Original Research Article

A study on topographic variants of Guillain-Barré Syndrome in a tertiary care hospital in South India

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Abstract

Background: The first clinical description of GBS dates back to 1859 by Jean Baptiste Octave Landry. It was further characterised by George Guillain and Jean Alexandre Barré and simultaneously by Andre Strohl in 1916

Objective: To report the frequency of occurrence of topographic variants of Guillain-Barré Syndrome (GBS) among patients attending tertiary teaching government hospital, Hyderabad, Telangana.

Material and methods: We have analyzed 746 consecutive patients admitted for acute onset rapidly progressive weakness in our Institute from May 2010 to July 2015. GBS was diagnosed as per NINDS criteria and GBS variants as per Asbury's and other investigators criteria described vide infra.

Results: Out of 746 patients, only 668 were diagnosed GBS as per NINDS criteria. Among 668 GBS patients, only 47 were identified as topographic subtypes of GBS. The Electrodiagnostic subtypes identified were AIDP 347 (56%); AMSAN 127 (20%); AMAN 85 (14%) and 62 (10%) of the patients were 'Equivocal'. Among the topographic subtypes GBS patients, 28/47 Paraparetic Variant; 8/47 PCB Variant; 6/47 Miller Fischer Variant; 3/47 Facial Diplegia; 2/47 Pure Sensory variants were identified.

Conclusion: Topographic variants GBS accounted for 7% of GBS patients in our institute. Paraparetic variant was more common among our population and had a better prognosis. PCB Variant had poorer outcome. There was strong association with antecedent infection. There were some seasonal trends with predilection in winter and rainy seasons.

Key words

Topographic variants of GBS, Guillain-Barré Syndrome, Regional variants of GBS, Subtypes of GBS, Miller Fisher Syndrome, Bickerstaff's Brainstem Encephalitis, Paraparetic GBS, PCB .

Introduction

The first clinical description of GBS dates back to 1859 by Jean Baptiste Octave Landry. It was further characterised by George Guillain and Jean Alexandre Barré and simultaneously by Andre Strohl in 1916 [1]. GBS encompasses a heterogenous group of acute neuropathies characterised by monophasic immune mediated hyporeflexic ascending quadriparesis with albuminocytological dissociation (ACD) in CSF which defies a comprehensive classification. The spectrum of this syndrome is highly variable ranging from mild weakness to flaccid paralysis of limbs, cranial nerves, autonomic dysfunction and occasionally respiratory failure. Some less frequent manifestations include vocal cord paralysis, ataxia, papilledema and variable sensory loss. Unusual presentations of GBS can be an asymmetrical and descending type of weakness affecting more profoundly some regions and sparing yet others. Such clinical situations where patients do not fall in the ambit of the diagnostic criteria of GBS are labelled as topographic variants, clinical variants, regional variants or simply variants of GBS [2-4]. There is paucity of literature on these poorly characterised syndromes. GBS variants are those illnesses which have close resemblance to a portion of typical GBS illness with considerable overlap among various members, presence of ACD in CSF and Electro-diagnostic tests (EDX) abnormalities in at least later part of illness. No other cause should explain this form of illness. This suggests that the pathologic and immunologic abnormalities of GBS can be localized and selective. Lack of awareness often leads to delay in the diagnosis and therapeutic interventions which could be highly rewarding. The clinical spectrum of variants of GBS is ever expanding and its boundaries remain undetermined. The frequency of GBS variants is reported to be 0.35/100,000/persons/year in Italian population [5].

GBS can be categorized into Electrophysiological subtypes viz., Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN) based on EDX findings as to whether demyelination/ axonal degeneration or motor/ sensory nerves are predominantly involved. In addition GBS can further be categorized into Topographic subtypes exclusively based on the region of involvement and dominant disease phenotype. The following are the various topographic subtypes of GBS described in the literature.

Topographic subtypes

Miller Fischer Syndrome (MFS)

It was first described in 1956 as a triad of ataxia, areflexia and ophthalmoplegia. Bulbar dysfunction, ptosis, pupillary abnormalities and facial weakness are additional features [6]. CSF protein is mildly elevated. EDX shows loss of sensory potentials, with milder axonal degeneration.MFS accounts for 5% of all cases with GBS.

