

Case Report

"Coma vigil" - case report of a rare neuropsychiatric complication in pan sensitive *Salmonella* infection

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Abstract

A 25 year old previously healthy male presented with low grade intermittent fever for ten days and confusion for two days. On examination he was febrile and confused, making abnormal unpurposeful gestures with his hands. He was not aggressive. There was no nuchal rigidity or cervical lymphadenopathy. He was started on empirical intravenous antibiotics and steroids to cover meningo encephalitis. He had a marginally elevated CRP, a normal full blood count and an unremarkable CSF analysis. The patient was started on chloramphenicol to cover typhus encephalitis. The CSF culture was sterile. *Salmonella enterica* serovar Typhi was isolated from blood culture.

Keywords: Typhoid, Salmonella, coma vigil, delirium

Introduction

A 25 year old previously healthy young man from the outskirts of Jaffna with no family history of any psychiatric illness presented with fever accompanied by chills and rigors of ten days duration. The fever was low grade and intermittent in nature and responded to antipyretics. The patient had generalized myalgia and arthralgia. He did not give a history of contact with anyone with a febrile illness. He regularly ate food prepared in restaurants.

Presenting Concerns

The patient was admitted to the local hospital on the 6th day of fever as there was no response to antipyretics. Soon after admission, his parents noticed behavioural changes. His food and water intake was poor with lack of sleep. He began to make abnormal hand and face gestures accompanied by babbling incoherent words. He was disoriented and was unable to recognize familiar objects or persons. He remained bladder and bowel continent. He continued to have low grade fever with chills. On day seven of the febrile illness he was taken home by the parents seeking traditional remedies. He was readmitted to Teaching Hospital Jaffna, the tertiary care centre of the region on the 10th day of fever with marked self neglect and altered behaviour.

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Clinical Findings

On admission he was febrile, not pale or icteric. No cervical or peripheral lymphadenopathy was evident. There were no visible rashes or eschar. It was evident that he had self-neglected himself and was unkempt. The pulse rate was 110/min and regular. Blood pressure was 110/80 mmHg and the heart was clinically normal.

Respiratory examination was unremarkable. No organomegaly was noted on abdominal examination. The patient was confused with GCS of 13/15 and was mumbling inappropriate words without any meaning. He was making unpurposeful gestures with his hands. He was not aggressive. His upper and lower limbs were neurologically normal with good muscle power, normal reflexes and intact sensation. His cranial nerve examination including optic fundoscopic findings were unremarkable.

Diagnostic Focus and Assessment

Initial investigations revealed a normal full blood count, ESR of 50 mm/hr and CRP of 43 mg/dl. He underwent a non contrast CT brain which was unremarkable. The subsequent CSF analysis was sterile without cells and a protein value of 43.7 mg/dl. CSF glucose was 56 mg/dl and the concurrent random blood sugar was 74 mg/dl. Biochemical work up to exclude a metabolic derangement was unremarkable (Serum Na 138 meq/l, K 4.6 meq/l, Calcium 8.9 mg/dL, serum magnesium 2.3 mg/dl, AST 23 U/L, ALT 83 U/L). The *Salmonella* serovar Typhi and *Salmonella* serovar Paratyphi O and H antibody titres using the Standard Agglutination Test (SAT) were negative at a titer of <1/30). An EEG confirmed diffuse slowing. A clinical diagnosis of typhoid fever complicated with neuropsychiatric disturbances was made which was confirmed with a positive blood culture for *Salmonella* Typhi sensitive to chloramphenicol, ampicillin, ciprofloxacin, norfloxacin, cotrimoxazole, ceftriaxone, gentamicin and amikacin.

Therapeutic Focus and Assessment

As the patient presented with fever and confusion, he was empirically treated with ceftriaxone 2 g and acyclovir 500 mg three times a day intravenously to cover bacterial and viral meningo-encephalitis. He was also given intravenous dexamethasone 8 mg three times a day to reduce the meningeal inflammation. Risperidone 1mg daily and clonazepam 0.5 mg at nights was added to treat the restlessness and confusion. On the third day following admission (12th day of fever), intravenous chloramphenicol 500 mg 6 hourly was added to the regimen to cover typhus encephalitis as scrub typhus was one of our main differentials.

Follow-up and Outcome

His confusion improved over the next few days and he was afebrile thereafter. Acyclovir was omitted and chloramphenicol and ceftriaxone were continued for a total of ten days. Antipsychotics and steroids were tailed off and discontinued.

Discussion

Enteric fever is caused by *Salmonella* Typhi and *S. Paratyphi*, Gram negative non-spore-forming, facultatively anaerobic bacilli of the family Enterobacteriaceae. Infection occurs by ingestion of organisms, either by contaminated food or water. Once the bacteria enter the small intestine they penetrate the mucosa and reside in the Peyer's patches till they get phagocytosed by macrophages. They survive inside the macrophages and get carried throughout the body via lymphatics and colonize and replicate in the reticulo-endothelial system, namely the spleen, liver, lymph nodes and bone marrow. The fever and abdominal pain are likely to be due to cytokine release from the activated mononuclear cells.

