CASE REPORT

Mild Encephalopathy/Encephalitis with Reversible Splenial Lesion in a Patient with *Salmonella typhi* Infection: An Unusual Presentation with Excellent Prognosis

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Abstract

Mild encephalopathy/encephalitis with reversible splenial lesion (MERS) is an uncommon clinicoradiological entity reported mainly in East Asian population. Mild encephalopathy/encephalitis with reversible splenial lesion is characterized by neuropsychiatric manifestations, magnetic resonance imaging (MRI) findings of the reversible lesions in the splenium of corpus callosum, and good clinical outcomes. These transient splenial lesions are not specific to a particular condition and have been described mainly in children in various situations including epilepsy or peri-ictal state, antiepileptic drug use, and infectious agents such as influenza virus, *Mycoplasma pneumoniae*, *Legionella pneumophila*, and O-157 *Escherichia coli*. Mild encephalopathy/encephalitis with reversible splenial lesion is an uncommon complication of *Salmonella* infection and has been described earlier in a child who made excellent clinical recovery. We report a case of *Salmonella typhi* encephalopathy in a young adult who presented with reversible transient splenial lesions on MRI. The patient recovered without neurological sequelae. Awareness of these lesions is important as these are uncommon findings on MRI and carry excellent prognosis.

Keywords: Magnetic resonance imaging, Mild encephalopathy with reversible splenial lesion, *Salmonella* encephalopathy.

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Introduction

Mild encephalopathy/encephalitis (MERs) with reversible splenial lesion is a clinicoradiological entity, reported mainly in the pediatric age group.[1] This entity has been reported with diverse conditions including epilepsy, use of antiepileptic drugs, and certain infections such as influenza, *Legionella*, *Mycoplasma*, and *E. coli*.[2–6] Transient splenial lesions have been previously described in a child with nontyphoid *Salmonella*.[7] However, there is limited literature on MERS in adults with *Salmonella* infection. We report a case of MERS in a young adult with culture-proven typhoid fever.

Case Description

A previously healthy 21-year-old male was referred to our hospital with a high-grade fever, decreased oral intake, generalized abdominal discomfort, and altered sensorium for 3 days. He was a resident of the United States with parents of Indian descent and had come to India for the first time on a personal visit. 10 days prior to admission, the patient developed diarrhea and low-grade fever and he self-medicated with paracetamol tablet with initial improvement in symptoms. He was brought to the emergency department in view of persisting fever and altered sensorium. On evaluation, the patient was disoriented to time, place, and person. There was slurring of speech and ataxia. He was moving all four limbs equally and had bilateral extensor plantar reflexes, normally elicitable deep tendon reflexes, and no neck stiffness. His cranial nerve examination was normal. Systemic examination was unremarkable except for hepatosplenomegaly.

A diagnostic possibility of tropical infection or meningoencephalitis was considered. Laboratory investigations revealed normal total leukocyte count, thrombocytopenia (platelets 96×10^9/L), serum creatinine 1.70 mg/dL (normal range: 0.5–1.3 mg/dL), aspartate aminotransferase (AST) 286 units/L, and alanine aminotransferase (ALT) 106 units/L. Cerebrospinal fluid study found glucose 66 mg/dL (blood glucose 94 mg/dL), protein 17 mg/dL, and nil white blood cell. Brain MRI on admission revealed an abnormal T2 hyperintensity in the splenium of corpus callosum showing restricted diffusion. There were no hemorrhagic residues or abnormal postcontrast enhancement of the lesion (Fig. 1).

Leptospiral, malarial, scrub typhus, and HIV serology were negative. Widal test was strongly positive with a *S. typhi* flagellar (TH) agglutinin level of ≥960. On day 5, blood cultures isolated *Salmonella* enteric serotype typhi. A diagnosis of typhoid fever with encephalopathy was made in view of positive blood culture and clinical features. The patient was managed with intravenous ceftriaxone twice daily for 14 days. There was improvement in sensorium by day 6 of hospital admission. Repeat MRI performed on day 8 revealed complete resolution of changes in the splenium of corpus callosum (Fig. 2). He was discharged from hospital without any central nervous system impairment.

