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GUILLAIN-BARRE SYNDROME - IN BRIEF

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ABSTRACT

The Guillain-Barre Syndrome (GBS) is a life-threatening postinfectious disease characterised by rapidly progressive, symmetrical weakness of extremities and acute areflexic paralysis with albuminocytologic dissociation (i.e., high levels of protein in the cerebrospinal fluid). Guillain-Barre syndrome is the m ost common and most severe acute paralytic neuropathy, with about 10,0000 people developing the disorder every year worldwide. Under the umbrella term of Guillain-Barre syndrome, there are several recognisable variants with distinct clinical and pathological features. The clinicopathological classification suggests AIDP, AMAN, AMSAN, and Miller Fisher Syndrome which affects the cranial nerves. The symptoms progress very rapidly. In some people, the disease becomes serious in just a few hours. Treatment can help reduce the severity of symptoms and shorten the duration of the illness.

KEYWORDS: Guillain-Barre Syndrome, Clincopathological classification, Pathogenesis, Clinical features, Diagnosis, Management.

INTRODUCTION

GBS is a heterogeneous disease characterised by rapidly progressive symmetrical lymph weakness with hyporeflexia/areflexia, sensory disturbances and cranial nerve deficits occuring in some patients.[1] The earliest description on Guillain-Barre Syndrome is found in Landry's report (where he found 10 patients with ascending paralysis in 1859). Despite this, French neurologist Guillain, Barre and Strohl reported 2 soldiers who developed acute paralysis with areflexia, and recovered soon.

The reported incidence of the Guillain–Barre syndrome in Western countries ranges from 0.89 to 1.89 cases (median, 1.11) 100,000 persons/year, although an increase of 20% is seen with every 10 year rise in age after the first decade of life. The ratio of men to women with the syndrome is 1.78 (95% confidence interval, 1.36 to 2.33).

Causative association with GBS: Campylobacter jejuni, Cytomegalovirus Epstein-Barr virus Mycoplasma pneumonia, Rabies vaccine, swine flu vaccine.[4]

CLINICOPATHOLOGICAL TYPES

The histologic features of the Guillain–Barre syndrome are suggestive of a classification, based on nerve-conduction studies that includes; demyelinating and axonal subtypes-acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy.[1]

There is a remarkable difference in the geographic distribution of subtypes of the syndrome, the proportion of cases classified as the demyelinating subtype decreased from 67% to 58%, and the proportion classified as the axonal subtype increased from 18% to 38%.[2]

Table 1: Clinicopathological Types

GBS subtypes	Main clinical features	NCS findings	Antibodies*
Acute inflammatory demyelinating polyneuropathy (AIDP)	Sensorimotor GBS, often combined with cranial nerve deficits and frequent autonomic dysfunction	Demyelinating polyneuropathy	Various‡
Acute motor axonal neuropathy (AMAN)	Pure motor GBS; cranial nerves rarely affected	Axonal polyneuropathy, sensory action potential normal	GM1a, GM1b GD1a GalNAc-GD1a
Acute motor sensory axonal neuropathy (AMSAN)	Resembles severe AMAN, but sensory fibres are affected, leading to sensory deficits	Axonal polyneuropathy, sensory action potential reduced or absent	GM1, GD1a
Pharyngeal–cervical brachial variant	Prominent weakness of oropharyngeal, facial, neck and shoulder muscles	Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern	GT1a>GQ1b>>GD1a
Miller Fisher syndrome	Ataxia, ophthalmoplegia, areflexia	Normal in most patients; discrete changes in sensory conduction or H-reflex may be present	GQ1b, GT1a

PATHOGENESIS

Guillain-Barre Syndrome (GBS) is a post infectious disorder, it is a heterogeneous disease characterized by rapidly progressive, symmetrical limb weakness with hyperreflexia or areflexia: sensory disturbances and cranial nerve deficits occur in some patients. There are Infections and other events which lead to GBS, which is having a strong evidence of causative association: Campylobacter jejuni, Cytomegalovirus Epstein–Barr virus, Mycoplasma pneumonia, Rabies vaccine, ‘‘Swine flu’’ vaccine.[3]

Campylobacter jejuni

C. jejuni is widely distributed in the environment, found in many mammals and is a common occurrence; it is a genetically highly variable spiral, flagellated bacillus.

