EARLY ABNORMAL SPONTENEOUS ACTIVITY FINDINGS IN AXONAL VARIANT OF GUILLAIN BARRE SYNDROME: IS THIS A NEW VARIANT OF GUILLAIN BARRE SYNDROME?

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ABSTRACT

Objective: To evaluate the earliest denervation potentials in axonal variant of GBS. Background: Guillain Barre Syndrome (GBS) is one of the most important acute neurolological emergency. Denervation potentials on needle EMG is the hallmark of axonal damage. Usually this is a time dependent phenomenon. The degeneration of axon depends upon length of axon to be degenerated. Studies claim variable time duration for denervation potentials from two weeks to three weeks. Material/Methods: This is a cross-sectional survey of patients admitted and referred for neurophysiologic assessment. Clinical and neurophysiological data of GBS patients over a period of three years and three months and ten days was collected. NCS/EMG performed by a qualified neurophysiologist. Diagnosed cases of GBS with available data of NCS/EMG were included. Patients with history of Diabetes Mellitus, previous history of any sort of neuropathy and demyelinating variants after diagnosis were excluded as well. Clinical and Neurophysiologic data were collected on Performa for analysis. Result: Total forty- three patients were diagnosed as GBS and those with axonal variants were finally included. Out of forty-three, eighteen had axonal variant of GBS and rest of them demyelinating variants. Twelve patients of axonal variant (31%) showed fibrillation potentials, positive Sharp Waves and increased insertional activity within 4-12 days of symptoms onset and six (69%) beyond that period. Total twelve patients were finally included. Active denervation in the form of fibrillation potentials and positive sharp waves were noted frequently and decreased interference pattern in almost all patients. NCS were performed before EMG examination. Conclusion: Fibrillation Potentials, Positive Sharp Waves and decreased interference pattern were noted in early course of disease in GBS patients interestingly before two weeks of symptoms onset. This study raises the query for a possible new Hyperacute or Fulminant variant of GBS. These findings need further histopathology and etiologic correlation as well as further prognostic importance.

Key Words: GBS GuillainBarre Syndrome, NCS Nerve Conduction Study, EMG Electromyography.

INTRODUCTION

GuillainBarre Syndrome is a clinical syndrome that manifests as an acute inflammatory polyradiculoneuropathy with resultant motor weakness and hypo/areflexia. It is described in 1859 by Landry and hence known as Landry Ascending Paralysis, he reported 10 patients with GBS1. Pathophysiologically there is a probable correlation with post-infectious immune-mediated disease, cellular and humoral immune mechanism. Antibodies cross-react with specific gangloids and glycolipids such as GM1 and GD1b has been noted2. Approximately two thirds of patients report an antecedent bacterial or viral illness prior to the onset of neurologic symptoms3,4. It has been reported that 69% of GBS cases are preceded by Campylobacter Jejuni in Dhaka Bangladesh5. However other agents like post-vaccination (Influenza vaccine or 2009 H1N1), drugs and other conditions are also rarely reported6-8. In USA, the incidence of GBS is 1.2-3 per 100,000 inhabitants, making it the most common cause of acute flaccid paralysis9,10. International statistics are not different in respect of incidence11. Introduction of immunoglobulin therapy markedly decreased the mortality of GBS; however morbidity is still a significant in terms of functional outcome.

METHODOLOGY

This is a single center hospital based cross sectional

survey. Initially all those patients, who have been admitted under neurology team as well as those who have been referred from other draining clinics and hospitals and subsequently admitted in our hospital by informing the referral physician. Armed Forces Hospital Southern Region is the largest tertiary and government teaching hospital in the southern region of Saudi Arabia, providing totally free of cost services to the military and their relatives. The catchment area is more than one million people. There are seven small hospitals, some of these are providing primary and others are providing primary as well as secondary care. Patients are being referred to the main tertiary care center for further management particularly for Neurophysiological assessment. Clinical data for the age, gender, duration of onset of symptoms, neurological findings, respiratory involvement like respiratory rate and if less than 10 then referred to pulmonologist and other relevant information were collected by the neurologist on Performa. The nerve conduction studies and electromyography findings were initially collected on the special form of neurophysiology and then transferred to a separate Performa. Lumbar Puncture was offered to all patients but written consent was given by only seven patients out of twelve. The data was collected from June 30, 2009 to October 10, 2012. Approval of study has been taken from the local research and ethical committee. Written consent from all the patients, those who were stable enough to sign the form and rest of them from their next legal guardian were taken. All patients with age of more than 12 years and above were included in study. Diabetes Mellitus and Previous were kept in exclusion criteria.

Those patients, who have been included in the study, have been assessed for Clinical presentation, CSF findings and Nerve Conduction Study/Electromyography findings. Details of latter were displayed in detail subsequently.

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RESULTS

CLINICAL PRESENTATION AND RELEVANT FINDINGS

Patients have been assessed for gender, duration of symptoms, Motor power as per Medical Research Council Scale, Deep Tendon Reflexes, respiratory muscle involvement and CSF analysis (most of the patients did not give the consent for lumbar puncture). Demographic details are shown in Table 1.1.

