

**BICKERSTAFF BRAINSTEM ENCEPHALITIS AND MILLER FISHER SYNDROME – VARIANT OF GUILLAIN-BARRÉ SYNDROME A SPECTRUM OF CLINICAL MANIFESTATION OF SAME DISEASE**MANISH KULSHRESTHA<sup>1</sup>, ANJALI KULSHRESTHA<sup>2\*</sup><sup>1</sup>Department of Medicine, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India. <sup>2</sup>Department of Microbiology, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India.Email: [anjalikulshrestha2185@gmail.com](mailto:anjalikulshrestha2185@gmail.com)

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**ABSTRACT**

Guillain-Barré syndrome (GBS) and its variants are parainfectious (2/3 cases) neurological illness involving the lower motor neuron but they can also involve central nervous system (CNS). Bickerstaff brainstem encephalitis (BBE) and Miller Fisher syndrome (MFS) are the two variants of GBS with CNS involvement. The present case series highlights the variable presentation and laboratory findings in BBE and MFS, which may help clinicians in early recognition and timely management of the condition.

**Keywords:** Guillain-Barré syndrome, Miller Fisher syndrome, Parainfectious neurological illness.

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**INTRODUCTION**

Guillain-Barré syndrome (GBS) is an autoimmune disorder. The most common presentation of which is acute onset motor predominant ascending paralysis leading to quadriplegia and sometimes respiratory failure needing mechanical ventilation [1]. Cranial nerves supplied muscles are usually spared except frequent involvement of VII cranial nerves (50%) [2]. The illness usually preceded by febrile infection involving upper respiratory or GI tract. Miller Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE) are two variants of GBS which presents with external ophthalmoplegia, areflexia, and in case of BBE, varying degree of altered sensorium [3,4]. Due to rarity of the central involvement in GBS, these variants are frequently misdiagnosed in the initial course of disease. Here, we are going to present series of three cases with the central nervous system (CNS) involvement in GBS. 2 cases were BBE and one was diagnosed as MFS.

**CASE 1**

A 12-year-old female patient without any significant previous medical comorbidity and perinatal history developed fever and diarrhea 7 days before admission for which she was treated at local facility. Fever relieved after 2 days but diarrhea continued. She developed acute onset difficulty in speaking in the form of nasal twanged voice rapidly followed by imbalance while walking over the next 8–10 h following which she was admitted at our hospital.

Examination at admission revealed a conscious and alert patient who was able to follow commands. Nasal twang voice was present and she also admitted the nasal regurgitation of liquids. Deep tendon reflexes (DTRs) were all present though ankle reflex was hypoactive. Neck flexion and extension were also weak. Palatal movement was absent.

All relevant investigations including magnetic resonance imaging (MRI) brain with whole spine screen, CPK total, and nerve conduction study performed at admission were normal. A provisional diagnosis of GBS or its variant was considered and IVIG started according to weight. Patient developed further worsening in clinical condition in the form of altered sensorium with aphonia progressed rapidly to decreased responsiveness. DTR in the lower limbs was absent. Hence, she was electively intubated. Repeat MRI brain revealed no interval change. Cerebrospinal fluid (CSF) revealed pleocytosis (P69S72C150). HIV serology was found to be negative. CSF pan neurotropic viral panel and autoimmune panel were negative, but ANA was high. Anti GQ1b

antibody was positive. On day 4 of IVIG infusion, patient developed decreased urine output and raised creatinine levels (2.5 mg/dl). IVIG stopped and patient managed conservatively and she improved. At this stage, she was on mechanical ventilation and was localizing to pain. Patient developed secondary deterioration and developed one episode of seizure. MRI brain revealed changes of PRES which subsided on subsequent MR scan over next 7 days. After this, patient showed continuous improvement in sensorium and she was extubated after 26 days of admission and subsequently shifted toward from where she was discharged in a stable condition. On subsequent follow-up visits, she improved completely over next 3 months.

**CASE 2**

A 30-year-old male patient with no previous comorbidity developed fever with upper respiratory tract infection 10 days before admission. He developed paresthesia and pain in bilateral lower limb with weakness 2 days after the initial symptoms. Following which he was admitted to our hospital. Examination at admission revealed a conscious alert though lethargic patient with mild weakness of lower limb (4+/5 MRC Grade). He was also having left eye ptosis and bilateral facial weakness. Sensory examination was normal and DTRs were hypoactive. Single breath count was 38/min at admission. Routine hematological and biochemical investigation including CPK revealed no significant abnormality. MRI brain with whole spine screen was normal. NCV revealed poor F wave. On day 2 of admission, patient developed worsening of symptoms in the form of neck flexion weakness and tachypnea (Respiratory rate 44/min). Hence, he was electively intubated and put on mechanical ventilation. CSF revealed elevated cell (100, 97% lymphocytes), normal sugar and high protein. CSF HSV PCR, TB PCR, Gram stain, and AFB stain was negative so was the ADA. IVIG was started. On next day, patient developed drowsiness which progressed to stuporous state and later coma over the period of 3 days, repeat MRI revealed no significant abnormality. Tracheostomy was done. Anti GT 1 b antibody was positive. Repeat CSF revealed protein 300 mg/dl and normal cell count and sugar. Patient developed fever on 10<sup>th</sup> day of admission and was diagnosed as having right lower lobe pneumonia which was managed with appropriate antibiotics. The clinical condition further worsened and he developed ARDS. Patient remained comatosed and succumbed to his illness at 15<sup>th</sup> day of inpatient care.