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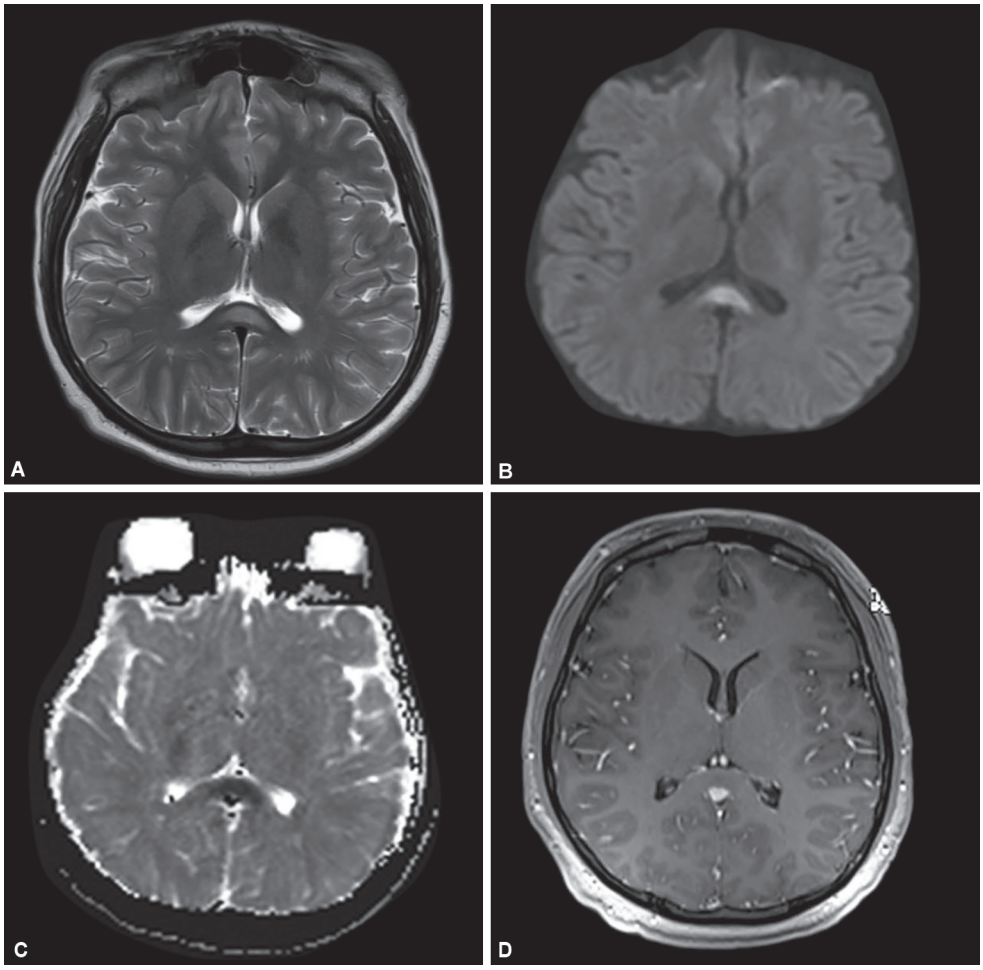
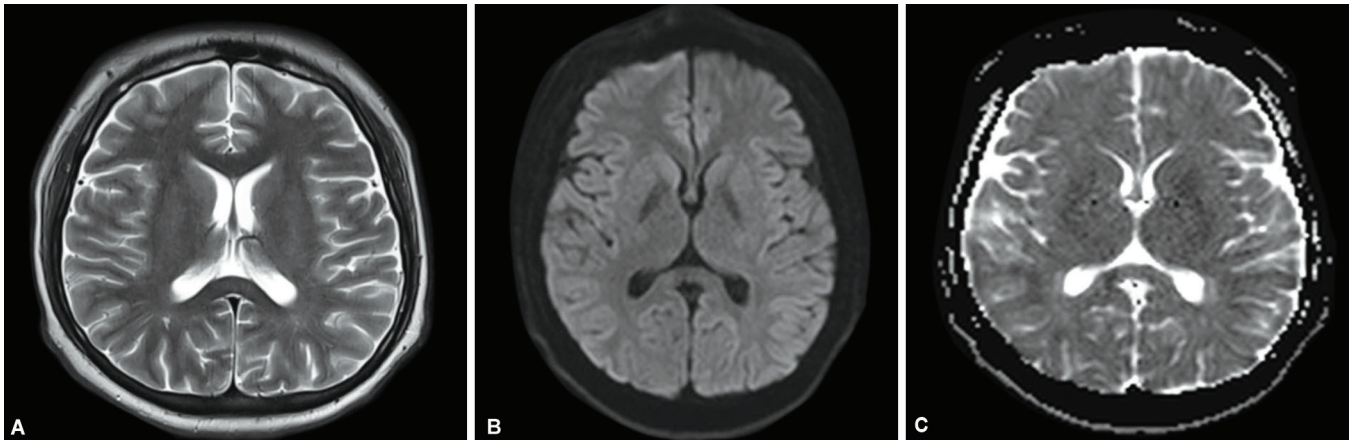