Cytomegalovirus

Cytomegalovirus is as a relevant antecedent infection, the association between CMV and GBS includes: the stimulation of immune responses to viral glycoconjugates or peptides which are shared by myelin peptides or Schwann cell epitopes.[3]

Table 2: Etiology.

Causative agents	infections
Campylobacter jejuni	Food –borne infections
Mycoplasma Pneumoniae	Respiratory infections(URTI) Encephalitis Meningitis
Haemophilus influenza	Respiratory infections(by colonizing the nasopharynx)
Cytomegalovirus	Pneumonitis Encephalitis Retinitis
Epstein-Barr virus	Mononucleosis Hepatitis

Acute inflammatory demyelinating polyneuropathy

The conventional description of AIDP is a multifocal inflammatory process throughout the peripheral nervous system where activated lymphocytes migrate across the endoneurial capillary walls and attract macrophages As. Bury et al., 1969. The macrophages penetrate the Schwann cell basal lamina and rapidly insinuate processes between the myelin lamellae and ingest and digest the myelin leaving demyelinated axons, which can then be myelinated. The localization of the lesions accounts for the distribution of neurological deficit which may be predominantly proximal, proximal and distal or predominantly distal, motor, motor and

sensory, or sensory and with or without autonomic features. The characteristic electrophysiological abnormalities are multifocal slowing of nerve conduction and partial conduction block.

Acute motor axonal neuropathy

The clinical and electrophysiological findings in AMAN demonstrates a purely motor disorder with a reduction in distally evoked muscle action potential amplitudes and relatively preserved motor nerve conduction velocity. Pathological studies indicate that the motor axon is the primary target of the autoimmune process.

Acute motor and sensory axonal neuropathy

Rare cases of GBS is depicting repeated electrophysiological studies early in the disease, which indicate the diminution of muscle and sensory action potentials consistent with what was first described as an axonal variant of GBS, but which has come to be called acute motor and sensory axonal neuropathy AMSAN.

Fisher syndrome

Fisher in 1956 described three patients with an acute disorder characterized by ophthalmoparesis, ataxia and tendon areflexia. Because of the spontaneous recovery and raised CSF protein and despite the absence of limb weakness, Fisher proposed that these cases were related to GBS. The precise anatomical distribution of lesions in Fisher syndrome is not known as it is a benign condition.[4]

CLINICAL FEATURES

In the majority of patients, the GBS continues to progress for up to 1 to 3 weeks after the onset of symptoms. Two thirds of patients are unable to walk independently when maximum weakness is reached. Respiratory insufficiency occurs in 25% of patients, with major complications like pneumonia, sepsis, pulmonary embolism, and gastrointestinal bleeding, developed in 60% of intubated patients. Among severely affected patients, 20% remain unable to walk 6 months after the onset of symptoms. The variations in the rate and extent of recovery in the Guillain–Barré syndrome make prognostication difficult.[2]

Table 3: Clinical features of Guillain-Barré syndrome.

Motor dysfunction	**Sensory dysfunction**
· Symmetrical limb weakness · proximal, distal or global Neck muscle weakness · Respiratory muscle weakness · Cranial nerve palsies: III–VII, IX–XII Areflexia · Wasting of limb muscles	· Pain Numbness · paresthesia · Loss of joint position sense · Vibration
Autonomic dysfunction	**Others**
Sinus tachycardia and bradycardia · Other cardiac arrhythmias (both tachy and brady) · Hypertension and postural hypotension · Wide fluctuations of pulse and blood pressure · Tonic pupils Hyper salivation · Anhidrosis or excessive sweating · Urinary sphincter disturbances · Constipation · Gastric dysmotility · Abnormal vasomotor tone causing venous pooling and facial flushing	· Papilledema

Table 4: Electrophysiological Features.

