: The atypical presentation of a globally obtunded state followed by mutism in typhoid coma in this case should be brought to the attention of clinicians worldwide. Additionally, the enduring speech limitations and potential psychiatric consequences may be linked to the prolonged duration of the infection.

KEYWORDS: *Salmonella*; Salmonellosis; Coma vigil; Typhoid fever

1. Introduction

Typhoid fever is a systemic infection caused by *Salmonella enterica* serotype typhi and paratyphi, a highly adapted human-specific pathogen that can persist and transmit in the host. Typhoid fever is endemic in developing countries with poor sanitation, where it causes an estimated 26 million cases and 215 000 deaths annually[1]. It is usually transmitted by contaminated food or water and presents with fever, headache, abdominal pain, diarrhoea or constipation, and rose spots. Common complications of the systemic disease are intestinal perforation, haemorrhage, hepatitis, cholecystitis, osteomyelitis, endocarditisand and development of antibacterial resistance[1−3]. Encephalopathy is a rare but serious complication of typhoid fever that is associated with high mortality and characterized by altered mental status, seizures, coma, and neurological signs[4].

2. Case presentation

A 19-year-old male patient residing in urban slums of Raipur city, with a history of substance abuse of cannabinoids, alcohol and other unknown agents over the past year, developed symptoms of irritability, agitation and violent behaviour. As a result, he was presented to a hospital for evaluation. He was stabilised, treated and discharged after a 5-day hospital stay with olanzapine and sodium valproate as his post-discharge medication regimen.

4 Days after discharge, the patient developed high-grade fever up to 40.5 ℃, followed by decreased responsiveness, muttering, and self-talking after 2 days of fever. When the patient presented to our hospital, he was febrile with altered mentation and Glasgow Coma Scale/Score of E4 V1 M3. Fever was intermittent, responding to

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Table 1. Initial blood results of a 19-year-old male who was diagnosed with coma vigil secondary to salmonellosis.

Laboratory value	Observed	Normal range
Hemoglobin, g/dL	13.9	12-16
Total leukocyte count, cells/μL	4 750	4 000-11 000
Differential leukocyte count, as % of total		
Neutrophils	75%	40-60%
Lymphocytes	15%	20-40%
Monocytes	9.50%	2-10%
Eosinophils	1%	0-4%
Basophils	0%	0-1%
Platelet count, cells/μL	50 000	150 000-450 000
Blood urea, mg/dL	58	15-39
Serum creatinine, mg/dL	1.94	0.9-1.3
Total bilirubin, mg/dL	1.2	0.3-1.3
Direct bilirubin, mg/dL	0.2	0.1-0.3
Aspartate transaminase, U/L	>1 000	12-38
Alanine transaminase, U/L	450	7-41
Prothrombin time, seconds/International normalized ratio	13.4/1.4	10-14/1-1.4

antipyretics associated with chills and rigors. He had pulse rate of 62 beats/minute (Normal range: 60-100 beats/minute), BP of 130/82 mmHg (Normal range for systolic: 90-140 mmHg, Diastolic: 60-90 mmHg), respiratory rate of 18 times/minute (Normal range: 12-18 times/minute), and SpO_2 of 98% at room air (Normal range: >94%).

Abdominal examination revealed a soft abdomen with splenomegaly 6 cm below the costal margin and nontender hepatomegaly 5 cm below the costal margin with normal bowel sound. Neck rigidity and Kernig's sign was presented. Increased tone, brisk deep tendon reflexes, and ankle joint clonus were observed. Additionally, his bilaterally babinsky sign was positive. The initial blood work is as summarized in the Table 1.

On neurological examination the Glasgow Coma Scale Score of patient was 8/15 (E4 V1 M3) (Normal range: 15/15, mild injury 13-14, moderate injuries 9-12, severe injury <8). The cranial nerve examination was within normal limits with equally responsive bilateral pupils. The motor and sensory examination was normal globally with no localizing findings. Neck rigidity and Kernig's sign was present. Brisk deep tendon reflexes and ankle joint clonus were observed.

Ultrasonography of the whole abdomen showed hepatosplenomegaly with normal colour doppler of portal vein. Bilateral increased renal cortical echogenicity suggestive of renal parenchymal disease. Electrocardiogram was suggestive of sinus bradycardia. Lumbar puncture results were within normal parameters. Scrub typhus IgM, *Leptospira* IgM, dengue NS1 antigen and malaria rapid antigen were negative. Viral panel for heptatis A, B, C, E virus were all-negative along with negative test for human immunodeficiency virus.

The patient was initiated on antibiotics and dexamethasone for meningitis, with doxycycline administered considering possibility of tropical fever. On the 3rd day of admission, his blood culture turned to be positive for *Salmonella* typhi. It was found to be susceptible to ampicillin, azithromycin and ceftriaxone but resistant to the fluoroquinolone.

