SM Journal of Infectious Diseases

Case Report

Acute Cerebellar Ataxia as a Rare Manifestation of Complicated Typhoid Fever: A Case Report

Paroma Agarwal, Zulquar Nain*, Shaad Abqari and Iraj A Khan

Department of Paediatrics, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Abstract

Enteric fever is a very common infection in south East Asian countries with varied complication including neurological complications. However most common neurological complication of enteric fever is aseptic meningitis. This a case report of rare presentation of enteric fever with cerebellar signs and neuroimaging showing cytotoxic lesions. Furthermore, this case came out to be a case of drug resistant enteric fever. This is a concern in recent area of antimicrobial resistance as this atypical presentation can be attributed to resistant salmonella infection.

Keywords: Enteric Fever; Ataxia; Typhoid Fever

Introduction

Enteric fever is a common infectious disease with about 80% disease occurring in the Asian countries [1]. Characteristic features include fever, relative bradycardia, diarrhea or constipation, and abdominal pain. Although neurological complications are not much common, they usually occur in the second or third week of illness with the main presenting symptoms being delirium, meningismus, convulsions, or coma. Acute abdomen, intestinal perforation and pneumonia are likely to develop in third to fourth week of illness. Gullian Barre syndrome, cranial nerve palsies, stroke like illness, brain abscess and peripheral neuropathy are some other unusual manifestations of enteric fever. We are here presenting a case of enteric fever with acute cerebellar ataxia as a main presenting feature.

Case Report

Patient Information

A 12-year-old boy presented to the paediatric emergency of a tertiary care hospital with complaints of fever for the last four days, ataxia and slurring of speech since morning. There was no history of loss of consciousness, seizures, headache, vomiting, and deviation of eyes or angle of the mouth, diplopia, diminished vision, nasal regurgitation, ear discharge, or rash. No history of any trauma, drug intake or similar episode in the past. There was no significant family history. The patient was not a known case of any chronic illness and was not on any prolonged medication.

Submitted: 20 December, 2023 | **Accepted:** 23 January, 2024 | **Published:** 25 January, 2024

***Corresponding author(s):** Zulquar Nain, Department of Paediatrics, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Citation: Agarwal P, Nain Z, Abqari S, Khan IA (2024) Acute Cerebellar Ataxia as a Rare Manifestation of Complicated Typhoid Fever: A Case Report: Analysis of 2013-2017 Routine HIV Data Tanzania. SM J Infect Dis 7: 3.

Clinical Findings

On examination, the child was conscious, alert, oriented, and febrile (100.7 F) with a pulse rate of 98 bpm. There was no pallor, icterus, lymphadenopathy, cyanosis or rash. On examination of central nervous system, all cranial nerves were normal with no signs of meningeal irritation; muscle bulk and tone were normal in all four limbs, power was noted to be grade 5/5 in all four limbs; plantar reflexes were flexor bilaterally; sensory system was normal. Cerebellar signs were present in the form of wide-based gait, slurred speech, motor ataxia, dysdiadokinesia and positive finger-nose test in both limbs. Fundus examination showed no significant findings and was normal at presentation. No nystagmus, hypotonia, rebound phenomenon, or pendulum knee jerk were elicited. Evaluation of vestibular function was normal. Other systemic examination including that of respiratory, cardiac and abdominal systems was normal (Figure 1).

Diagnostic Assessment

Haematological investigations showed haemoglobin 12.7 g/dL; total leucocyte count of 4500/mm^3; differential count: neutrophils 10%, lymphocytes 74%, monocytes 8%; and platelet count of 1.36 lac/mm^3. Mildly raised transaminases were found with SGOT - 129 U/L and SGPT - 91U/L. ALP - 130 U/L and total serum bilirubin of 0.5mg/dL. Blood sugar, renal functions, and serum electrolytes were found to be normal. Cerebrospinal fluid examination was inconclusive (Cells = 2/mm3, Glucose = 57 mg/dL, proteins = 45 mg/dL, Chloride = 102 mg/dL, gram stain = negative). The CSF culture and viral panel were sent and reports were expected after one day. Stool examination (routine microscopy and culture) was negative. Subsequently, neuroimaging (MRI) was done which showed altered signal intensity region involving selenium of the corpus callosum which appears hyper intense on T2W and FLAIR sequences and is intense on TIW sequences with evidence of restriction of DWI. The final impression regarding the lesion was reported to be cytotoxic lesion of corpus callosum by radiology department. The child showed no improvement with persistent fever. Blood culture, C-reactive protein and Typhoid (IgM) was done. The result of Typhoid was weakly positive. The patient further evaluated with Widal test, the titre was positive with T(O) reactive up to 1:160 and T(H) reactive up to 1:80. Repeat Wedel test was done which

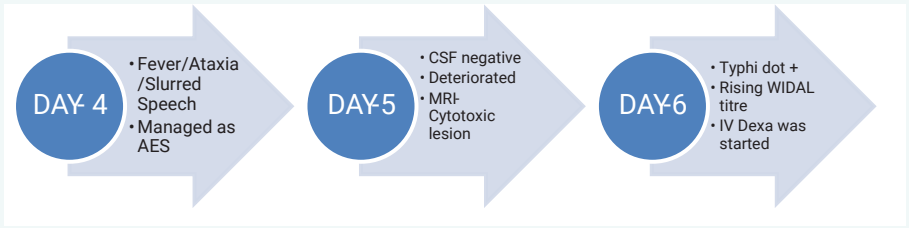

Figure 1

came out to be also positive with T(O) reactive 1:160 and T(H) reactive up to 1:160. Stool culture was also sent.

