



NEUROPSYCHIATRIC MANIFESTATIONS IN TYPHOID FEVER - A CASE REPORT

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ABSTRACT Enteric fever presenting with atypical manifestations is challenging even to astute clinicians and is not a new occurrence in the tropics. Various authors have highlighted the dynamic manifestations of this common tropical infection. The rarity of acute psychosis in typhoid fever can result in delayed and misdiagnosis of the condition. We report a case of a 36-year-old previously healthy man with nil comorbidities having travel history presented with fever, loose stools and acute psychotic symptoms. This was associated with headache, dizziness, vomiting, body weakness, hyperpathic variety of akinetic mutism, which was mistaken for a dissociative state. There were no other significant symptoms like nuchal rigidity or cervical lymphadenopathy. Neurological examination revealed reduced muscle tone of bilateral upper and lower limbs but otherwise unremarkable. MRI scan of his brain showed no abnormality. Blood specimens for microbiological culture grew Salmonella Typhi. He was treated with intravenous ceftriaxone for 14 days and responded well.

KEYWORDS :

INTRODUCTION

Typhoid fever is a disease caused by salmonella Typhi bacteria. Typhoid fever is endemic in many countries in Southeast Asia. The word 'enteric' suggests predominantly early involvement of the ileum and other parts of the gastrointestinal and biliary system in typhoid and paratyphoid fever. The term typhoid is derived from the Greek word typhus, by a French Pathologist Louis Pierre in 1829. Typhus means 'hazy' or 'smoky' and typhoid means 'Typhus like', differentiating it from the typhus group of fevers. The 'hazy' could have been a reference to the CNS manifestation where the patient have manifestations like delirious.

The infection is mainly transmitted through contaminated food and water supply. Symptoms vary from mild to severe, and usually begin at 6 to 30 days after exposure. Often there is a gradual onset of a high fever over several days accompanied by weakness, abdominal pain, headache, loose stools and vomiting. In severe cases, people may experience confusion. Neurological manifestation is one of the clinical presentations of extra-intestinal typhoid fever and this can occur in up to 84% of the cases. Nevertheless, acute psychosis or akinetic mutism is not a common clinical manifestation of typhoid fever.

CASE REPORT

A 36 years old male with nil co-morbidities presented with complaints of multiple episodes of loose stools, vomiting and intermittent fever for past 5 days. He had history of travel for holiday for 7 days with his friends following which family members noticed he had low mood, decreased appetite with low grade fever. He presented to hospital on day 5 of fever, loose stools and vomiting. It was associated with headache, dizziness and generalized fatigue. On physical examination, he was febrile with body temperature of 100.0°F and tachycardia with pulse rate of 120 beats per minute. His blood pressure was normal at 110/80 mmhg, apart from that, he did not have any other significant clinical findings.

Patient was initially treated for acute gastroenteritis with fluids and probiotics. On day 2 of hospital stay he had acute onset of behavioural changes whereby he was frequently talking to himself noticed by bystanders. He claimed that he was responding to the voices he heard in his head. On Day 3 he became restless and tried to jump out of the bed and climb up the window. At this stage working diagnosis was acute meningoencephalitis, cerebral malaria, acute psychosis of unknown cause. Thus, his blood sample was taken for laboratory investigations including full blood count, serum electrolytes, serum creatinine, blood film malaria parasite and culture sensitivity. Urine for drug screening was done in suspicion of elite drug use. On Day 4th of hospital stay he developed Akinetic mutism, he was apparent alert with lack of almost all motor function including speech, gesture and fascial expression. MRI brain with contrast was also performed which showed no evidence of increased intracranial pressure and no evidence

of any other abnormal findings. He was empirically started on intravenous ceftriaxone 2 grams 12-hourly and acyclovir 500 mg 8-hourly.

The laboratory investigation results showed his full blood count was within normal limit. His serum creatinine level was 1.29 mg/dl with serum electrolytes being within the normal range. The C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were raised. The lactate dehydrogenase was raised at 1468 U/L. The Blood film for malaria parasite was negative. His blood for bacterial culture was positive on the same day of isolation. The bacterial isolate was identified as Salmonella Typhi with an excellent identification profile. The isolate was susceptible to ampicillin, ceftriaxone, ciprofloxacin, and trimethoprim-sulfamethoxazole. Patient widal test was strongly positive and was started on injection Ceftriaxone 2 gm 12th hourly for 10 days following tapering dose to 1 gm 12th hourly for next 5 days. His sensorium started to improve on day 4th of treatment and at present he has no behavioural symptoms and was discharged on later date.

Table no-1 Blood investigation on the day of Admission

Haemoglobin	12.2 gm/dL
Total counts	3550 c/cumm
Neutrophils	77 %
Lymphocytes	18 %
Eosinophils	0 %
Monocytes	3 %
Basophils	0 %
ESR	53 mm/hr
Platelets	57,000 c/cumm
MPFT	Negative
Renal Parameters	
Urea	56 mg/dL
Creatinine	1.29 mg/dl
Sodium	137 mmol/L
Potassium	3.38 mmol/L
Uric acid	6.28 mg/dL

LDH - 1468 U/L

Stool microscopy – No inflammatory exudates, no cysts or ova seen.