AIDP (Acute inflammatory demyelinating polyneuropathy)	Reduced conduction velocity Conduction block or abnormal temporal dispersion Prolonged terminal latency Absent F wave or prolonged F wave latency
AMAN (Acute motor axonal neuropathy)	AMAN Absent or reduced compound muscle action potential (CMAP) amplitude Normal motor terminal latency and conduction velocity Normal sensory nerve action potential (SNAP)
AMSAN (Acute motor sensory axonal neuropathy).[7]	Absent or reduced SNAP amplitude Absent or reduced CMAP amplitude Normal motor terminal latency and conduction velocity

DIAGNOSIS

Guillain-Barre syndrome is a recognizable entity for which the basis for diagnosis is descriptive in our present state of knowledge. The features which allow a diagnosis include; clinical, laboratory, and electro diagnostic criteria.[8]

GBS occurs over days, beginning with numbness and weakness in lower limbs, weakness progression is rapid, resulting in quadriplegia within a few days. The progression after 4 weeks is unusual and should be careful as it may often lead to many other illnesses, like chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).[7]

Approximately 50% patients develop facial weakness, Opthalmoparesis is seen in 20%, 30% of patients with GBS develop respiratory failure from phrenic nerve disease resulting in intubation and ventilation.

Some progress to tracheostomy, autonomic involvement is common in GBS, with tachycardia bradycardia, hypertension hypotension, GI hypo motility, urinary retention as common manifestations. Autonomic involvement may be the cause of death in GBS patients.

INVESTIGATIONAL DIAGNOSIS

Diagnostic criteria for Guillain-Barré syndrome have been laid down, based on clinical, laboratory, and electrophysiological features. Progressive motor weakness and areflexia are prime requirements for diagnosis. Cerebrospinal fluid analysis is the only laboratory criteria. However, other laboratory tests provide corroborative evidence for diagnosis and are useful in the management; Magnetic resonance imaging can be useful in diagnosis, especially when the electrophysiological findings are equivocal. It is a sensitive but unfortunately non-specific test.[9]

Table 5: Investigations.

Cerebrospinal fluid
Antiganglioside antibodies
Stool culture for C jejuni
Antibodies to C jejuni, Cytomegalovirus, EBV, HSV, HIV, M pneumonia.
Biochemical screening: urea, electrolytes, liver enzymes
Full blood count
Erythrocyte sedimentation rate
ECG
Autonomic function tests
Electrophysiology

Cerebrospinal Fluid

Cerebrospinal fluid (CSF) findings are normal during first week,elevated protein level on serial lumbar puncture and ten or fewer mononuclear leukocytes per cubic millimetres is the expected finding, but 11 to 50 mononuclear leukocytes per cubic millimetre may on occasion be a variant feature. In the presence of human immunodeficiency virus (HIV) seropositivity, these limits require modification.[5]

Electrodiagnosis

Understanding of the electrophysiological features supporting the diagnosis of GBS has evolved considerably in the past ten years. In the majority of GBS patients, electrodiagnostic studies reveal an evolving picture of multifocal demyelinating polyneuropathy with secondary axonal degeneration.

Proposed Electrodiagnostic Criteria for Demyelination of Peripheral Nerve: These criteria criteria concern nerve conduction studies (including proximal nerve segments) in which the predominant process is demyelination.[10]

Table 6: Electrophysiologic Diagnostic Criteria.

Must have three of the following four features
1. Reduction in conduction velocity in two or more motor nerves.
a. <80% of lower limit of normal (LLN) if amplitude
b. <70% of LLN if amplitude <80% of LW.
2. Conduction block or abnormal temporal dispersion in one or more motor nerves: either peroneal nerve be- tween ankle or below fibular head, median nerve be- tween wrist and elbow, or ulnar nerve between wrist and below elbow.
Criteria for partial conduction block:
a. <15% change in duration between proximal and distal sites and >20% drop in negative-peak area of peak-to-peak amplitude between proximal and distal sites. >go% of LLN
Criteria for abnormal temporal dispersion and possible conduction block
a. >15% change in duration between proximal and distal sites and >20% drop in negative-peak area or peak-to-peak amplitude between proximal and distal sites.
3. Prolonged distal latencies in two or more nerves.
a. >125% of upper limit or normal (ULN) if ampli
b. >150% of ULN if amplitude <80% of LLN.
4. Absent F-waves or prolonged minimum F-wave latencies (10-15 trials) in two or more motor nerves.
a. >120% of ULN if amplitude >80% of EN.
b. >150% of ULN if amplitude <80% of LLN.