Therapeutic Intervention

The presumptive diagnosis was kept as acute meningoencephalitis and the patient was initially managed as per the protocol for Acute Encephalitis Syndrome (AES). This included supportive treatment and intravenous ceftriaxone (100 mg/kg/d), IV acyclovir (60 mg/kg/d), IV doxycycline and IV articulate. However, there was no response after 24 hours of treatment and patient's condition declined. Hence an urgent neuroimaging and blood investigation to look for other infections was done. IV articulate was stopped after smear demonstrated no malarial parasite and rapid diagnostic test for falciparum was negative. After receiving report of cytotoxic lesion on MRI and weakly positive Typhoid, the child was managed as a case of enteric encephalopathy. IV ceftriaxone was continued and IV dexamethasone (3 mg/kg loading dose followed by 1 mg/kg/dose six hourly for next two days) was added for the management of complicated enteric fever. Dysdiadokinesia and slurring of speech reduced markedly after day three of treatment. By day five, child started walking with support. The fever persisted with same intensity and duration. Blood culture (VITEC-2) reported later on was suggestive of *Salmonella tophi* (resistant to ampicillin, third-generation cephalosporin's, aminoglycosides, and fluoroquinolones). Antibiotics were changed as per culture sensitivity and were switched to meropenem (60 mg/kg/d). Child improved over next 3-4 days and the fever subsided. The CSF culture was sterile after 48 hours of incubation. The child was discharged after completion of 14 days of antibiotic treatment. A follow-up examination was done after three weeks of discharge which showed no signs of neurological complication or any relapse of enteric fever.

Discussion

Neurological complications in enteric fever usually occur by second week of illness with encephalopathy being the most common presentation. Acute cerebellar ataxia is a rarely reported neurological symptom of enteric fever. Wadia, et al. described 28 cases of enteric fever with neurological symptoms out of which only two of them presented with isolates cerebellar ataxia, remaining had a combination of ataxia with pyramidal, extrapyramidal signs, deafness or protracted confessional states [2]. Syngenta, et al. reported a patient with enteric fever developing cerebellar ataxia in first week of illness [3]. A seven-year-old boy was reported by Dew a, et al. with cerebellar ataxia on day two of fever [4]. Shawnee, et al. reported three adult patients with cerebellar ataxia on day two and three of enteric fever [5]. Faruk, et al. reported a seven-year-old boy with cerebellar ataxia during first week of fever [6]. In our case child presented primarily with cerebellar signs on day four of fever. Usually, cerebellar signs occur in the second week of illness, but as in our case, it may appear earlier. Although the pathophysiology of this neurological manifestation is not clear but metabolic disturbances, hyperpyrexia, dehydration, electrolyte imbalance, toxaemia and non-specific cerebral changes (enema and haemorrhage) have been described as the possible mechanism [7].

Due to high drug resistance with fluoroquinolones in India, the first line treatment to Salmonella Tophi has switched to cefixime and ceftriaxone and azithromycin [1]. This has further led to a resistance to third generation cephalosporin as is observed in our case and is also reported in Pakistan as XDR salmonella Tophi [8]. Similar cases of third-generation cephalosporin-resistant salmonella cases are also being reported from Kolkata and Pondicherry in India [9,10].

MRI findings are usually rare in cases of enteric fever [11]. Ahmed, et al. reported a fatal case of S. Tophi-associated encephalopathy with MRI findings of diffuse hyper intense signals on Fluid Attenuated Inversion Recovery (FLAIR) sequence in centrum semi vale, periventricular and deep white matter, splenium of corpus callosum with restricted diffusion in the corresponding areas [12]. Cytotoxic lesions of corpus callosum are usually a rare finding in children with postulated causes of the lesions being infection, trauma and drugs [13]. Enteric fever as cause of cytotoxic lesion of Corpus callosum is rarely reported with only a handful of cases present in literature [12,14,15]. Gagneja, et al. reported a case of 4-year-old boy with enteric fever showed lesions in the corpus callosum with restricted diffusion in the white matter of bilateral cerebral hemisphere in MRI [14]. Similarly, in our case the child showed cytotoxic lesions in the corpus callosum. These lesions are usually reported to be reversible with radiological clearing in 3 weeks to 4 months.

Conclusion

Acute Cerebellar Ataxia is an uncommon manifestation of the enteric fever and can appear even in the first week of illness. The case is interesting in the sense that it describes a major complication of enteric fever. However, the link between the clinical presentation and the resistance to antibiotic treatment cannot be proven. Besides, neurologic manifestation can be due

to the bacteria per se, or to the immunological reaction, which is more likely the case in this observation, given normal CSF analysis. Hence, the resistance to the initial antibiotic regimen might not have influenced the course of the disease and third generation cephalosporin should be initial drug even in suspected enteric fever. As it a treatable condition, a differential diagnosis of enteric fever should be considered when investigating a case presenting with fever and cerebellar ataxia.