Table no -2 WIDAL TEST Method - Tube agglutination

S.Typhi O	1:160 (Positive)
S.Typhi H	1:320 (Positive)
S.Paratyphi AH	Negative

S.Paratyphi BH	Negative
Result	Positive

Table no – 3 Antibiotic susceptibility testing result for this Salmonella Typhi isolate Method – Disc Diffusion Method

Antibiotic	MIC	Result
Ampicillin	0.75	Sensitive
Ceftriaxone	<=0.25	Sensitive
Ciprofloxacin	0.5	Intermediate
Trimethoprim/Sulfamethoxazole	<=20	Sensitive



Figure 1. The bacteria isolated in this case showing growth on MacConkey agar.

DISCUSSION

According to Global Burden of Disease estimates, more than half of the 14.3 million global cases of enteric fever in 2017 occurred in India, where it is estimated as 8.3 million cases and with 72000 deaths. Enteric fever is a systemic disease characterised predominantly by fever and abdominal pain, caused by dissemination of *Salmonella* Typhi or *Salmonella* Paratyphi. Enteric fever can affect many organ systems including liver, gastrointestinal tract, kidney and brain. Neurological manifestations occur in 2%–40% of patients and include spastic quadriplegia as a rare complication.¹

The neuropsychiatric symptom is one of the clinical presentations of typhoid fever that can be divided into two major groups, acute onset and slow onset. Acute onset is characterized by delirium or confusional state without much fever and the slow insidious onset with varying degrees of temperature with toxemia. Although the central nervous system involvement in typhoid fever is not uncommon but acute psychosis followed by atonia, such that experienced by the patient, in this case, is indeed very rare. The usual presentation of “typhoid toxemia” is at the onset of fever. It is in the form of “muttering delirium” or “coma vigil” with picking at bed clothes or imaginary objects and it usually subsides within 2–3 days of defervescence. Review of literature has failed to reveal any presenting symptom other than encephalopathy with varying stages of coma.

Our patient's behaviour with abnormal gestures was more in favour of the typhoid encephalopathy. The pathogenesis of typhoid encephalopathy remains unknown. In the past it was said typhoid delirium, stupor and coma carry a mortality of around 40%.² In an extensive study of neuropsychiatric manifestations of typhoid in Nigeria, Osuntokun et al 3 reported toxic delirium in 57% of 959 cases; 3.5% had varying depths of coma, 3.1% had bilateral pyramidal signs, 1% had transient extrapyramidal signs, 1% had peripheral neuropathy, mononeuritis multiplex and late development of post typhoid schizophreniform psychosis. In another case, the patient started talking irrationally, expressing inappropriate guilt and feeling of worthlessness on day three of illness (Ukwaja, 2010).⁴

In a study conducted by M Lakhota and RS Gehlot, at Mahatma Gandhi hospital, Jodhpur, a total of 232 patients of enteric fever, admitted between 1999 and 2001, were evaluated. The average age of patients was 36.9 ± 8.3 years, with males comprising of 71.4% and females 28.6% with mean duration of fever being 14.8 ± 5.6 days. 27% of patient had neurological manifestations of which 42% of these patients had typhoid delirium state and 57% had had specific neurological complications. Amongst specific neurological complications, 25% had features of encephalitis, 19% had psychiatric manifestations, 19.44% with cerebellar ataxia, and 13.89% with meningitis as the dominant features. Mortality rate amongst patients with neurological manifestations was 6.35%.⁵

Similarly, a study by Gazanfar Ali and Samia Rashid from SMHS

Hospital, Srinagar conducted a study on 791 patients with multidrug-resistant typhoid fever over a period of 6 years, of whom 84% individuals developed neuropsychiatric manifestations. These manifestations included, acute confusional state (73%); myelitis (6%), psychosis (0.6%), meningo-encephalitis (0.5%), encephalitis (0.25%), sensory motor polyneuropathy etc.

Administration of the appropriate antimicrobial therapy results in complete resolution of psychotic symptoms without the need to use antipsychotic medication. Although there is concern about the increasing number of multidrug-resistant *Salmonella* Typhi isolated globally, culture isolates have to be obtained on day of suspicion. The bacterial isolate from our patient was sensitive to all the tested antibiotics. He was successfully treated with intravenous ceftriaxone and his symptoms resolved completely.

CONCLUSION

Given the rarity of neuropsychiatric manifestations in typhoid fever, it can result in delayed and misdiagnosis of the condition. Acute infection with *Salmonella* Typhi should be included in the differential diagnosis of persons originating or traveling from a typhoid-endemic area with acute febrile neurologic illness, particularly if viral and bacterial aetiologies more typically associated with neurologic illness are not apparent. With high degree of clinical suspicion, it is important to take the appropriate sample for the isolation of the *Salmonella* Typhi, as the yield of the laboratory diagnosis benefits to establish diagnosis and initiate appropriate measures to prevent further complications. Early initiation of specific antibiotics ensures complete recovery without residual complications.

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