Bickerstaff Brainstem Encephalitis (BBE)

Bickerstaff in 1957 reported cases with Opthalmoplegia, Ataxia, Areflexia and impaired consciousness under the title of "mesencephalitis and rhomboencephalitis" [7]. Anti GQ1b antibodies are seen. It may be considered as a

central nervous system subtype of MFS associated with altered consciousness [8].

Pharyngeal Cervical Brachial Variant (PCB)
It characteristically involves cervical, brachial and oropharyngeal muscles, hyporeflexia or areflexia in upper limbs and sometimes facial palsy, blepharoptosis, sensory disturbance, and preserved tendon jerk in the legs [9].There can be incomplete forms and considerable overlap with MFS and BBE. These clinical observations and serological evidence suggest that PCB, FS, and BBE form a continuous spectrum.EDX tests reveal dominant axonopathy.

Sensory GBS
It is acute onset symmetrical paresthesias in the feet and hands, absence of weakness, areflexia involving all four limbs. Diminished sensation mainly vibration/joint position sense distally with normal muscle power [10]. Electrophysiological evidence of demyelination is present in at least 2 nerves. It has monophasic course, no alternative cause for neuropathy, no family history of neuropathy and elevated cerebrospinal fluid protein. Antibodies to ganglioside GD1b and GD3 are present [11].

Acute Small Fiber Neuropathy
Acute onset numbness associated with burning dysesthesia, normal muscle strength, symmetrical glove and stocking type sensory loss for pain and temperature, normal proprioception and vibration senses and normal or brisk tendon reflexes. EDX studies are often normal.

Ataxic GBS
Ataxia, distal paraesthesias, areflexia, and raised CSF protein concentrations, anti-GQ1b IgG antibodies positivity is present [12].

Pandysautonomia
The clinical features are hypertension, orthostatic hypotension, vomiting, diarrhoea or constipation, paralytic ileus, sweating disturbances and cardiac arrhythmias.CSF examination shows ACD in CSF. Routine EDX studies are normal; autonomic testing such as heart rate variability, tilt-table testing, sympathetic skin responses, and sweat testing (QSART) may be abnormal [13].

Paraparetic
Isolated weakness of both lower limbs and areflexia, with minimal or no paraesthesia or sensory loss is present. Typically sphincters are spared. Usually slight elevation of CSF protein concentration is seen. Electrophysiological findings are confined to lower limbs showing abnormal motor conduction and late responses in the legs [14].

Oropharyngeal Palsy
It may occur in isolation or with MFS/PCB. EDX tests show motor and sensory abnormalities. Anti-GM1b IgG antibody may be useful in the diagnosis [15].

Recurrent GBS
Two or more episodes of GBS with a minimum time between episodes of 2 months (full recovery in between) or 4 months (only partial recovery). It is important to distinguish between recurrent GBS patients and GBS patients with treatment-related fluctuations (GBS-TRF) or CIDP with acute onset (A-CIDP) [16].

Hand Onset GBS
In this type, pure motor symptoms confined to hands and arms with presence of IgG antibodies against GM1b and GD1a, as well as those against GM1. A serial electrophysiological study confirmed the diagnosis of an axonal variant of GBS, indicating that anti-GM1 IgG and C jejuni infection are related to hand-predominant weakness in GBS [17].

Acute Facial Diplegia
Isolated facial diplegia with minimal to no motor limb weakness has been described as a GBS variant. CSF shows ACD. Antiganglioside serology is often positive. Hyperreflexia does not exclude GBS or one of its variants [18].

Polyneuritis Cranialis
5^{th}, 7^{th}, 9^{th}, 10^{th} and 12^{th} pairs of cranial nerves are affected along with ataxia and areflexia. CSF shows ACD [19].

Unilateral 3rd CN Palsy

It is exceptionally rare. Appropriate alternative differential diagnosis should be ruled out [20].