Table 1.1: Demographic and Clinical Data

Patient No.	Age/ Sex	Onset of Symptoms	CSF	Maximum Deficit
1	38 Y/M	4 days	ND	Quadriparesis, areflexia, Increased respiratory rate
2	25 Y/M	5 days	Normal	MTR.PWR MRC scale 2/5 DST and 4/5 PRX, WR/K +1, rest were absent
3	56 Y/F	7days	High protein	Quadriparesis, areflexia, using Accessory muscles
4	29 Y/M	6 days	ND	Quadriparesis, areflexia
5	30 Y/M	4 days	ND	Quadriparesis, areflexia
6	47 Y/M	8 days	Hi9h Protein	Quadriparesis, areflexia and using accessory muscles
7	18 Y/F	5 days	Normal	MTR.PWR MRC scale 1/5 DST, 2/5 PRX, areflexia
8	29 Y/M	6 days	ND	MTR.PWR MRC scale 2/5 DST and 4/5 PRX, BR/KN +1, rest were absent
9	48 Y/M	9 days	High Protein	Quadriparesis and areflexia
10	33 Y/F	2 days	ND	MTR.PWR MRC scale 1/5 DST, 2/5 PRX, areflexia
11	51 Y/M	3 days	Normal	MTR.PWR MRC scale 1/5 DST, 2/5 PRX, areflexia
12	15 Y/F	7 days	High Protein	Quadiparesis and areflexia

M=Male, F=Female, CSF=Cerebrospinal Fluid, MTR=Motor, MRC=Medical Research Council, PRX=Proximal, DST=Distal, WR=Wrist, KN=Knee, ND=Not Done, PWR=Power

NERVE CONDUCTION STUDY AND ELECTROMYOGRAPHY

NCS/EMG is performed by a qualified neurologist &neurophysiologist and supported by trained qualified technologist. Before preceding the test, patients have been informed and for needle examination written consent was taken as per recommendation of local research ethical committee. All the patients agreed for test and most of the consents were signed by their legal guardians. Median, ulnar and common Peroneal nerves were selected for sensory and motor studies. For EMG studies deltoid, First Dorsal Interossei, Vastus Medialis and Tibialis Anterior were selected.

MOTOR NERVE CONDUCTION STUDY

In Motor Nerve Conduction Studies two nerves in upper limbs (median and ulnar) and Common Peroneal Nerve with H-Reflex were selected in lower limbs. Distal Latencies, Compound Muscle Action Potential, Conduction Velocity and F-Wave latencies were recorded bilaterally. Difference between two sides was checked. Almost all patients have decreased CMAP amplitudes; some having mildly prolonged distal latencies with slow conduction velocities were noted. Prolonged F-wave Latencies and abnormality of H-Reflex in all patients were noted. For further details refer to Table 1.2.

Table 1.2: Motor Nerve Conduction Study Data Interpretation

Patient No	Motor Nerve Conduction Studies													
	Median				Ulnar				Common Peroneal				H-Reflex	Difference in both sides
	DL	CMAP	CV	FW	DL	CMAP	CV	FW	DL	CMAP	CV	FW		
1	4.9	2.2	38	40	4.1	2.8	35	36	4.8	1.2	28	NR	NR	Almost same
2	4.7	3.1	38	30	4.0	3.9	40	26	4.2	2.4	36	40	ABST	---
3	4.6	2.0	40	NR	3.8	3.2	32	34	5.0	1.8	32	36	ABST	---
4	4.8	3.8	36	34	3.6	3.0	34	26	5.5	2.2	34	NR	ABST	---
5	4.6	4.0	42	20	3.8	3.6	38	20	4.8	1.8	36	38	ABST	---
6	5.0	2.0	32	NR	4.2	2.4	20	NR	4.8	1.2	28	NR	NR	---
7	4.8	3.6	30	42	4.0	3.5	38	24	5.0	1.6	34	32	ABST	---
8	4.8	3.9	40	38	4.2	3.2	34	30	4.6	1.4	30	35	ABST	---
9	5.0	2.8	32	NR	4.9	3.0	30	NR	5.5	1.0	28	NR	NR	---
10	4.6	4.0	42	26	3.8	4.0	32	28	3.8	2.4	38	36	ABST	---
11	4.8	3.6	38	28	4.0	3.9	36	30	4.0	2.2	36	36	ABST	---
12	4.7	3.3	34	32	3.8	3.0	38	32	4.4	1.8	34	NR	NR	---

DL= Distal Latency, CMAP =Compound Muscle Action Potential, CV=Conduction Velocity, FW=F Wave , NR=Not Recordable, ABST=Absent

SENSORY NERVE CONDUCTION STUDY (NCS)

In NCS two nerves were selected from upper limbs (median and ulnar) and Sural nerve in the lower limbs. Study conducted bilaterally. Peak Latencies, Sensory Nerve Action Potential and Conduction Velocities were recorded. No spastically significant difference was noted in bilateral recording. No sensory abnormality detected. For further details are given in Table 1.3.

