Japanese encephalitis (JE) is a mosquito borne disease caused by a virus belonging to the Flaviviridae family. It is endemic in northern India and generally occurs in the monsoon season. Even though vaccination has been introduced in India, there’s not much reduction in the incidence. It causes acute encephalitis syndrome and has been rarely associated with myelitis. The disease has a high mortality and is associated commonly with long term neurological sequelae.

Case definition of a suspected case of acute encephalitis syndrome (AES) is described as a case of acute onset fever (5–7 days) with change in mental status with or without seizures. Longitudinally extensive transverse myelitis is a variant of acute transverse myelitis (ATM) which involves three or more vertebral segments. It is most commonly associated with neuromyelitis optica (NMO).

We report a case of a young male with altered sensorium and quadriparesis, and diagnosed to have JE with longitudinally extensive transverse myelitis (LETM).

Case Report
A 35-yr-old male resident of Delhi presented with a history of fever and altered sensorium for five days, and two generalised tonic-clonic convulsions. There was no history of recent travel or vaccination. On examination, the pulse rate was 84/min, blood pressure was 130/90 mmHg and glasgow coma score (GCS) was E1VTM1. Neurological examination revealed generalised hypotonia, weakness and areflexia. Plantars were mute and there were no signs of meningeal irritation. No rash or eschar was visible. After a lumbar puncture, he was started on antibiotics (according to meningitis protocol), acyclovir; antimalarials (artesunate) and antiepileptics (levetiracetam). A clinical diagnosis of suspected AES was made with pending investigations.

Routine haematological, biochemical and metabolic parameters were normal. Cerebrospinal fluid (CSF) showed $40 \times 10^6$ leucocytes/l (55% lymphocytes and 45% polymorphs), sugar and protein of 4.44 mmol/l (corresponding blood sugar of 6.11 mmol/l) and 1.10 g/l respectively. Serum tests were negative for malaria, dengue, chikungunya, scrub typhus and HIV. The CSF was found negative for herpes virus, cryptococcal antigen and tuberculosis (gene Xpert test). However, both the serum and CSF samples were found to be positive for IgM against Japanese B virus. Accordingly, the patient was managed for JE.

MRI of the brain revealed features of encephalitis (Fig. 1). Over the next two days, the patient’s fever subsided and sensorium gradually improved to a GCS of E4VTM1. His quadriplegia and areflexia however persisted. A nerve conduction velocity and electromyography were normal, but the MRI spine showed cord oedema and altered signal involving segments from C2 to C6 level (Fig. 2). With the diagnosis of transverse myelitis, the patient was given a pulse of methylprednisolone for five days.

The patient remained on mechanical ventilation however, the muscle power did not show significant improvement and the patient succumbed to ventilator acquired pneumonia two weeks later.

DISCUSSION
Japanese encephalitis causes an array of neurological manifestations and does not have specific antiviral therapy. The mortality rate in India varies from 20–40% . Clinical manifestations includes fever, altered sensorium, seizures, movement disorders and brainstem involvement . Rare findings include paralysis, dystonia and dysarthria . Multiple seizures, respiratory pattern changes, flexor or extensor posturing and abnormalities of the papillary and oculocephalic reflexes are associated with poorer prognosis .

The diagnosis was done by using JE specific IgM antibody capture enzyme linked immunosorbent assay (MAC-ELISA) as recommended by WHO . IgM against the virus is detected in CSF by four days and in serum by
7–9 days after clinical illness\(^9\). It may show cross reactivity with other Flavivirus, but presence of CSF antibody is a more accurate way to confirm CNS infection of the virus; as in the present case. Also, the test for dengue was negative.

The patient’s sensorium improved, but the quadriplegia persisted likely due to myelitis. He could not be weaned-off mechanical ventilation, as he continued to have type-II respiratory failure, likely due to the bilateral diaphragmatic palsy caused by cervical cord involvement. Even with steroids, the patient did not show significant improvement in muscle power over the first week, and developed ventilator acquired pneumonia. The high dose of steroids may have predisposed the patient to super added infection. The role of steroids in idiopathic transverse myelitis is well documented\(^{10}\), but there are few such records in case of acute infectious myelitis.

Acute transverse myelitis, an inflammatory myelitis, has been reported to be associated with autoimmune, infectious and inflammatory pathologies\(^{11}\). When associated with acute encephalitis or encephalopathy, the differential diagnoses include non-infectious causes like acute disseminated encephalomyelitis (ADEM), NMO, post-vaccination encephalomyelitis, neuro lupus, extraglandular Sjogren’s syndrome and rarely neoplasms. Infectious causes which must be considered are mostly viruses (including herpes family, flaviviridae, enterovirus and retrovirus), cerebral malaria, neurocysticercosis, CNS aspergillosis and rarely bacterial infections. These
causes were excluded in this case systematically, till a diagnosis was confirmed. Association of ATM with JE is rare, and to the best of our knowledge it is only the third case where it has been documented. Both the earlier described cases showed signal alternations in the cervical region of spinal cord and were treated by a short course of intravenous methylprednisolone. One of the cases was of the parainfectious variety likely due to autoimmunity, which occurred after three weeks of infection while the second was in the acute phase of illness which may indicate an alternate pathogenesis, possibly acute infectious myelitis. Hence, myelitis may present in the acute phase or few weeks later in the parainfectious form. Motor weakness in JE has been observed and even quadriplegia is known which has been shown to occur due to anterior horn cell damage. In the present case anterior horn cell damage was ruled out by the normal electromyography (EMG) and nerve conduction velocity (NCV), and by the abnormalities seen in MRI.

The present case is also unique, for the way, the patient required prolonged mechanical ventilation due to his diaphragmatic involvement, and this complication led to a change in the patient’s clinical outcome.

In conclusion, Japanese B virus infection can cause spinal cord involvement in the form of LETM with a predilection for the cervical region, even in the acute phase as observed in this as well as other reported cases. Associated complications like diaphragmatic palsy may also occur. The current treatment for myelitis remains early initiation of high dose steroids (when specific antibiotic therapy is not available) but further research is required to determine its efficacy and role of other modalities like plasma exchange, cyclophosphamide, etc.

Conflict of interest

There is no conflict of interests to declare.

Ethical statement

Consent was taken from the patient’s kin for the treatment administered and for publication of the case.

REFERENCES


Correspondence to: Dr Animesh Ray, Assistant Professor, Room No. 3070, III Floor, Department of Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi–110 029, India.
E-mail: doctoranimeshray@gmail.com

Received: 2 March 2017 Accepted in revised form: 27 June 2017