The patient's treatment was switched from injection meropenem 2 g/d to injection ceftriaxone 2 g/d given in 2 divided doses. Additionally, high-dose dexamethasone was given as per the patients' weight, *i.e.* 3 mg/kg first dose followed by 1 mg/kg every 6 hours for the next 8 doses. It took 5 days for the patient's fever to subside and his mentation started improving on day 7 but he was persistently mute until day 11 of treatment. A psychiatry consultation was obtained and the brain MRI did not show organic lesion. The patient was discharged after 15 days of hospitalisation. At the time of discharge, he had residual generalised hypotonia as well as paucity of speech with change in speech intonation according to the family members. At 1-month follow-up, the hypotonia had improved though marginally but the paucity of speech continued as the patient used only few words at a time. The family members also reported unusual behavioural changes following discharge, such as a blank stare, not eating food, talking to self as well as giving unusual responses to questions. On psychiatry consultations, the patient was given olanzapine 10 mg for schizophrenic symptoms. At 3-week follow-up, the family reported increased appetite of the patient and improvement in other behavioural aspects.

3. Discussion

In this case, the 19-year-old male, known addict to alcohol, cannabinoids and other agents presented with complaints of decreased responsiveness, muttering and altered mentation to our

emergency department. the patient was diagnosed with neuro-salmonellosis based on clinical presentation and managed with antibiotics. Following resolution of active infection he developed a prolonged mutism and paucity of speech afterwards that has continued to this despite clear Neuro-imaging. Such an unusual presentation of coma vigil with a globally obtunded state and persitent paucity of speech has never been described in literature.

With the advancement of modern diagnostic modalities and the use of antibiotics, it is unusual to see such extensive manifestations of salmonellosis. What is particularly rare are the CNS manifestations associated with the disease, the so-called "coma vigil" characterized by altered sensorium and classical bed picking in the patient[4]. The prolonged development of mutism is peculiar as it has no identifiable focal lesion in reported cases, as far as we know[5]. In addition, the post-typhoidal schizophrenic psychosis is highly variable in presentation and has been infrequently reported[6].

The CNS presentations of salmonellosis, the "typhoid toxaemia" presents within 48 hours of onset of fever are in line with what we experienced, but the presentation was rather that of an obtunded state with drowsiness than a delirious state that has been described in literature[6]. Besides, the signs of meningeal irritation , the residual CNS sequelae in form of prolonged mutism and speech difficulties has not been reported yet[4].

The probable pathophysiological mechanisms behind such presentations are unclear. Many possible hypothesis have been put forward such as direct invasion of CNS by the microbe, production of cell wall toxins that produce such effects, cytokine mediated injury, metabolic disturbances secondary to systemic inflammation or vascular thrombosis[5]. However, a detailed serological and autopsy analysis by several different studies failed to reach a consensus as to the origin of such presentations in *Salmonella* infections[6–8]. In our case, the CSF failed to show evidence of the bacteria. Despite the hepatitis and liver injury, the markers for liver synthetic functions remained within acceptable limits with no elevation of any known metabolic toxin to attribute the findings. MRI findings also failed to show any focal sequelae that may have arisen due to any vascular compromise. This leaves a possibility of bacterial toxin mediated or cytokine mediated injury, and the answer may lie in a combination of both. Manifestations such as meningeal symptoms and a globally obtunded and delirious state more parallel a CNS injury seen in sepsis associated encephalopathy[9]. However, certain specific features of "coma vigil" such as muttering delirium and bed picking might be due to interaction between specific bacterial products and circum ventricular organs and vagal afferents outside the blood brain barrier. Of particular interest are the circum ventricular organs due to their potent interactions with the hypothalamus, amygdala and hippocampus in producing behavioural changes[9].

In tropical settings, even in the presence of *Salmonella* infection, the diagnosis of coma vigil is made after ruling out more common conditions such as cerebral malaria, scrub typhus, leptospirosis, infectious meningitis and encephalitis. Only after these conditions along with non-infectious conditions such as substance abuse, iatrogenic drug reactions, intracranial bleeds and stroke have been excluded, should typhoid be labelled as the causative agent. The management approach remains straightforward, to begin with standard empirical antibiotics based on local sensitivity patterns for meningoencephalitis covering prevalent organisms. Adding a dose of steroid before starting antibiotic therapy to improve post-inflammation scarring and better long-term neurological prognosis with less long-term sequelae[10,11]. Once a diagnosis of coma vigil due to *Salmonella* is confirmed, antibiotics should be continued according to sensitivity patterns. There is evidence in favour of continuing steroids as it improves long-term neurological outcome.

4. Conclusions

We delve into the description of a case of 19-year-old male with disseminated salmonellosis and its atypical neuropsychiatric manifestations. The case brings to light the various unsual manifestations of the so-called coma vigil and informs clinical practice of its varied presentation; furthermore, the prolonged mutism and the sequential paucity of speech and development of psychiatric manifestations in the following months shed light towards novel findings that have yet to be described in clinical practice.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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Authors' contributions

PB: Manuscript preparation, editing and review; JS: Manuscript preparation, editing and review; PNW: Manuscript preparation, editing and review; RR: Manuscript preparation, editing and review.

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