Anti GQ1b Antibody syndrome

Odaka M, et al. tried to clarify the nosological relation among MFS, GBS with ophthalmoplegia, BBE and acute ophthalmoparesis without ataxia. The clinical findings together with the common autoantibody anti- GQ1b for MFS and BBE with cross reactivity with anti-GT1a for PCB suggest that a common autoimmune mechanism functions in the pathogenesis of these illnesses [21].

Hyper acute GBS

Maximal incapacity is reached within a day or two [22].

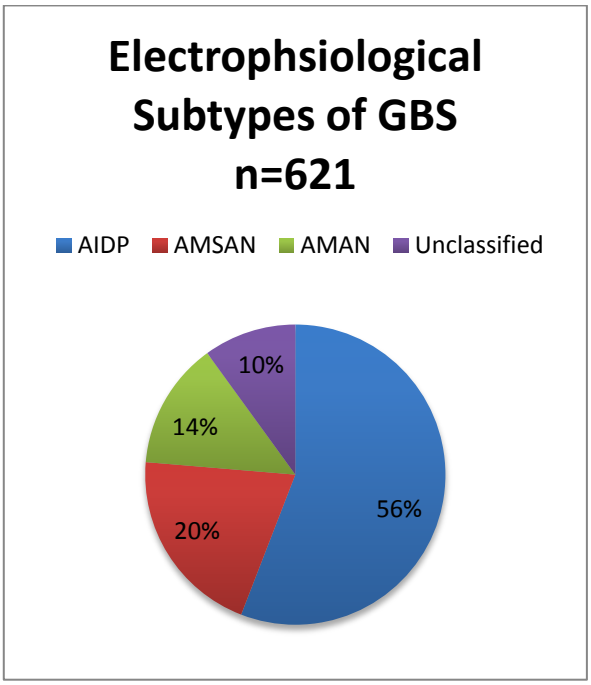
Materials and methods

We have analyzed 746 consecutive patients admitted for acute onset rapidly progressive weakness in our Institute from May 2010 to July 2015. GBS was diagnosed as per NINDS criteria [1] and GBS variants as per Asbury's and other investigators criteria described vide supra. EDX were done on Nicolet – Viking. Modified Ho, et al. criteria was used to detect demyelination, axonal degeneration and 'Equivocal' [23, 24]. EDX were repeated at the time of discharge which was 2-3 weeks for the GBS variants. Routine biochemical tests, CSF analysis, connective tissue disorder profile, CK, urinary porphobilinogen, serum B12, thyroid function tests were done in all patients to exclude primary cause of neuropathy. MRI was done as and when required to exclude spinal cord and brain lesions. Antiganglioside antibodies were done by immunoblot method in suspected MFS and PCB variants. Hughes functional grading scale (HFGS) was used for evaluating the severity of the disability as follows: 6-death; 5-need mechanical ventilation; 4-bed bound; 3-walk with aid; 2-walk without aid; 1- run with minor deficit; 0- normal. Patients with grade 4 and 5 on HFGS were treated either by IVIg in a dose of 0.4 gm/kg body weight/ day for 5 days or plasma exchanges as one plasma volume 50 ml/kg body weight on five separate occasions spread over 10 to 15 days. The data was separately evaluated by DP and VN. Whenever there was discrepancy about the diagnosis, a consensus opinion was taken by collective discussion by all authors. This study has approval from Dr. NTR University of Health Sciences. Informed consent was taken from the patients or their attendants when the patient was unable to give a valid consent. Standard protocols of our Institute were followed. The data was computed for statistical analysis.

