

## Atypical Association of Japanese Encephalitis with Sixth and Seventh Cranial Nerve Palsy during Outbreaks : Does it Require a Second Thought? A Case Report

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### Abstract

Last year in the month of August and September there had been an increased incidence of Japanese Encephalitis being reported all over West Bengal, India. Keeping this public and medical interest in the backdrop, the authors are reporting a 28 years old female patient admitted to the medical ward with acute onset flaccid paralysis of both lower limbs, diplopia, nasal intonation of voice, difficulty in swallowing and features suggesting facial nerve palsy.

The intensivist was called for management of gradually worsening respiratory failure and the patient was put on mechanical ventilator after being shifted to Intensive Therapy Unit. On neurological examination, power of lower limb was diminished with sixth and seventh cranial nerve palsy. The patient was diagnosed to have Japanese Encephalitis infection by a four-fold rise in virus-specific antibody detected in paired acute and convalescent sera by enzyme-linked immunosorbent assay. In nerve conduction velocity test she had bilateral symmetrical demyelinating sensory>>motor polyradiculoneuropathy suggestive of Sural nerve sparing acute inflammatory demyelinating polyneuropathy. Cerebrospinal fluid study revealed albumino-cytological dissociation. She was off the ventilator after 3 days of full course of plasmapheresis and she gradually regained her motor power with physiotherapy and nursing care.

Japanese Encephalitis patients are mainly admitted with feature of central nervous system insults and have poor prognosis. Syndromic association of Japanese Encephalitis with sixth/seventh cranial nerve palsy having Guillain-Barré Syndrome without any features of meningo-encephalitis is a rare phenomenon and there are very few case reports in literature regarding this topic. This case report highlights the successful management of such rare experience.

**Keywords:** Japanese encephalitis; Guillain-Barré Syndrome; Sixth and seventh cranial nerve palsy; Plasmapheresis

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### Introduction

Japanese Encephalitis (JE) virus is the sole etiologic agent of Japanese Encephalitis. It is one of the major causes of viral encephalitis in human population [1]. Since the isolation of this virus in Japan in 1935, it has spread worldwide becoming a major public health concern [2]. JE is of major public health importance due to its high epidemic potential, high case fatality rate (CFR),

and sequelae among survivors [3,4]. Last year in the month of August and September there has been an increased incidence of Japanese Encephalitis being reported all over West Bengal with significant mortality rate. High grade fever with or without rigors, headache, general malaise, nausea, vomiting followed by altered sensorium, convulsions, neck stiffness, muscular rigidity, mask-like facies, and abnormal movements are the classic clinical picture of the disease. Apart from the classical presentation other

atypical presentations of JE have been reported. Among them an acute flaccid paralysis-like illness with multiple cranial nerve palsy and bulbar palsy has been reported [5-7].

## The Case

A non-diabetic, non-hypertensive 28 years old female patient was admitted to the medical ward with features suggesting acute onset flaccid paralysis of both lower limbs, diplopia, nasal intonation of voice, difficulty in swallowing and facial nerve palsy for last 3 days. Weakness started with leg and progressed in ascending order. There was no alteration of sensorium at the time of admission. Bladder and bowel habits were normal.

There was no history of such neurological disorder running in her family. There was neither history of recent respiratory tract infection nor gastrointestinal infection. Over the next 72 hours her illness evolved to acute respiratory failure requiring intubation and mechanical ventilation at Intensive Therapy Unit (ITU).

On neurological examination-

Higher function - patient was conscious and oriented

Motor functions -power of both lower limbs were 3/5

Power of both upper limbs were 5/5

Sensory functions - bilateral symmetrical distal limb sensory loss were seen which had no definite level.

Reflexes-knee and ankle jerks were diminished, planter reflex was non-responsive in both lower limbs,gag reflex was absent.

In cranial nerve examination bilateral 7<sup>th</sup> (more in left side) and 6<sup>th</sup> nerve palsy were seen. Bilateral pupillary reflexes were normal. Bilateral palatal movements were sluggish.

There were no abnormality with spine and cranium.

The patient was proved to have Japanese Encephalitis infection by a four-fold rise in virus-specific antibody detected in paired acute and convalescent sera and CSF by enzyme-linked immunosorbent assay.

Cerebrospinal fluid(CSF) study revealed-protein 66 mg/100 ml, glucose 73 mg/100 ml, leukocyte count 5/cu.mm (all lymphocytes).There was no evidence of sepsis in routine blood investigations as suggested by total leukocyte count (TLC) of 8400/cu.mm ( $N_{69}L_{27}M_2E_2B_0$ ). Blood, sputum and urine culture showed no growth of organisms. Serial monitoring of serum electrolytes were unremarkable. Mild hypernatremia was seen which was corrected.Haemoglobin value was 12 gm%.

On the 6<sup>th</sup> day after onset of symptoms, nerve conduction velocity (NCV) test showed bilateral symmetrical demyelinating sensory>>motor polyradiculoneuropathy, (upper<<lower) with sural sensory nerve action potential (SNAP) sparing.

Immediately after admission to ITU one course of plasmapheresis was done. Simultaneously respiratory therapy, cardiac monitoring, physiotherapy, nutritional supplementation by ryles tube, postural care, deep vein thrombosis (DVT) prophylaxis were given. With treatment, power and tone of both upper limb and lower limb were improving. Weaning trials from ventilator were carried on with continuous monitoring of FEV<sub>1</sub>, negative Inspiratory force, respiratory rate, vital capacity, tidal volume and she was taken out of ventilator successfully with spontaneous normal breathing

pattern and without complication after 3 days of full course of plasmapheresis. Oral feeding was initiated on the same day. The patient was shifted to the ward after gaining normal neurological function. Patient was discharged and transferred to a local centre for rehabilitation after 20 days of admission.