**CASE 3**

A 5-year-old child with normal perinatal history, fully vaccinated according to AIP protocol developed one episode of fever 6 days before

current admission. After 2 days of index symptoms, he complained of double vision and headache and family noticed squint. Initially, he was treated and evaluated elsewhere. MRI brain with contrast revealed meningeal enhancement. Routine biochemical and hematological investigation along with CSF revealed no significant abnormality. NCV was normal. Patient developed difficulty in walking over next 3 days following which he was admitted at our center.

Examination at admission revealed a conscious and alert patient. External ophthalmoplegia was observed along with neck flexion weakness. Upper limb motor power was 4/5 and lower limb 3/5. DTRs were absent. Sensory examination was normal. Single breath count was 24/breath. Poor cough reflex was observed. IVIg was started according to the weight.

AntiGQ1b antibody was positive. On the day 3 of IVIg course, disease progression halted and after 3–4 days, patient showed signs of improvement of increased single breath count to 28/breath. Motor power was also improved to 4+/5 in both upper and lower limb but residual ataxia was evident. He showed significant improvement in next 3 days and he was discharged with a residual squint and mild ataxia (was able to walk unsupported).

## DISCUSSION

GBS is an acute self-limiting polyneuropathy named after Guillain-Barré and Strohl who first reported it in 1916 [1]. It commonly presents as predominantly motor neuropathy through sensory symptoms and signs can be found. CNS and cranial nerves are usually spared except frequent involvement and VII cranial nerve. MFS and BBE are two variants of GBS which presents with external ophthalmoplegia, are flexia and in case of BBE, varying degree of altered sensorium [3,4]. Taken together with available literature, this case series highlights the core clinical features of BBE and MFS with variation in clinical presentation of GBS variant and also pull attention toward the complication during immunomodulatory therapy.

We will begin our discussion with history. In case 1, the illness preceded by episodes of diarrhea and fever. The index neurological symptoms was difficulty in speaking leading to aphonia S/O palatal paralysis which further spread to involve other cranial nerves in the form of external ophthalmoplegia and ataxia followed by altered sensorium. In second case, the illness started with history of radicular pain and paresthesia followed by weakness of lower limb and dropping of eyelids facial weakness and neck flexor weakness (suggesting cranial nerve involvement) which progressed to altered sensorium and coma.

In the third case, first symptom was double vision followed by headache (holocranial) which progressed to ataxia and quadriparesis. Areflexia was present in all three cases. In the third case, the sensorium was preserved throughout the course of illness. The severity was variable where second case developed deep coma while first case was stuporous at its nadir of sensorium. All three patients had febrile illness before the neurological illness which suggest that some para infectious process is involved in the pathogenesis in these cases.

In the second case, the diagnosis was challenging but depending on acute onset rapidly progressive peripheral neuropathy and absent DTRs with quadriparesis (LMN type) and cranial nerve involvement

suggested the diagnosis. Nerve conduction study revealed decreased CMAP amplitude and absent H and F wave which further added to the diagnosis. AntiG1T1 b antibody was also positive.

CSF picture was interesting where the usual CSF finding in GBS and variants is albinocytological dissociation (Cells – <10/microliter and Protein >45 mg/dl) in the first two cases, it was pleocytic and in Case 3, it was normal. Pleocytic CSF creates the diagnostic confusion but it does not exclude GBS [4,5]. This type of CSF picture may be found in patients of GBS with HIV infection.

MRI brain was normal in Case 2 and 3. While in Case 1, it was normal initially but later she developed changes of PRES which got reversed in the due course of time. The Case 1 and 3 resolved completely but the Case 2 succumbed to the septicemia and ARDS suggesting that like other variants of GBS the condition is reversible but there are higher chances of getting infection in an intubated patients with indwelling catheter and cannula.

## CONCLUSION

The case series highlights the variable clinical features and CSF picture in GBS variants with CNS involvement. Clinicians should be vigilant and also have high index of suspicion for the condition, antibodies are helpful in establishing the diagnosis.

## CONSENT FOR PUBLICATION

Written and informed consent was obtained from the patient and from the parents in case of minor.

## AUTHORS CONTRIBUTION

Dr Manish Kulshrestha (MK) was the clinician who diagnosed and treated the cases and the laboratory assistance was provided by Dr Anjali Kulshrestha (AK). MK and AK both reviewed and drafted the manuscript and both have approved the final version of this in the end.

## CONFLICTS OF INTERESTS

None.

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