

Case report

A case of typhoid fever with neurological presentation

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ARTICLE INFO

Keywords:

Typhoid
Aseptic meningitis
Optic neuritis
Neuro involvement

ABSTRACT

Introduction: Typhoid fever, leading to systemic disease due to *Salmonella enterica* serotype Typhi, typically has gastrointestinal manifestation, however, neurologic complications—although uncommon, can arise. Aseptic meningitis and optic neuritis are rare manifestations that can be challenging to diagnose.

Case summary: Our patient a 31-year male presented with fever for 18 days associated with headache, rash, vomiting, diarrhea and progressive neurological symptoms in form of disorientation and blurred vision. On examination there was bilateral sixth cranial nerve palsy. Investigations were positive for typhoid fever with aseptic meningitis and optic neuritis. He was successfully treated with intravenous ceftriaxone and corticosteroids.

Conclusion: Atypical neurological symptoms of typhoid fever must be recognized. To prevent complications, early diagnosis and treatment are important. Typhoid fever should be considered in febrile patients with unexplainable neurological symptoms, especially in an endemic region.

Introduction

Enteric fever represents one of the most prevalent infectious diseases, especially in Asia and developing nations [1]. It's caused by bacteria after ingestion of contaminated foods and drinking water. The classic culprits are *Salmonella enterica* serotypes Typhi (formerly *Salmonella* Typhi) and Paratyphi A–C; the only reservoir of *Salmonella* Typhi and *Salmonella* Paratyphi A is humans [2].

Typhoid fever presents with fever, headache, abdominal pain, and gastrointestinal manifestations such as anorexia, nausea, vomiting, and constipation during the first week of illness [3]. In the 2nd week of the disease few distinct manifestations do develop such as relative bradycardia, hepatomegaly, splenomegaly and abdominal tenderness. Complications such as acute abdomen, intestinal perforation, pneumonia, altered sensorium, ataxia, psychosis, pancreatitis, hepatitis and nephritis are likely to develop after the third or fourth week of illness [3]. The full spectrum of neurological manifestations is only a small subset of an emerging spectrum [4], with the most classical clinical features not consistently evident across all patients, and disease possibly presenting in an atypical manner and thus likely underdiagnosed.

This case reports a young man with initially presenting with fever,

headache, visual blurring and disorientation subsequently diagnosed as having aseptic meningitis with optic neuritis secondary to typhoid fever.

Case summary

A 31-year-old man from Dhaka working in private service, arrived at the emergency department with a high-grade fever that lasted 18 days with a maximum temperature of 104 °F. The fever was associated with chills, body ache, and rash. Persistent vomiting and diarrhea started from 8th day. On the tenth day, he started getting a headache, and as the days passed, his condition worsened. His wife grew increasingly concerned when, on the 14th day, he started speaking incoherently. The next day, he developed of blurring of vision. History of taking any antibiotic prior to admission was uncertain.

On admission patient was conscious but disoriented with a Glasgow Coma Scale (GCS) of 14/15 (E4M6V4). He was mildly icteric with mild dehydration and tachycardia (pulse-110/min) and temperature 99.7 °F with bilateral conjunctival congestion and coated tongue. A maculopapular rash was present all over the body but more concentrated over trunk. Abdomen was soft, non-tender with just palpable spleen. Neurological examination revealed bilateral sixth cranial nerve palsy

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<https://doi.org/10.1016/j.idcr.2025.e02203>

Received 14 March 2025; Received in revised form 20 March 2025; Accepted 21 March 2025

Available online 24 March 2025

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with no signs of meningeal irritation. In light of the above findings, a provisional clinical diagnosis of typhoid fever was made, with differential diagnoses including dengue fever, leptospirosis, and malaria.

A CT brain was performed immediately which showed no abnormality. Ultrasonogram of abdomen revealed hepatosplenomegaly with liver measuring about 16.2 cm and spleen about 15.9 cm. Liver function test was deranged and urine routine microscopy showed significant proteinuria and mild hematuria. His blood culture was positive for *Salmonella* Typhi. The organism was sensitive for ceftriaxone, azithromycin, cefixime, and amikacin and resistant to amoxicillin, cotrimoxazole, cefotaxime. This was supported by a high titer triple antigen of *Salmonella* Typhi, H (TH) of 1:640 done by Widal agglutination tests. He was started on Inj. Ceftriaxone 2 gm, 12 hourly. Detailed investigation profile described in Table 1.

Over the next two days, patient became afebrile; however, his state of confusion persisted. Gadolinium contrast MRI brain was unremarkable (Fig. 1). Although an orbital MRI would add diagnostic value, it was not performed in our case, which could be a limitation. Ophthalmological examination revealed bilateral optic neuritis. CSF study showed

Table 1
Investigation comparison at admission and at discharge.

