Journal of Innovations in Applied Pharmaceutical Science [JIAPS]

Content available at: www.saap.org.in ISSN: 2455-5177

GUILLAIN-BARRE SYNDROME: A PAEDIATRIC CASE SCENARIO IN A TERTIARY CARE HOSPITAL AT SOUTHERN INDIA

Nevin Joseph[1], Alfin Baby[1], Eldhose Elias George[1], Gopikrishnan T.S[1], Merrin Joseph*[2]

[1]PharmD Intern, Nirmala College of Pharmacy, Muvattupuzha, Kerala, India

[2*]Asst. Professor, Dept. of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha, Kerala, India, 686661

Article History

Received: 06-10-2023
Revised: 26-10-2023
Accepted: 17-10-2023

Keywords: Guillain-Barre Syndrome, GBS, Case Study, Treatment, Antibody, Polyneuropathy

Abstract

Background: During hospital a ward round which was conducted as a part of Doctor of Pharmacy curriculum at Caritas Hospital, Thellakom, the first author got a chance to deal with a case of GBS.

Case: 12 year old female patient admitted with complaints of weakness on both legs; later diagnosed by the neurologist with demyelinating poly neuropathy and Guillain-Barre Syndrome. **Aim:** The aim of this particular study was to study more about Guillain-Barre Syndrome which is an auto immune disorder involving peripheral nervous system which usually occurring very rarely, affects 1.55 people per 100,000 in the world's population, and is characterised by flaccid paralysis of limbs. It typically happens as a result of an earlier illness or other triggering events that excite the immune system of the body and result in the development of various antibodies.

Materials and Methods: Analyse various case reports published in various scientific databases like PubMed, Medline, CrossRef etc.

Results: This particular case was treated as follows: The treatment involves intravenous infusion of IVIg at a dose which varies according to the weight and severity of condition in each individual. Supplementation with Methyl cobalamin, Alpha lipoic acid, Levo-carnitine, and Vitamin E can improve the neural health and hasten the healing of nerve injuries.

Conclusion: Data till now tells us that out of all GBS diagnosed population, 80% have recovered completely, 15% of patients have shown some neurological disabilities, and 5% have succumb to death. Here, the therapy was successful and the patient got discharged from hospital.

***Corresponding Author**
Merrin Joseph

https://doi.org/10.37022/jiaps.v8i3-S.533

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Introduction

Evidences of involvement of the immune system after the occurrence of certain infections or sometimes after receiving vaccinations have been established. The specific source of this immune system activation is unclear. Gullain-Barre Syndrome, commonly known as Landry's paralysis, is such an immune-mediated inflammatory reaction of the neurological system, involving peripheral nervous system which usually affects 1.55 people per 100,000 in the world's population, and is characterised by flaccid paralysis of limbs [1]. It is either or not followed by an infection vaccination, or surgery. A typical triggering factor is often an infectious disease caused primarlyby *Campylobacter jejuni*, which is the major cause, other pathogens include *cytomegalovirus* (CMV), Epstein–Barr virus, *Mycoplasma pneumonia*, *Haemophilus influenza*, and *Influenza A* virus. People can also develop Guillain–Barre syndrome due to vaccines like a meningococcal vaccine, poliovirus vaccine, influenza vaccine, and rabies vaccine [1-2].

Subtypes of GBS include acute inflammatory demyelinating polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor Sensory Axonal Neuropathy (AMSAN), Pharyngeal-Cervical brachial variant and Miller Fisher Syndrome. AIDP is a sensorimotor GBS that is frequently associated with cranial nerve abnormalities and autonomic dysfunction. It is caused by a variety of antibodies. AMAN is purely a motor involving GBS comprising antibodies like GM1a, GM1b, GD1a, GaINAc-GD1a.in case of AMAN cranial nerves are less affected. AMSAN resembles severe AMAN with sensory fibre damage and is mediated by GM1, GD1a antibodies. Motor fibres are damaged in Acute Motor and Sensory Axonal Neuropathy (AMSAN), which might be regarded a severe form of AMAN. Miller Fisher Syndrome (MFS) is a rare variant of GBS characterized by paralysis of the muscles within or surrounding the eye, the loss of full control of bodily movements and the absence of deep tendon reflexes. In most patients, diplopia is the presenting symptom. Patients with MFS usually have a good clinical outcome but rarely some of t

he patients develop limb weakness and respiratory insufficiency (termed MFS–GBS overlap syndrome). Other local variants of GBS, such as the pharyngeal–cervical–brachial variant, have also been reported [3].

