PARKINSONISM AND BRAIN MRI FINDINGS IN A RELAPSED CULTURE-PROVEN *SALMONELLA TYPHI* INFECTION: A CASE REPORT IN MALAYSIA

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ABSTRACT

Typhoid fever is a systemic infection caused by *Salmonella typhi*, which may be associated with extra-intestinal complications. Neurological manifestations, particularly Parkinsonism, are rarely reported. We report a 17-year-old patient with relapsed culture-proven *Salmonella typhi* infection who developed septic shock and subsequently Parkinsonism. Lumbar puncture revealed acellular cerebrospinal fluid with raised protein level. Magnetic resonance imaging revealed cerebral petechial haemorrhages resulted from small vessels vasculitis. His symptoms resolved spontaneously after 3 months.

Keywords*: Typhoid fever, Salmonella typhi, neurological manifestation, Parkinsonism, MRI brain*

Background

Typhoid fever is a systemic infection caused by *Salmonella typhi* or *paratyphi A*. Headache is a common symptom in 44-94% of cases (1-3) but other neurological manifestations such as encephalopathy, meningitis, Parkinsonism, motor neuron disorders, ataxia, cerebral abscesses, cerebral oedema, seizures and Guillain–Barré syndrome are infrequently reported. This is a case report describing the clinical presentation and features of the magnetic resonance imaging (MRI) of the brain of a patient with relapsed culture-proven *Salmonella typhi* with Parkinsonism.

Case Report

A 17-year-old male presented to the Emergency Department with a 5-day history of high-grade fever as well as diarrhoea that lasted for 2 days. He was previously treated for typhoid fever and had completed a course of treatment with ceftriaxone one month prior to admission. On examination, he was febrile and had hepatosplenomegaly. A diagnosis of relapsed typhoid fever was considered and he was started on empirical intravenous (IV) ceftriaxone therapy.

Laboratory tests showed the following results: white blood cell count 4400/µl (neutrophils 62.4%, lymphocytes 29.9%, monocytes 7.2%); haemoglobin 13.6 g/dl; C-reactive protein 125.8 mg/dl; platelet count 37,000/mm^3; total bilirubin 41.8 µmol/l; aspartate aminotransferase 251 IU/l; alanine transaminase 109 IU/l; lactate dehydrogenase 1481 IU/l; creatine kinase 2418 IU/l; and normal renal function. Serum rapid HIV test was negative.

Blood culture taken at admission grew *Salmonella typhi* on day 2 of admission, with susceptibility to Ampicilin, Ceftriaxone, Chloramphenicol, Ciprofloxacin, Trimethoprim/Sulfamethoxazole, Imipenem and Meropenem. He was continued on Ceftriaxone. His platelet count increased to a normal level since day 5 of admission following a total of 12 units of random platelet transfusion from day 2 to day 4 of admission. He had septic shock complicated by myocarditis and was transferred to the Intensive Care Unit. The patient received an initial bolus of high dose intravenous dexamethasone 3 mg/kg, followed by eight consecutive doses of the drug at 1 mg/kg administered 6-hourly. Subsequently, he developed nosocomial infection. On day 22 of admission, his fever settled but he was found to have bilateral pill-rolling tremor and cogwheel rigidity. Lumbar puncture was done and the result showed that his cerebrospinal fluid was acellular and had protein level of 876 mg/dl and glucose level of 3.9 mmol/dl (blood glucose 4.9 mmol/dl). The cerebrospinal fluid gram stain and culture were negative for bacterial and fungal growth. Magnetic resonance imaging (MRI) of

the brain performed on day 30 of hospitalization revealed multiple petechial haemorrhages in the brain parenchyma involving the junction between the grey and white matter, corpus callosum and internal capsule bilaterally [Figure 1]. His symptoms resolved spontaneously over a period of 3 months.