The most common symptom is prolonged fever which occurs in about 75% of patients and can last up to four weeks if left untreated. Although abdominal pain and constipation/diarrhoea are considered classical symptoms, they occur in only about 35% of the population.¹ This patient had fever for ten days before admission to TH Jaffna and did not have any gastrointestinal symptoms. Other symptoms such as headache, chills, sweating, anorexia, arthralgia may also occur in patients with enteric fever. Around 10% can develop hepatosplenomegaly. Typical "rose spots" rash in typhoid occur in about one third of infected patients and are mostly seen in patients with a fair complexion.¹

Complications in typhoid occur in 10 to 15 percent of patients and are particularly likely in patients who have been ill for more than two weeks. Many complications have been documented, of which gastrointestinal bleeding, intestinal perforation, and typhoid encephalopathy are the most important. Other complications include meningitis, disseminated intravascular coagulation, haematophagocytic syndrome, hepatic and splenic abscesses and granulomas, pancreatitis, endocarditis, myocarditis, pericarditis, orchitis, hepatitis, glomerulonephritis, pyelonephritis and haemolytic-uraemic syndrome, severe pneumonia, arthritis, osteomyelitis, and parotitis.²

Typhoid encephalopathy, also known as "typhoid state" "muttering delirium" or "coma vigil" is observed in 2-40% of typhoid patients. Picking at the bedclothes and at imaginary objects (carphology and floccillation) are characteristic, as is muscular twitching (subsultus tendinum).³ Even though not previously reported in Sri Lanka, around 27% of patients diagnosed with typhoid in India are reported to have some neurological manifestation, either due to typhoid toxemia causing delirium or as specific neurological manifestations such as encephalitis, polyneuropathy, nerve palsies or cerebellar ataxia.²

Our patient's behaviour with abnormal gestures was more in favour of the typhoid state. The pathogenesis of typhoid encephalopathy remains unknown. In the past it was said typhoid delirium, stupor and coma carry a mortality of around 40%.⁴

Typhoid fever should be suspected in any patient from the Asian sub continent with prolonged fever without an obvious focus of infection, especially in the monsoon season. Culture of the organism is the only recommended diagnostic test for typhoid. Blood culture is the widely used method but bone marrow, intestinal secretions, stool or rose spot punch biopsy can also be used to isolate the organism. Bone marrow culture has the highest sensitivity (90%) but is rarely performed.¹ Unlike the blood culture, it remains positive even after initiation of antibiotics. Other investigations (FBC, SAT) have low sensitivity and low positive predictive value as seen in this patient.

Empirical treatment for *S. Typhi* is with ceftriaxone 2 g daily or azithromycin 1 g daily. Ciprofloxacin is the optimal treatment for typhoid but quinolone resistance in Asia makes it a poor choice as empirical treatment.¹ Ampicillin, chloramphenicol and cotrimoxazole can also be used as treatment. There have been trials stating efficacy of high dose dexamethasone in the past with combination of chloramphenicol but no evidence with other drugs.¹ It has been proposed that steroids decrease mortality in typhoid encephalopathy by reducing the production and release of prostaglandins and free oxygen species by macrophages induced by *S. Typhi* endotoxin.⁵ However, evidence is still lacking to prove the definite benefit of steroids in typhoid delirium.

Oral live attenuated vaccine and a parenteral vaccine are available which needs booster dosing at five and two years respectively. People who travel to countries with high risk of infection are advised to get vaccinated. Proper sanitation and good personal hygiene play a main role in preventing the spread of this disease.

Conclusion

Typhoid delirium is a known neurological complication of typhoid fever which has not been previously reported in Sri Lanka. This patient presented on day nine of fever with typical muttering delirium and picking at bedclothes and imaginary objects. The diagnosis could have easily been missed if not for the high degree of clinical suspicion. Early initiation of specific antibiotics ensured complete recovery without residual complications.

References

1. Kasper L, Fauci A, Hauser S, et al. Harrison's Principles of Internal Medicine. 19th ed. 2015 New York. McGraw-Hill Medical. p.1049-1053. *No doi*
2. Parry CM, Hien TT, Dougan, et al. Typhoid fever. *N Engl J Med.* 2002; 347:1770–1782. *doi: 10.1056/NEJMra020201*
3. Verghese A. The “typhoid state” revisited. *Am J med.* 1985; 79(3):370-2. *PMID: 3898837*

4. Haque A. Neurological manifestations of enteric fever. In: Chopra JS, Sawhney IMS, editors. *Neurology in tropics*. 1st ed. BI Churchill Livingstone; New Delhi: 1999. pp. 506–512. *No doi*
5. Leung DT, Bogetz J, Itoh M, et al. Factors associated with encephalopathy in patients with *Salmonella enterica* Serotype Typhi bacteremia presenting to a diarrheal hospital in Dhaka, Bangladesh. *Am J Trop Med Hyg*. 2012; 86(4):698–702. *doi* : *10.4269/ajtmh.2012.11-0750*