Investigations	At Admission	At Discharge
Hemoglobin (gm/dl)	13.5	13.2
Packed Cell Volume (%)	40.5	39.1
White Blood Cell (WBC) (10 ⁹ /L)	6.2	9.85
Neutrophils (%)	66.9	51.3
Lymphocytes (%)	31	41.7
Platelet (10 ⁹ /L)	160	377
Serum Bilirubin (mg/dl)	2.3	1.2
Alanine Transaminase (IU/L)	543	228
Aspartate Transferase (IU/L)	295	29
Alkaline Phosphatase (IU/L)	224	121
Serum Albumin (g/dl)	2.6	2.9
Serum Urea (mg/dl)	32	
Serum Creatinine (mg/dl)	1.11	0.98
Serum Sodium (m mol/L)	134	129
Serum Potassium (m mol/L)	4.1	4.2
C-Reactive Protein (mg/dl)	25.5	1.94
Prothrombin Time (Seconds)	10.3	
INR	0.85	
Triple Antigen- <i>Salmonella</i> Typhi, H (TH)	1:640	
Dengue Virus Antibody IgM & IgG	Negative	
Leptospira IgM & IgG	Negative	
Blood Culture and Sensitivity	<i>Salmonella</i> Typhi	No growth
Urine Profile –		
Protein	+++	
Pus cells	2–4	
Red blood cells (RBC)	7–8	
Urine C/S	No growth	
CSF Analysis:		
Color	Watery	
Appearance	Clear	
Glucose (mg/dl)	37.8	
Protein (mg/dl)	173	
RBC	0–2	
Total count of WBC	0.079	
Differential count of WBC-		
Polymorphonuclear cells (%)	25	
Mononuclear cells (%)	75	
Adenosine Deaminase (U/L)	4	
Mycobacterium tuberculosis (MTB) PCR	Not detected	
Culture	No growth	
Meningitis Panel	No organism found	
Brain Plain CT Scan	Normal CT scan findings	
Ultrasound of Whole Abdomen	Hepatospleno megaly with hypochoic hepatic parenchyma	
Brain MRI with contrast	Unremarkable MRI findings	

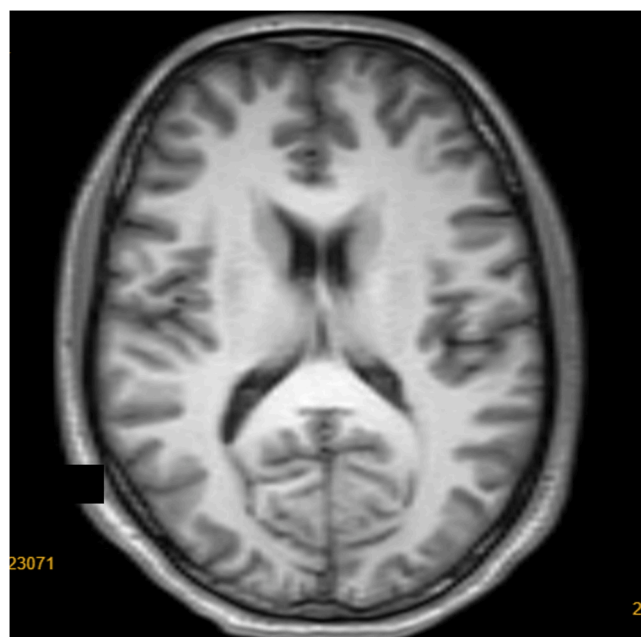


Fig. 1. Normal brain MRI.

high protein with pleocytosis predominantly mononuclear cells, but CSF culture yield no growth. With a working diagnosis of aseptic meningitis with optic neuritis due to typhoid fever, he was then initiated on Inj. Methylprednisolone 500 mg once daily for 3 days and later converted to oral prednisolone starting from 50 mg once daily later tapered. Over the next few days, his mental status, visual disturbance and overall well-being improved, with no further episodes of confusion. He was subsequently discharged with a total 14-day course of antibiotic and a steroid tapering regimen over 6 weeks.