Figs 1A to D: Magnetic resonance images in a patient with typhoid fever and encephalopathy on hospital admission: (A) T2-weighted axial image shows a hyperintense signal in splenium of corpus callosum; (B and C) Diffusion-weighted image shows hyperintensity on diffusion and hypointensity on apparent diffusion coefficient (ADC) image suggestive of restricted diffusion; (D) No abnormal postcontrast enhancement seen on contrast-enhanced T1-weighted image



Figs 2A to C : Magnetic resonance images in a patient with typhoid fever and encephalopathy on 8th hospital day: (A) T2-weighted image; (B and C) Diffusion-weighted and ADC image. There is complete resolution of T2 hyperintensity and restricted diffusion in splenium of corpus callosum

Discussion

Our patient presented with fever, had a disoriented behavior, and had reversible neuroradiological findings on MRI in the splenium of corpus callosum with good clinical outcomes, consistent with MERS. This entity has been rarely reported as a complication of typhoid fever in the adult age group.

Complicated *S. typhi* infection has variable neurological manifestations including encephalitis, delirium, meningitis,

psychotic state, tremors, cerebellar ataxia, seen in about 27% of cases.[8] Age (10–24 years), severe dehydration, Widal TH ≥640, and leukopenia have been implicated as the risk factors associated with higher rates of typhoid encephalopathy, probably reflecting prominent inflammatory response.[9]

There is limited literature on MRI findings in neurological complications of *S. typhi*. Ahmed et al. reported a fatal case of *S. typhi*-associated encephalopathy with MRI findings of diffuse hyperintense signals on fluid attenuated inversion recovery (FLAIR) sequence in centrum semiovale, periventricular and deep white matter, splenium of corpus callosum with restricted diffusion in the corresponding areas.[10] Alternatively, patients with typhoid fever-associated encephalopathy can have no signal abnormalities on MRI.[11]

Tada et al. proposed the terminology "mild encephalopathy/encephalitis with reversible splenial lesion" to describe clinicoradiological syndrome sharing common features of mild encephalopathy, reversible lesions in corpus callosum, and good clinical outcomes. Although there are no definite clinical criteria to define MERS, the most common presenting features are fever and neurological symptoms including delirium, altered sensorium, ataxia, and seizures. The key radiological features include T2 hyperintensity, restricted diffusion, and nonenhancing lesions located in the splenium of corpus callosum.[1,2] Mild encephalopathy/encephalitis with reversible splenial lesion has been reported with diverse etiologies including metabolic disturbances, epilepsy or postictal state, use of antiepileptic drugs, and infections. The various infectious agents associated with MERS include influenza, *E. coli*, *Legionella*, *Mycoplasma*, mumps, rotavirus, measles, and varicella.[1–6] Kobuchi et al. previously reported MERS in a child with nontyphoid *Salmonella* infection.[7] The exact pathogenesis of these transient splenial lesions in diverse situations is undetermined. The restricted diffusion in MERS may occur due to cytotoxic edema, which is more pronounced in the splenium of corpus callosum, considering the high density of neurons, astrocytes, oligodendrocytes, including cytokine and glutamate receptors in this area of brain.[12]

Mild encephalopathy/encephalitis with reversible splenial lesion as an entity has been more commonly reported in children of Asian descent, suggesting genetic predisposition.[13] Although our patient was born in the United States, his parents were of Indian descent. Acute disseminated encephalomyelitis (ADEM) is one of the differential diagnoses in a patient with encephalopathy and white matter changes. However, MRI appearance in ADEM includes multiple asymmetric hyperintense lesions in the subcortical white matter on T2 and FLAIR sequences with varying degrees of postcontrast enhancement. Splenial involvement in ADEM is also asymmetric and damage to white matter can be permanent.[13,14] MRI findings in our case were isolated T2 hyperintense splenial lesion showing restricted diffusion which resolved quickly within days.

There is no specific treatment of MERS presentation besides treatment of the underlying cause. In our case, the patient responded well to intravenous ceftriaxone with the resolution of neurological symptoms within a week. Although the changes similar to MERS have been described earlier in a child of *Salmonella* encephalopathy. This is one of the first case report to describe MERS in an adult patient with typhoid encephalopathy. In conclusion, MERS can be associated with various infectious etiologies including *S. typhi*, and awareness about this entity is important for its distinct neuroradiological features and benign prognosis.

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