The pathophysiology behind occurrence of GBS after an infection can be described as below: After *C. jejuni* infection, antibodies are generated and these antibodies cross react with specific gangliosides, like GM1 and GD1a on peripheral nerves. The antigens targeted in AMAN (Acute Motor Axonal Neuropathy) are seen at or near the node of Ranvier.In response to the anti-GM1 and anti-GD1a antibodies binding to the nodal axolemma, complement is activated, MAC is formed, and voltage-gated sodium channels vanish.This injury causes para-nodal myelin separation, which leads to failure of nerve conduction.Macrophages then infiltrate the peri-axonal area from those nodes, roaming the damaged axons. Antigens on the myelin sheath are targeted in AIDP (Acute Inflammatory Demyelinating Polyneuropathy).In brief, antibodies that activate the complement system cause the development of the MAC on the outer surface of Schwann cells, causing vesicular degeneration and macrophage invasion of myelin [4].

Most common symptoms are the weakness of the legs(areflexia) and paralysis, accompanied by tingling dysesthesias in lower extremities3 or even pain (especially in children), often starting in the legs or back.Insufficient respiration necessitating artificial ventilation may develop, autonomic dysfunction (most often cardiovascular dysregulation) may also happen to occur.

Diagnosis is based on symptoms such as bilateral weakness, rapid progression, and hypo/areflexia. Blood tests are not required to diagnose this pathology.Nerve conduction studies (NCS) are the only way to diagnose GBS and distinguish between axonal and demyelinating subtypes5. After 2 weeks of paralysis, nerve conduction problems tend to peak.GBS subtypes have different abnormalities. NCS exhibits demyelination-related characteristics in AIDP, such as extended distal motor latency, decreased nerve conduction velocity, prolonged F-wave latency, increased temporal dispersion, and conduction block. Whereas reduced motor and/or sensory amplitudes without demyelinating characteristics are seen in axonal GBS (AMAN or AMSAN).Additionally, sensory-nerve studies will be performed to help distinguish between AMAN and AMSAN, whereas neurophysiological findings in AMAN are very complex, indicating transient conduction block or slowing that quickly recovers during the course of the disease-a phenomenon known as reversible conduction failure; which is not present in AMSAN.However, reversible conduction failure might be mistaken for demyelination, as antiganglioside antibodies can cause reduced conduction at the node of Ranvier. As a result, patients with reversible conduction failure may be misdiagnosed with AIDP rather than AMAN. To avoid such scenarios, serial NCS may be required. Compound Muscle Action Potential (CMAP) scanning, a new electrophysiological method, has improved the diagnosis even further [3-4].

Treatment mainly includes administration with IVIg which inhibits Fc-mediated immune cell activation.Serum IgG-Fc glycosylation in GBS patients appears to be linked to illness severity and may impact IVIg immunomodulatory effects. When administered at a dose of 0.4 g/kg daily for 5 days (or 1 g/kg daily for 2 days) within 2 weeks after the onset of weakness, it is helpful in those who are unable to walk 10 metres on their own and have a GBS Disability Scale score of 3.Alternative therapeutic options for antibody treatment include plasma exchange, which eliminates neurotoxic antibodies, complement factors, and other humoral inflammatory mediators. Supportive therapy for respiratory distress should be provided in the form of oxygen supplementation in addition to the primary treatment. Chances for occurrence of DVT and pulmonary embolism are there; thus Low molecular weighted Heparin can be given prophylactically. Treatment-related fluctuation (TRF) is deterioration after initial improvement or stability that generally improves following treatment with IVIg or plasma exchange; in patients who develop TRF, a retreatment with IVIg (2 g/kg over 5 days) is recommended.

Data till now tells us that out of all GBS diagnosed population, 80% have recovered completely, 15% of patients have shown some neurological disabilities, and 5% have succumb to death. We witnessed a scenario of a young girl who acquired paralysis in both lower limbs without any preceding illness, immunisation, or surgery, at a tertiary care hospital.

