Typhoid Fever Presenting as Acute Cerebellar Ataxia and Severe Thrombocytopenia

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SUMMARY

Typhoid fever being a systemic infection can present in a multitude of ways, involving various systems. Here we describe a case of typhoid fever presenting with acute cerebellar ataxia and marked thrombocytopenia. This atypical presentation is not common in typhoid fever and can lead to misdiagnosis as well as a delay in the initiation of appropriate therapy. Prompt clinical improvement and the return of platelet counts to normal were noted after the patient was started on IV Ceftriaxone.

KEY WORDS:
Typhoid fever, Acute cerebellar ataxia, Thrombocytopenia, Ceftriaxone

INTRODUCTION

Typhoid or enteric fever is a systemic infection which can present in a multitude of ways. Characteristic presenting features include fever, relative bradycardia, diarrhea or constipation and abdominal pain. Neurological involvement in typhoid fever is not uncommon. Complications such as meningism, delirium, coma and convulsions have often been reported. Here we present a case whereby the main presenting feature was acute cerebellar ataxia with marked thrombocytopenia.

CASE REPORT

A 28 year old Malay man from Bagan Datoh, working as a laborer in a coconut plantation, presented to us with one week history of fever followed by four days of unsteady gait, slurring of speech and vomiting. He did not have any headache, diarrhea or abdominal pain. On initial examination, the patient was febrile but there was no evidence of relative bradycardia or 'rose spots'. He had no neck stiffness but walked with a broad-based gait. Romberg's test was negative. Dysdiadochokinesia and past-pointing were present bilaterally. There was no obvious nystagmus and his tone and reflexes were normal. He was also noted to have left sided upper motor neuron VII nerve palsy. Hearing was reduced bilaterally although formal audiology testing was not done. There were no other neurological signs apart from those mentioned. The liver and spleen were not enlarged. The patient gave no history of taking any medication, alcohol or recreational drugs prior to this.

An urgent CT brain was reported as normal. Lumbar puncture was not done as the patient had marked thrombocytopenia (26,000/ul). He also had mild anemia and leucopenia (hemoglobin 11.5 g/dl and total white count 4,200/ul). He was found to have a markedly raised creatine kinase (7659 iu/l) as well as liver impairment (serum albumin 33 g/l, total bilirubin 16 mmol/l, ALP 129 iu/l, AST 956 iu/l, ALT 301 iu/l). Initial renal profile was also deranged (urea 9.2 mmol/l, Na 127 mmol/l, potassium 2.8 mmol/l, chloride 96 mmol/l, creatinine 207 umol/l). Repeated blood films did not show any malarial parasites. Screening for HIV, hepatitis B and hepatitis C were negative. Both Dengue IgG and IgM were found to be positive. The differential diagnoses at that time included dengue encephalitis and leptospirosis. The patient was empirically started on IV Ceftriaxone 2 g bd as well as IV Acyclovir 500 mg tds.

The patient made rapid recovery with the treatment given. Dysdiadochokinesia and past-pointing were no longer obvious by the second day. Ataxia and dysarthria improved by day 6 and he was afebrile by the 7th day. His platelet counts also improved and returned to normal. His blood culture results came back as *Salmonella typhi* (non multi-drug resistant). Widal test was negative despite being repeated twice, 12 days apart. Leptospira serology came back negative.

The patient's diagnosis was changed to typhoid encephalitis. Ceftriaxone was continued for 14 days and Acyclovir discontinued. On discharge, the patient showed complete neurological recovery with all blood investigations returning to normal. Three consecutive stool cultures were also negative for *Salmonella typhi*. No other case of typhoid fever was reported during the subsequent weeks.

DISCUSSION

In the progression of typhoid fever, the second week is commonly described as the week of complications. Literature describes meningism, delirium, coma and convulsions as common neurological complications of typhoid fever. Acute cerebellar ataxia associated with typhoid fever is rare. It commonly occurs in the second week but can manifest within the first few days of illness. In cases which have been reported, neck stiffness is typically absent and gait ataxia is usually marked as in our patient. Op Kalra, *et al* described a similar case in a 19 year old Indian patient [1]. Cerebrospinal fluid (CSF) examination of that patient showed only mildly elevated protein level (45 gm/dl) with no cells seen and no growth when cultured. The exact pathogenesis of this complication is unknown although it has been postulated that non-specific inflammation of the cerebellum may play

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an important role. Recovery with appropriate treatment is often complete but may take as long as two weeks.

The preferred treatment for uncomplicated typhoid fever currently is a short-course of Ceftriaxone (3g daily for three days) or Fluroquinolones (e.g. Ciprofloxacin 500mg bd for 7-10 days) as compared to traditional therapy with Chloramphenicol which requires up to 14 days of treatment and carries the risk of developing bone marrow suppression and aplastic anemia. Antibiotics may need to be continued for up to 14 days in severe cases. There are no clear recommendations on the duration of therapy in cases of typhoid fever presenting with cerebellar ataxia. Kang JK, *et al* reported the success of high doses of intravenous dexamethsone together with antibiotics in the treatment of a patient presenting with cerebellar ataxia [2].

The above case also presented with thrombocytopenia and mild leucopenia. Malik AS and Malik RH found thrombocytopenia (< 150,000/ul) in 26% of cases of typhoid fever in Malaysian children [3]. Toxic arrow suppression is believed to be a cause of thrombocytopenia in typhoid fever. Complete recovery is expected following successful treatment of the underlying infection. In countries where dengue fever is endemic, the diagnosis of dengue will undoubtedly be entertained. As single qualitative dengue serology testing carry false positive rates of up to 42.5% [4], withholding the appropriate antibiotics in such a case would certainly be catastrophic. Therefore, a high index of suspicion is needed not to miss a diagnosis of typhoid fever. Perhaps it is also prudent for us to recognize clinical features which suggest a diagnosis other than dengue fever early and investigate further.

The above case illustrates the need to re-look at typhoid fever as an entity as it mimics a myriad of other possible diseases. The epidemiology as well as the travel history of a patient becomes increasingly important as well as a high index of suspicion especially in cases coming from endemic areas.

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