Results

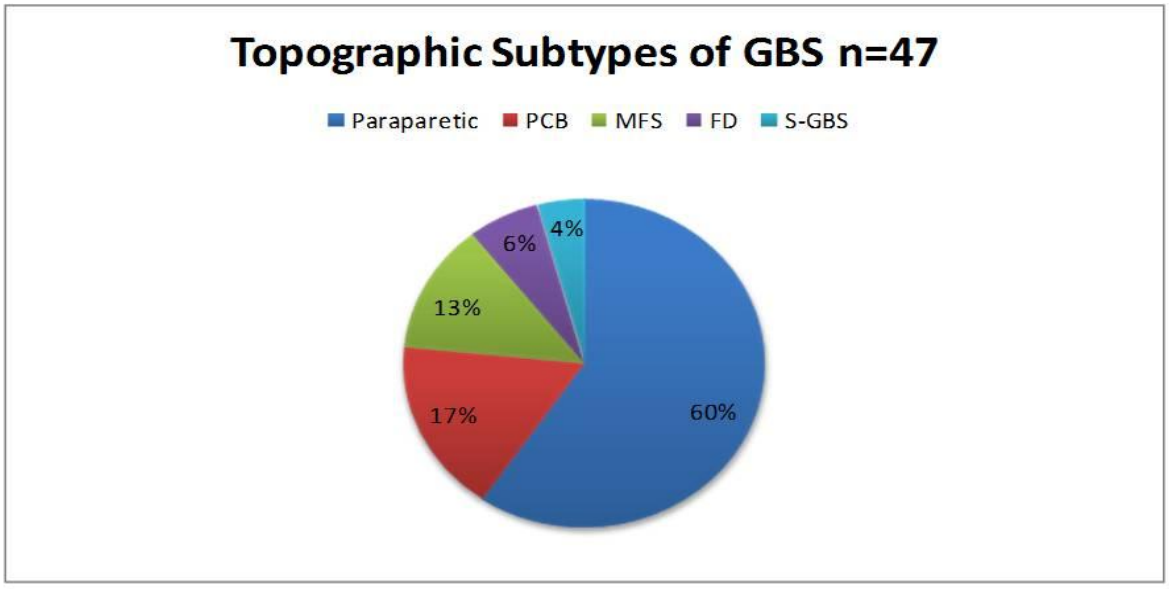
Out of 746 patients, only 668 were diagnosed GBS as per NINDS criteria. The rest of 78 patients were excluded from the study for failing to meet these criteria. Among 668 GBS patients, only 47 were identified as topographic subtypes of GBS. The Electrodiagnostic subtypes identified were AIDP 347 (56%); AMSAN 127 (20%); AMAN 85 (14%) and 62 (10%) of the patients were 'Equivocal' (**Figure – 1**). Among the topographic subtypes GBS patients, 28/47 Paraparetic Variant; 8/47 PCB Variant; 6/47 Millar Fischer Variant; 3/47 Facial Diplegia; 2/47 Pure Sensory variants were identified (**Figure – 2**).

Figure – 1: Electrophysiological subtypes.



EDX abnormalities consistent with GBS were found in all variants. ACD in CSF was seen in all 45 tested patients, the mean CSF protein being 219 mg/dl. CSF could not be collected in two patients as they were on invasive ventilation and died, however they had typical features of PCB their antiganglioside antibody titres were positive. The topographic subtypes of GBS patients had seasonal trends with predilection in winter and rainy seasons. Antecedent events were present in ninety six percent of patients. Upper respiratory tract infection was seen in 57%, gastro-intestinal infection in 33% and rest were associated with pregnancy or surgery. The mean age of onset was 34.5 years (range 12 to 51 years). The male female ratio was 3:1.

Figure – 2: Topographic subtypes of GBS.



Discussion

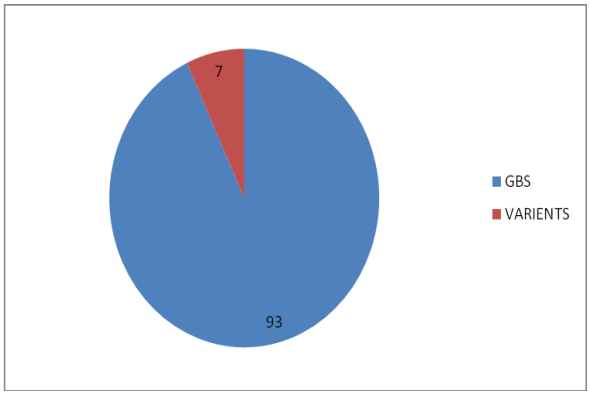
We tried to analyse the data apart from the routinely classifying GBS from electrophysiological view point viz., AIDP, AMAN, and AMSAN but also from topography/ region of involvement to identify these poorly characterized variants of GBS. In the present study, topographic subtypes of GBS constituted 7% of GBS patients reporting to our Institute (**Figure – 3**). All patients had acute progressive weakness of less than four weeks duration, relatively symmetric involvement; they showed albuminocytological dissociation and had EDX abnormalities conforming to the diagnostic criteria of GBS. All five variants identified in the current study fulfilled the diagnostic requirement as described above.