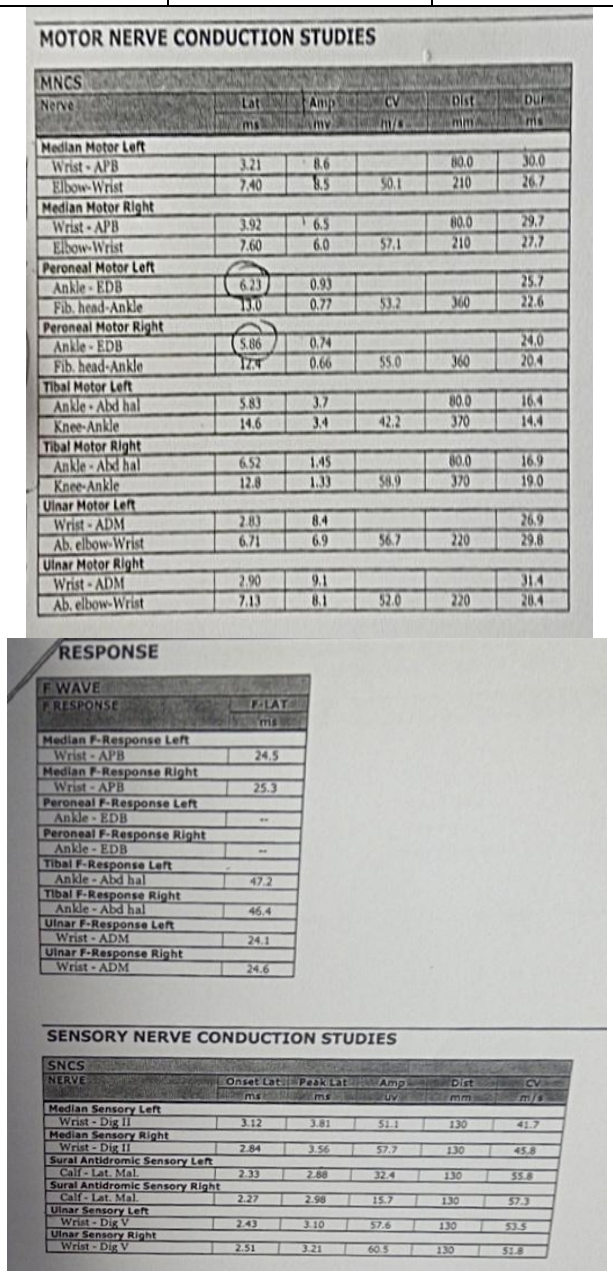
Case Details

A 12 year old female patient was admitted in the hospital with chief complaints of weakness on both lower limbs. The patient admitted with fever, body ache on exertion and buckling of legs, four days ago. The patient came by walking, accompanied by relative. The breathing was adequate and level of consciousness was good. The patient was vulnerable and the risk on full assessment found to be low. The patient was having a past history of hemiplegic migraine. On examination, B/L hand gripping, LL proximal 4- right, LL proximal 4-left, distal 4+. The patient was admitted in the neurological department.

Table no: 1 Laboratory investigations

PARAMETER	NORMAL	OBSERVED VALUE
Haematological Parameters		
Hb	12-17 gm/dl	13.7
Neutrophil	45-75 %	52
Lymphocyte	20-40 %	43
Monocyte	2-10 %	2
Basophil	0-1 %	0
Eosinophil	1-6 %	3
ESR	0-22 mm/hr.	11
Platelet	1.5-4 Lcells/cu.mm	3.25
Liver Function Test		
Total protein	6-8 mg/dL	7.3
S. Albumin	3.5-5 mg/dL	4.4
SGOT	10-40IU/L	21
SGPT	10-37 IU/L	14
Total bilirubin	0.3-1 mg/dL	0.5
ALP	20 to 140 IU/L	216
Renal Function Tests		
Blood urea	10-50 mg/dL	21.9
S. Creatinine	0.6-1.1 mg/dL	0.5
S. Sodium	130-145mEq/L	135