Discussion

Typhoid fever is mainly known for its enteric presentations, but it can also affect the central nervous system (CNS), resulting in different neurological complications. Historically, in untreated typhoid fever, meningoencephalitis and neuropsychiatric manifestations, such as “coma vigil” in late stages, were reported [5]. Although severe neurological complications have been greatly diminished since the introduction of antibiotics, drug-resistant *Salmonella* Typhi outbreaks have highlighted the wide range of clinical manifestations [6]. Neurological involvement is known to occur with typhoid, though infrequently, and may present as encephalopathy, focal deficits, cranial nerve palsies, or immune-mediated syndromes such as Guillain-Barré syndrome (GBS) [7]. The identification of these neurologic characteristics is important, especially in endemic areas where febrile illnesses with unusual presentations could be misdiagnosed initially. We consider typhoid as our first differential as because, it is endemic in Dhaka city because of high density population, poor sanitary system and limited clean water. On the other hand, leptospirosis also a common diagnosis, in this setting but the patient wasn’t exposed to any contaminated wastewater or farming. Also, malaria can be a differential for a febrile patient from Bangladesh, but it is less prevalent in this part (Dhaka) of the country.

Aseptic meningitis, defined as meningeal inflammation in the absence of identifiable bacteria in cerebrospinal fluid (CSF), is an uncommon but known complication of typhoid fever [4]. Although the exact mechanism is unknown, such an effect is thought to be an immune response to *Salmonella* endotoxins or an inflammatory response, induced by bacterial antigens [8]. Culture-confirmed true *Salmonella* meningitis is very uncommon in immunocompetent adults and occurs

primarily in neonates or immunocompromised patients [7]. If present, *Salmonella* Typhi-associated bacterial meningitis is associated with high morbidity and mortality, with significant long-term neurological sequelae among survivors [7]. However, typhoid fever-associated aseptic meningitis usually has a favorable outcome with antibiotic treatment. Its clinical presentation typically involves fever, headache, nuchal rigidity, as well as altered sensorium, as shown in this case. Two other similar cases presented in the literature demonstrated recovery with antimicrobial therapy only and lend credence to the hypothesis that aseptic meningitis in typhoid is an inflammatory phenomenon rather than a manifestation of direct bacterial invasion of the CNS [5].

Optic neuritis, the inflammation of the optic nerve that causes visual impairment is a post-infectious complication of typhoid fever that has been documented, although reported extremely rarely [9]. The mechanism is presumed to be illegitimate and related to the phenomenon of molecular mimicry; that is, *Salmonella* Typhi antibodies cross-react with proteins in the optic nerves, which in turn cause demyelination [10]. Affected persons demonstrate sudden bilateral or unilateral loss of vision, relative afferent pupillary defects and optic disc edema on fundoscopic exam [9]. MRI findings characteristically show inflammation of the optic nerve, supporting the diagnosis [10]. Literature reports indicate that early intervention with corticosteroids leads to significant visual recovery, supporting the hypothesis that post-typhoid optic neuritis is an immune-mediated phenomenon rather than a direct bacterial infection [11].

The management of neurological complications of typhoid fever is guided by the clinical presentation. For the management of aseptic meningitis, prolonged antibiotic treatment for *Salmonella* Typhi is indicated and supportive treatment, including hydration and analgesics, is recommended for symptomatic relief [7]. In cases of optic neuritis, the optimal treatment strategy, as with other immune-mediated demyelinating disorders, is high-dose intravenous corticosteroids administered followed by an oral taper [10]. With early detection and treatment, the outlook is generally good for both. Patients with post-typhoid optic neuritis described in reported cases improved significantly after corticosteroids therapy [9]. Similarly, typhoid fever-associated aseptic meningitis has been shown to completely resolve when appropriate antimicrobial treatment is instituted [5]. Early identification and receiving the proper care are significant because delayed recognition or poor management may lead to permanent neurological sequelae [11].

Conclusion

Neurological involvement in typhoid fever presents with diagnostic and therapeutic dilemmas. The current case illustrates an uncommon dual presentation of aseptic meningitis and bilateral optic neuritis, both of which responded well to antibiotics and adjunctive corticosteroid therapy. Awareness of these atypical presentations is important for clinicians practicing in endemic areas to permit recognition and appropriate management in a timely manner. Although these neurological complications are rare, they appear to be underdiagnosed and should be included in differential diagnosis among patients with persistent neurological symptoms in association with recent enteric fever.

Ethical approval

Ethics approval was not required for this case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Funding

No funding was obtained or used for the completion of this manuscript.

CRediT authorship contribution statement

Rahman Mohammad Mahfuzur: Writing – review & editing, Investigation. **Sami Chowdhury Adnan:** Writing – review & editing, Investigation. **Mohona Sayat Quayum:** Writing – review & editing. **Ashraf Sohely:** Writing – review & editing, Methodology, Investigation. **Marisa Sumaiya Farah:** Writing – review & editing, Conceptualization. **Afsar Nikhat Shahla:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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