Table 1.3: Sensory Nerve Conduction Study Data interpretation

Patient	Median PL CV	SNAP	Ulnar PL CV	SNAP	Sural	Difference in both sides
1	3.3 53	34	2.8 49	22	BER	No significant D/F noted
2	3.0 55	20	2.8 52	32	BER	-----
3	3.5 50	31	2.9 50	42	BER	-----
4	3.1 48	32	2.8 55	30	BER	-----
5	3.0 50	25	2.8 49	32	NR/T D	-----
6	3.2 52	35	2.6 52	26	BER	-----
7	3.4 50	26	3.6 50	32	BER	-----
8	3.1 49	40	2.7 48	40	BER	-----
9	3.0 48	28	2.6 49	41	BER	-----
10	3.1 53	32	2.8 50	34	BER	-----
11	3.2 49	30	3.0 47	32	NR/T D	-----
12	3.5 50	20	3.2 50	43	NR/T D	

PL= Peak Latency, SNAP =Sensory Nerve Action Potential, CV=Conduction Velocity, NR=Not Recordable, NR/T=Not Recordable/Technically Difficult, BER=Bilateral Equal Recordable, D/F=Difference

ELECTROMYOGRAPHY/EMG FINDINGS

For needle EMG examination two muscles in upper limbs (proximal and distal) and in lower limbs (VM and TA) were selected. Spontaneous activity in the form of Fibrillation Potentials and Positive Sharp Waves is seen and graded according to ANNEM classification from + is mild to ++++ severe axonal loss. Interestingly Fibrillation Potentials and Positive Sharp Waves have been noted frequently and almost all having decreased interference during MUAP assessment. For details are shown to Table 1.4.

Table 1.4: Electromyography Findings

Patient No	Deltoid		First Dorsal Interossei (FDI)		Vastus Medialis (VM)		Tibialis Anterior (TA)	
	FIBS MUAP	PSW	FIBS MUAP	PSW	FIBS MUAP	PSW	FIBS MUAP	PSW
1	ABST D I/P	+	+ I/P	++ D	ABST D I/P	ABST	+ I/P	+ D
2	ABST D I/P	ABST	ABST I/P	+ D	ABST D I/P	ABST	ABST I/P	+ D
3	+ D I/P	++	++ I/P	++ D	ABST D I/P	++	++ I/P	++ D
4	ABST D I/P	ABST	ABST D I/P	+	ABST D I/P	ABST	+ I/P	+ D
5	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST	ABST I/P	+ D
6	+ D I/P	+	+ ABST	+	+ D I/P	+	+ ABST	++
7	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST
8	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST
9	ABST D I/P	+	+ D I/P	++	ABST D I/P	ABST	+ I/P	++ D
10	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	ABST	ABST D I/P	+
11	ABST D I/P	ABST	ABST D I/P	+	ABST D I/P	ABST	+ D I/P	+
12	ABST D I/P	ABST	ABST D I/P	+	ABST D I/P	ABST	+ D I/P	+

FIBS=Fibrillation Potentials, PSW=Positive Sharp Waves, MUAP=Motor Unit Action Potentials, ABST=Absent, D=Decreased, I/P=Interference Pattern, +/++=Grading of active denervation grading from + to ++++ as per AANEM classification

DISCUSSION

Our article draws the attention to care being given generally and neurology particularly to the aggressive type of GBS. In literature different cases are reported and labelled as "Hyperacute Variant of GBS" 12 others also label it "Fulminant GBS" having rapid clinical course. In this study our main focus was on early NCS/EMG findings in the form of Fibrillation Potentials and Positive Sharp Waves as well as other findings like Interference Pattern and Recruitment. However, our team is planning to work on long term prognosis of possibly this new entity of GBS.

Guillain Barre Syndrome is usually a progressive disease up to certain time. Different people have different opinions but mostly the maximum motor weakness reaches from 3-4 weeks. By quoting one observation in 75% patients reached their peak motor incapacity within 2 weeks, 92% within 3 weeks and 94% within 4 weeks13. Data from one recently published study from a group of South East Asia, it showed the maximum

motor incapacity within 9.7 (6.7) days and median time 7 days14. As compare to above mentioned observation, it showed early maximum motor weakness. In our study the peak duration of motor paresis/paralysis is from 5-7 days. This clinical evidence is supported by electrophysiological studies done for these patients, in the form of severe axonal loss and early unstable potentials like Positive Sharp Waves and Fibrillation Potentials during spontaneous activity assessment. We did not investigate for possible etiology, bad prognostic factors and other associations; this may be a drawback of this survey, however such studies are warranted for the understanding of overall picture of this fulminant course of GBS. This study will definitely be a valuable addition to future research for possibly introducing a new variant of GBS, in the form of Fulminant or Hyperacute having bad prognosis.

CONCLUSION

The data of this study is possibly demonstrating an entity of a rapid clinical course with early abnormal findings on NCS/EMG in GBS, which lead to early motor incapacitance. This survey will be an initiative to identify a possible new variant of GBS. Further large studies in different regions of the world will be helpful to support our study.

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