S. potassium	3.5-5.4mEq/L	4.2
CPK	55-170 U/L (M) 30-135 U/L (F)	27
Thyroid Function Tests		
TSH	0.5 to 5.0 mIU/L	1.66



MOTOR NERVE CONDUCTION STUDIES

MNCS

Nerve	Lat ms	Amp mv	CV m/s	Dist mm	Dur ms
Median Motor Left					
Wrist - APB	3.21	8.6		80.0	30.0
Elbow-Wrist	7.40	8.5	50.1	210	26.7
Median Motor Right					
Wrist - APB	3.92	6.5		80.0	29.7
Elbow-Wrist	7.60	6.0	57.1	210	27.7
Peroneal Motor Left					
Ankle - EDB	6.23	0.93			25.7
Fib. head-Ankle	13.0	0.77	53.2	360	22.6
Peroneal Motor Right					
Ankle - EDB	5.86	0.74			24.0
Fib. head-Ankle	12.4	0.66	55.0	360	20.4
Tibal Motor Left					
Ankle - Abd hal	5.83	3.7		80.0	16.4
Knee-Ankle	14.6	3.4	42.2	370	14.4
Tibal Motor Right					
Ankle - Abd hal	6.52	1.45		80.0	16.9
Knee-Ankle	12.8	1.33	50.9	370	19.0
Ulnar Motor Left					
Wrist - ADM	2.83	8.4			26.9
Ab. elbow-Wrist	6.71	6.9	56.7	220	29.8
Ulnar Motor Right					
Wrist - ADM	2.90	9.1			31.4
Ab. elbow-Wrist	7.13	8.1	52.0	220	28.4

RESPONSE

F WAVE

F RESPONSE	F-LAT ms
Median F-Response Left	
Wrist - APB	24.5
Median F-Response Right	
Wrist - APB	25.3
Peroneal F-Response Left	
Ankle - EDB	--
Peroneal F-Response Right	
Ankle - EDB	--
Tibal F-Response Left	
Ankle - Abd hal	47.2
Tibal F-Response Right	
Ankle - Abd hal	46.4
Ulnar F-Response Left	
Wrist - ADM	24.1
Ulnar F-Response Right	
Wrist - ADM	24.6

SENSORY NERVE CONDUCTION STUDIES

SNCS

NERVE	Onset Lat ms	Peak Lat ms	Amp uv	Dist mm	CV m/s
Median Sensory Left					
Wrist - Dig II	3.12	3.81	51.1	130	41.7
Median Sensory Right					
Wrist - Dig II	2.84	3.56	57.7	130	45.8
Sural Antidromic Sensory Left					
Calf - Lat. Mal.	2.33	2.88	32.4	130	55.8
Sural Antidromic Sensory Right					
Calf - Lat. Mal.	2.27	2.98	15.7	130	57.3
Ulnar Sensory Left					
Wrist - Dig V	2.43	3.10	57.6	130	53.5
Ulnar Sensory Right					
Wrist - Dig V	2.51	3.21	60.5	130	51.8

Figure 1: Nerve Conduction Study Report

Nerve Conduction Study Report

Studies done and was found that bilateral peroneal distal latency was prolonged, F waves were absent in bilateral peroneals and the results were suggestive of demyelinatingpolyneuropathy. (From Figure 1)

Diagnosis

The person was identified as having demyelinating polyneuropathy and GBS after examining the findings of nerve conduction testing and other laboratory parameters.

Treatment

The neurologist advised to maintain the oxygen saturation above 95% all the time. Inj. Hydrocortisone 100mg and phenaramine maleate 1ml was given as IV stat. The patient was admitted for 9 days. And during hospital stay, the patient was treated with IVIG infusion and other supportive care. IVIG infusion was given at a rate of 50 ml/hr.; 20gm twice a day for 5 days, followed by 10 gm infusion once on the next day. Along with IVIG infusion an injection containing pyridoxine hydrochloride 100mg, Mecobalamin 1000mcg and Nicotinamide 100mg was given once for first five days. From the fourth day, tablet containing alphalipoic acid (100 mg), mecobalamin (1500 mcg), folic acid (1.5 mg), pyridoxine (3 mg) and Cholecalciferol (1000 IU) was given at noon; even after discharge. And from the day six, tablet containing Levo-carnitine (150mg) + Vitamin E (200mg) was given once daily as a drug to be continued thereafter. The patient was also advised with Diclofenac gel to be applied in the area where an algia is felt twice a day.

Discussion

Acute monophasic demyelinating neuropathy (GBS), which causes increasing are flexia and motor weakness in the limbs, is what is known as the condition (Lack of motor reflex). The areas we need to focus comprises of symptomatic manifestations, laboratory investigation reports, treatment regimen and final therapeutic outcome. The primary goal of the therapy is to improve the patient's clinical condition and to improve the patient's standard of life. Normally, GBS is manifested as rapidly evolving is flexic motor paralysis with or without sensory disturbance, usually an ascending flaccid paralysis. Sensory impairments such as numbness and/or paraesthesia are more commonly reported in leg muscles than in arms. Pain is usually accompanied. And in this case too, the subject came with similar clinical findings, especially the weakness of limbs and pain with minor sensory and motor neural conduction deficits. Now, as you can see in the laboratory parameters, the ALP is elevated (From Table 1). But, ALP levels will be higher in girl children with ages near to age 12 and they start to decline after 12 years. This happens so because their bones are in the growth phase at this age. This rise in ALP in this case in insignificant. But, if similar case arises in case of an adult indicates the chances of Heterotopic Ossification (HO), which a metabolic disorder, characterized by new lamellar bone formation outside the normal skeletal structure; which is a rare complication of GBS.7It is to be noted again that the CPK (Creatinine Phosphokinase) values for children lies between 27 to 170 IU/L; thus here too, the value remains in the normal range.(From Table 1)