Informed Consent

The informed consent was taken from father of the patient and can be provided if needed from editorial office.

Author's Contribution

PA wrote the original manuscript. ZN reviewed and edited the article. SA and IA did the final manuscript edit and quality check.

References

1. Kumar P, Kumar R. Enteric Fever. Indian J Pediatr. 2017; 84(3): 227-230. doi: 10.1007/s12098-016-2246-4. Epub 2016 Oct 29. PMID: 27796818.
2. Wadia RS, Ichaporia NR, Kiwalkar RS, Amin RB, Sardesai HV. Cerebellar ataxia in enteric fever. J Neurol Neurosurg Psychiatry. 1985; 48(7): 695-697. doi: 10.1136/jnnp.48.7.695. PMID: 4031914; PMCID: PMC1028413.
3. Sangeeta A. Acute Reversible Cerebellar Ataxia in Typhoid Fever Case Report. Int J Biol Med Res. 2014; 5(1): 3915–3916.
4. Dewan P, Pooniya V, Kaushik JS, Gomber S, Singhal S. Isolated cerebellar ataxia: an early neurological complication enteric fever. Ann Trop Paediatr. 2009; 29(3): 217-219. doi: 10.1179/027249309X12467994693978. PMID: 19689864.
5. Sawhney IM, Prabhakar S, Dhand UK, Chopra JS. Acute cerebellar ataxia in enteric fever. Trans R Soc Trop Med Hyg. 1986; 80(1): 85-86. doi: 10.1016/0035-9203(86)90202-6. PMID: 3727002.
6. İncecik F, Hergüner MÖ, Mert G, Alabaz D, Altunbaşak Ş. Acute cerebellar ataxia associated with enteric fever in a child: a case report. Turk J Pediatr. 2013; 55(4): 441-442. PMID: 24292041.
7. Cohen JI, Bartlett JA, Corey GR. Extra-intestinal manifestations of salmonella infections. Medicine (Baltimore). 1987; 66(5): 349-388. doi: 10.1097/00005792-198709000-00003. PMID: 3306260.
8. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Emergence of an Extensively Drug-Resistant Salmonella enterica Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins. mBio. 2018; 9(1): e00105-18. doi: 10.1128/mBio.00105-18. PMID: 29463654; PMCID: PMC5821095.
9. Dutta S, Das S, Mitra U, Jain P, Roy I, Ganguly SS, et al. Antimicrobial resistance, virulence profiles and molecular subtypes of Salmonella enterica serovars typhoid and Paratyphoid A blood isolates from Kolkata, India during 2009-2013. PLoS One. 2014; 9(8): e101347. doi: 10.1371/journal.pone.0101347. PMID: 25098613; PMCID: PMC4123848.
10. Menezes GA, Harish BN, Khan MA, Goessens WH, Hays JP. Antimicrobial resistance trends in blood culture positive Salmonella Typhi isolates from Pondicherry, India, 2005-2009. Clin Microbiol Infect. 2012; 18(3): 239-245. doi: 10.1111/j.1469-0691.2011.03546.x. Epub 2011 Jun 29. PMID: 21714829.
11. Sejvar J, Lutterloh E, Naiene J, Likaka A, Manda R, Nygren B, et al. Neurologic manifestations associated with an outbreak of typhoid fever, Malawi--Mozambique, 2009: an epidemiologic investigation. PLoS One. 2012; 7(12): e46099. doi: 10.1371/journal.pone.0046099. Epub 2012 Dec 3. PMID: 23226492; PMCID: PMC3513310.
12. Ahmed M, Sureka J, Mathew V, Jakkani RK, Abhilash KP. Magnetic resonance imaging findings in a fatal case of Salmonella typhi-associated encephalopathy: a case report and literature review. Neurol India. 2011; 59(2): 270-272. doi: 10.4103/0028-3886.79145. PMID: 21483131.
13. Aksu Uzunhan T, Maraş Genç H, Kutlubay B, Kalın S, Bektaş G, Yapıcı Ö, et al. Cytotoxic lesions of the corpus callosum in children: Etiology, clinical and radiological features, and prognosis. Brain Dev. 2021; 43(9): 919-930. doi: 10.1016/j.braindev.2021.05.001. Epub 2021 Jun 11. PMID: 34120800.
14. Gagneja V, Kumar P, Kejriwal N, Tucker S. Mild encephalopathy with reversible splenial lesion of the corpus callosum due to enteric fever. J Pediatr Crit Care. 2021; 8(3): 139-141.
15. Chopra P, Bhatia RS, Chopra R. Mild Encephalopathy/Encephalitis with Reversible Splenial Lesion in a Patient with Salmonella tophi Infection: An Unusual Presentation with Excellent Prognosis. Indian J Crit Care Med. 2019; 23(12): 584-586. doi: 10.5005/jp-journals-10071-23300. PMID: 31988550; PMCID: PMC6970213.