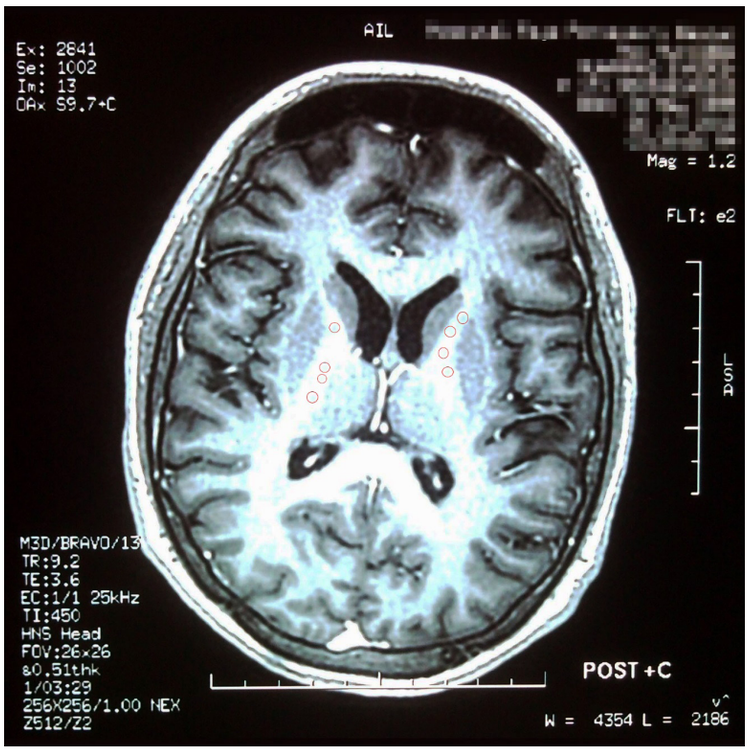

Figure 1: Axial T1W magnetic resonance image of the brain showing hypointense foci (red circles) in the internal capsule bilaterally. This finding is consistent with petechial haemorrhages.

Discussion

Typhoid fever is caused by facultative gram-negative bacillus *Salmonella typhi* or *paratyphi A*. It usually occurs in developing countries as a result of poor sanitation and poverty. The prevalence of the disease is estimated to be 12-33 million cases (4). It can affect multiple organs system, and therefore, neurological sequelae is not uncommon. Relapse typhoid fever occurs in 5-10% of cases and is usually less severe than the initial episode. However, hepatomegaly is a more common sign in relapse cases (5).

Parkinsonism is a rare neurological manifestation of typhoid fever, which was first described by Millis in 1927 (6). In a study by Ali et al., 84% of cases of multidrug-resistant typhoid fever developed neuropsychiatric manifestations, which include acute confusional state (73%), myelitis (6%), cerebellitis (1%), Parkinsonism (1%), acute psychosis (0.6%), meningoencephalitis (0.5%), encephalitis (0.25%) and others [3]. During an outbreak in Malawi-Mozambique in the year 2009, 40 out of the 303 identified cases were associated with neurological abnormalities but only 8 of them had Parkinsonism (7). Neurological symptoms usually appear during the first few days of the fever but may occur up to the third week or during the convalescence period, as seen in this case.

The exact pathophysiology of central nervous system involvement in Salmonella typhi infection is not clear, and various mechanisms such as neuro-endotoxin interaction and altered immune response have been proposed (3). Everest et al. suggested that both bacteria and host response are crucial in the mechanism of severe typhoid infection. Immune response triggered by bacteraemia may lead to necrosis of the venules and capillaries, and finally, haemorrhage (8). Subthalamic dysfunction is associated with Parkinson's disease. Subthalamic activity is regulated by direct (through pallidothalamic) and indirect (through pallidosubthalamic) signal pathways out of the striatum. Pallidothalamic fibers pass through the internal capsule and lesions in this region may affect the balance between these two pathways, leading to Parkinsonism (9). This may explain the MRI findings of small vessel petechial haemorrhage involving the internal capsules in our patient.

Previous studies have reported various features from MRI investigation, ranging from normal appearance, demyelinating changes, symmetrical diffuse abnormal

signal with central area of restricted diffusion to diffuse cerebral oedema (10-13). The literature on imaging findings of Parkinsonism is lacking. Talukdar et al. reported a normal appearance on MRI in a patient with catatonia and Parkinsonism (13), however, the MRI was done prior to the onset of Parkinsonism. To the best of our knowledge, this is the first case report demonstrating the MRI findings in a patient with typhoid fever and Parkinsonism.

In the present case, the patient's neurological symptoms resolved spontaneously over a period of 3 months. A recent case report indicated that a combination of amantadine and dopamine agonist resulted in a complete recovery of symptoms within a month of treatment (13). High-dose intravenous methylprednisolone has also been shown to be successful in treating patients with salmonella-associated encephalopathy (11); however, its benefit in Parkinsonism is yet to be evaluated.

Conclusion

Parkinsonism is a rare neurological manifestation, which may be a complication of relapsed typhoid fever. Petechial haemorrhages of the brain parenchyma affecting the subthalamic activity may be one of the mechanisms involved. Parkinsonism may resolve spontaneously but antiparkinsonian therapy could facilitate recovery from this condition.

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Competing interests

All authors declare that they have no competing interests.

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