Regarding the available treatments, as we have already mentioned, the standard of care entails the administration of IVIg, which prevents the Fc-mediated activation of immune cells connected to the formation of antiganglioside antibodies. The normal dosing of IVIg in GBS is a single dose of 0.4 g/kg IVIg every day for 5 successive days. In this particular scenario, to the patient during her hospital stay was given with IVIG infusion and other supportive care. IVIG infusion was given at a rate of 50 ml/hr.; 20gm twice a day for 5 days, followed by 10 gm. infusion once on the next day. For an average girl of age 12 years, the body weight lies in between 40-50 kg. The weight of the subject being approximately equal to 50kg the dose was appropriate; and to reduce the chances of TRF, a secondary dose of IVIg was given after five days of treatment. Since it is known that MeCbl improves nerve conduction, promotes the

regeneration of damaged or injured nerves, and inhibited ectopic spontaneous discharges of injured primary sensory neurons.8 Alpha lipoic acid being a good antioxidant, it can help with controlling harmful free radicle oxidation of nerve cells; further reducing the rate of demyelination.9Levo-carnitine highly appreciated for its analgesic and nerve fibre cluster regeneration, by inhibiting prostaglandin synthesis and lipid peroxidation- is given her for the same reason as mentioned.10 Vitamin E which is essential for normal neurological function, increases the integrity of membranes by inhibiting lipid peroxidation and enhances the rate of cellular regeneration after damage [11].

Conclusion

Acute monophasic demyelinating neuropathy, often known as Guillain-Barre Syndrome (GBS), is a disorder that causes increasing areflexia and motor weakness in the limbs (Lack of motor reflex). And in this case report, the subject was a female having 12 year old,who came with complaints of weakness on both lower limbs. The subject's motor nerve conduction studies were done and was found that bilateral peroneal distal latency was prolonged, F waves were absent in bilateral peroneals and the results were suggestive of demyelinating polyneuropathy. Treatment includes administration with IVIg which inhibits Fc-mediated activation of immune mediated cells. Serum IgG- Fc glycosylation in GBS patients appears to beintimately associated with severity of disease and can influence the immuno-modulatory effects of IVIg.When given within two weeks after the commencement of weakness, at a dose of 0.4 g/kg daily for five days (or 1 g/kg daily for two days), a better treatment effect was seen.The weight of the subject being approximately equal to 50kg the dose was appropriate; and to reduce the chances of TRF, a secondary dose of IVIg was given after five days of treatment. Along with the primary treatment regimen, since it is known that MeCbl, Alpha lipoic acid, Levo-carnitine, and Vitamin E improves nerve conduction, promotes the regeneration of damaged or injured nerves, those supplementations were also given. Data till now tells us that out of all GBS diagnosed population, 80% have recovered completely, 15% of patients have shown some neurological disabilities, and 5% have succumb to death. The treatment was successful and the subject has recovered. Thus, the personnel was discharged.

Acknowledgement

We would like to thank Dr. Joseph Sebastian MBBS, MD (medicine), DM (neurology), Fellowship in Cerebrovascular Diseases and other hospital authorities for their collaboration. This was not an industry supported study. The authors do not make any recommendations to use drugs or devices off-label.

Conflict of Interest

Authors have no conflict of interest to declare.

Abbreviations

GBS: Guillain-Barre syndrome
NCS: Nerve Conduction Study
AMAN: AcuteMotor Axonal Neuropathy
AMSAN: Acute Motor-Sensory Axonal Neuropathy
AIDP: Acute Inflammatory Demyelinating Polyradiculopathy
MFS: Miller Fisher Syndrome
MeCbl: Methyl cobalamin
Hb: Haemoglobin
SGOT: Serum Glutamic-Oxaloacetic Transaminase
SGPT: Serum Glutamic-Pyruvic Transaminase
ALP: Alkaline Phosphatase
CPK: Creatine Phosphokinase
CMAP: Compound Muscle Action Potential
TRF: Treatment-Related Fluctuation
IVIg: Intravenous Immuno-Globulin
DVT: Deep Vein Thrombosis

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