The Paraparetic variant was the commonest type (60%). All patients had symmetric weakness of the lower limbs of variable degree and had loss of reflexes in the lower limbs. 9/28 had additional weakness of grade IV/V on MRC scale in the upper limbs and loss of reflexes as well. None had sensory loss. No other cause for paraplegia was found. EDX showed axonopathy in 59%, demyelinating changes in 33% and combination of both in two patients. CSF findings were consistent with GBS. EDX abnormalities were seen in upper limbs even the when muscle strength was normal. None of the patients progressed to florid quadriplegia. All patients recovered by 1 to 2 grades on Hughes scale before being discharged from the hospital.

The PCB variant was seen in 17% of topographic subtypes. All patients had oropharyngeal weakness, neck weakness and arm weakness and areflexia in upper limbs of 7 to 12 days duration. Facial weakness was seen in 3/8 patients. Ankle

jerk was preserved in all cases. Antiganglioside IgG antibody titre was positive for GT1a, GQ1b, GM1 and GD1a in patients tested. This variant had fulminant course in our patients. Invasive ventilatory support was required by 5/8 patients and three patients died and the cause of death was cardiac arrhythmia in one and pneumonia in the other two. The high mortality among this variant is attributed to late referral to our center and delay in diagnosis. The rest of the patients made remarkable improvement of grade two in HFGS in four weeks time.

Figure – 3: GBS vs Variants.



MFS variant was seen only in 13% of topographic subtypes on contrary to those reported in literature. All had ophthalmoplegia, ataxia and areflexia. Diplopia was the main presenting symptom whereas ataxia was in two patients. Total external ophthalmoplegia was seen in three patients and partial in the rest. Half of the patient couldn't walk independently. Facial weakness and bulbar weakness was seen in one each. Sensory symptoms were seen in one patient. Limb weakness of grade IV/V on MRC scale was seen in one. EDX showed sensory motor axonopathy. Antiganglioside IgG antibody titre was positive for GQ1b in 3/6 tested patients. All patients responded well to IV Ig therapy.

Facial diplegia presented with isolated facial weakness of one week duration, none had ear pain or gustatory disturbance. Other cranial nerves were normal. One patient had grade IV/V on MRC scale weakness in upper limbs with hyporeflexia and distal paresthesias in upper limbs and hyper-reflexia in lower limbs. EDX revealed axonopathic changes in both facial nerves and upper limbs as well. CSF showed ACD and imaging was normal.

Pure sensory GBS presented with paresthesias of feet and hands of 10 days duration with loss of vibration and joint position sense. There was no limb weakness however there was areflexia. EDX showed demyelinating neuropathy mainly in the sensory nerves. CSF showed ACD and no other cause for neuropathy could be found.

The present study revealed that 62.5% cases occurred during winter and the rest of 37.5% during rainy season.

Conclusion

Topographic variants GBS accounted for 7% of GBS patients in our institute. Paraparetic variant was more common among our population and had a better prognosis. PCB Variant had poorer outcome. There was strong association with antecedent infection. There were some seasonal trends with predilection in winter and rainy seasons. High index of suspicion is required to diagnose these not very rare groups of disorders. Early diagnosis is important for therapeutic intervention and favourable outcome for these potentially treatable disorders.

Limitations of the study

The present study was not a population based study to reflect its incidence. It was not a multicenter study and the number of GBS variants was too small for drawing any logical conclusions of the true occurrence.

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