## Discussion

Japanese Encephalitis virus is endemic in the Indian subcontinent but knowledge regarding disease progression still reveals interesting facts. It is the leading cause of viral encephalitis in Asia, with 30,000-50,000 cases reported annually. Case-fatality rates range from 0.3% to 60% depending on the age and on population. The natural host of the Japanese Encephalitis virus is bird and many believe the virus will therefore never be completely eliminated [8]. Japanese encephalitis is diagnosed by detection of antibodies (IgM) in serum and CSF [9]. There is no specific treatment for Japanese Encephalitis and treatment is supportive, with assistance given for feeding, breathing or seizure control as required.

Japanese Encephalitis typically presents as fever, headache and mental state change due to meningo-encephalitis, but more rarely can also cause a polio-like illness without encephalitis. We have reported here a case of a lady who presented with acute flaccid paralysis due to JE virus. Electrophysiological studies suggests that Japanese Encephalitis virus myelitis is caused by anterior horn cell damage and the clinical presentation mimics poliomyelitis as was our case [6].

Guillain-Barré syndrome (GBS) is an acute polyradiculoneuropathy of variable etiology [10,11].

A number of etiological agents such as viral and bacterial infections, vasculitis, surgery, malignancy, vaccination and drug reactions are noted to be associated with GBS. Various viral infections may precede the onset of GBS like influenza, cytomegalovirus, Epstein-Barr virus, measles, mumps, adenoviruses etc.

GBS is most commonly characterized by combination of limb paraesthesia, generalized weakness and areflexia. The Brighton Collaboration is an international collaboration sponsored by the World Health Organization to facilitate the development, evaluation, and dissemination of high quality internationally standardized case definitions for various illnesses with the aim of improving vaccine safety. These innovatory 'Brighton criteria' also represents the level of diagnostic certainty based on the presenting findings at clinical and additional examinations, ranging from level 1 (highest level of diagnostic certainty) to level 4 (reported as Guillain-Barré syndrome, possibly due to insufficient data for further classification) [12].

### Key diagnostic criteria and Brighton case definitions for Guillain-Barré syndrome

The findings in our case were consistent with the first, second, fourth, sixth and seventh diagnostic criteria of the Brighton Collaboration as shown in the **Table 1**.

Pathogenesis of GBS not yet fully understood and current thinking is that GBS may not be a single disease, but a variety of acute neuropathies with a number of related immune-mediated pathogenic mechanisms. Most common immunopathologic findings are endoneural inflammation in spinal nerves roots, distal

**Table 1** Key diagnostic criteria and Brighton case definitions for Guillain-Barré syndrome

Diagnostic criteria		Level of diagnostic certainty			
		1	2	3	4
1	Bilateral and flaccid weakness of limbs	+	+	+	+/-
2	Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/-
3	Monophasic course and time between onset-nadir 12 h to 28 days	+	+	+	+/-
4	CSF cell count <50/ $\mu$ l	+	+ <sup>a</sup>	-	+/-
5	CSF protein concentration > normal value	+	+/- <sup>a</sup>	-	+/-
6	NCS findings consistent with one of the subtypes of GBS	+	+/-	-	+/-
7	Absence of alternative diagnosis for weakness	+	+	+	+

- $\pm$  present; - absent; +/- present or absent.
- $\pm$ NCS = nerve conduction studies.
- $\pm^a$  If CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis Guillain-Barré syndrome.

nerve segments or around potential nerve entrapment sites. Many viral proteins share some cross-reacting determinants with host tissue components. As a result, antibodies to self-proteins are often detected following viral infection. Theoretically, such a phenomenon would result in autoimmune-mediated tissue damage. Evidence for the role of molecular mimicry between some viral proteins and human myelin basic protein (MBP) has been provided earlier with respect to hepatitis B virus and measlesvirus [13,14]. Hence, it is plausible that viruses play a major role in the pathogenesis of demyelinating diseases. Target antigens appear to be common to the axon, myelin sheath or both. The exact antigens, the precipitating event or the resultant mechanism of injury remains somewhat unclear and hence requires further molecular research.

Virus-specific IgM antibody detection in serum and CSF is recognised as a sensitive, specific indicator of JEV infection. These antibodies can be detected as early as the first day after the onset of neurological symptoms and over 90% of the JE patients are positive for this antibody in the CSF by the seventh day of the illness.

About 30% of patients admitted to hospital with Japanese encephalitis die and around half of the survivors have severe

neurological sequelae [4]. About 30% of survivors have frank motor deficits. 20% of patients have severe cognitive and language impairment (most with motor impairment also) and 20% have further convulsions [15].

Japanese encephalitis presenting with bulbar palsy, multiple cranial nerve palsies and GBS without any feature of meningo-encephalitis is a very rare phenomenon [6,7,15].

## Conclusion

Patients affected with Japanese Encephalitis virus are mainly admitted with feature of CNS insults and have poor prognosis. This case depicts the rare association of JE with sixth nerve palsy along with a host of atypical features of Guillain-Barré Syndrome.

On the background of endemic outbreaks at various times, this case report brings out the notion that atypical presentation of Japanese Encephalitis might require further research to decipher exact mechanisms of such varied rare presentations.

Keeping this public and medical interest in the backdrop this case has highlighted the successful management of such rare experience.

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