Brighton Collaboration Diagnostic Criteria for Guillain-Barre Syndrome is another type of criteria which helps in diagnosis of the GBS.[10]

TREATMENT

- **General Care**

In many developed countries, 5% patients with GBS die from various complications such as sepsis, pulmonary emboli, cardiac arrest etc. Therefore, management needs measures for early detection of such complications.

Ideally, all patients should remain under hospital observation until it has been established that there is no evidence of clinical whenever feasible, patients should be treated in a critical care unit, where adequate resources are available to allow continuous cardiac and respiratory monitoring. Patients with very mild weakness and the ability to walk independently are unlikely to require any treatment beyond supportive care. Even in the absence of clinical respiratory distress, mechanical ventilation may be required.[21]

- **PHARMACOTHERAPY**

Specific Treatment

Plasma exchange

In 1978, Brettle et al first drew attention to the improved outcome in a patient with Guillain-Barre syndrome following plasma exchange. Subsequently the efficacy of plasma exchange was established by large multicentre trials. Plasma exchange beginning within the first two weeks of the illness reduced the period of hospital stay, the duration of mechanical ventilation, and the time to reach ambulation.[11]

Intravenous immunoglobulin

Intravenous immunoglobulin is used in the treatment of several immunologically mediated disorders. It is supposed to act through several mechanisms including anti-idiotypic suppression of autoantibodies. Corticosteroids Steroid treatment in Guillain-Barré syndrome has yielded disappointing results. A double blind, placebo controlled, multicentre trial looked into this issue. Two hundred and forty two patients were randomised to receive either high dose intravenous methylprednisolone (500 mg daily for five days within two weeks of onset) or placebo. The results did not show any significant difference in outcome between the two groups. However, a pilot study suggested that combined treatment with intravenous methylprednisolone (0.5 g/d) and intravenous immunoglobulin (0.4 g/kg body weight/d) for five days was more beneficial than intravenous immunoglobulin alone.[2][7]

Table 1. Management of the Guillain–Barré Syndrome.

Monitoring of cardiac and pulmonary dysfunction

Electrocardiography, blood pressure, pulse oximetry for oxyhemoglobin saturation, vital capacity, and swallowing should be regularly monitored in patients who have severe disease, with checks every 2–4 hr if the disease is progressing and every 6–12 hr if it is stable.63

Insertion of a temporary cardiac pacemaker, use of a mechanical ventilator, and placement of a nasogastric tube should be performed on the basis of the monitoring results.

Prevention of pulmonary embolism

Prophylactic use of subcutaneous heparin and compression stockings is recommended for adult patients who cannot walk.

Immunotherapy

Intravenous immune globulin or plasma exchange should be administered in patients who are not able to walk unaided. In patients whose status deteriorates after initial improvement or stabilization, retreatment, Immune globulin form of immunotherapy can be considered. However, plasma exchange should not be performed in patients already treated with immune globulin because it would wash out if the Immune globulin is still present in the blood. Also, immune globulin should not be used in patients already treated with plasma exchange because this sequence of treatments is not significantly better than plasma exchange alone.

Case Reports Describe 'Unusual' Guillain- Barre Variants Following Covid -19 Vaccination

Two studies were published in Annals of Neurology, reporting small clusters of an unusual variant of GBS, after the administration of COVID-19 vaccine, as per the American Neurological Association.11 cases of GBS were reported in those who received the vaccine 10 to 22 days prior to symptom onset.

Another study by Christopher Martin Allen, from Notiingham University Hospitals NHS Trust in the UK & colleagues reported 4 cases of bifacial weakness with paresthesias variant of GBS within 2 weeks of Oxford Astrazeneca ARS-CoV-2 vaccine, All cases occurred after 1st dose of Astrazeneca vaccine.

ZIKA VIRUS AND GBS

Zika virus (ZIKV) infection is linked to the Guillain–Barré syndrome. A study conducted by Beatriz Parra, PhD; Jairo Lizarazo, MD etal From November 2015 to March 2016 exhibits that a number of cases of GBS were reported during the outbreak of ZIKV infection in Colombia. A total of 68 patients with the GBS at six Colombian hospitals were evaluated clinically, and virologic studies were completed in 42 of them. They performed reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assays for ZIKV in blood, CSF, urine, and anti flavivirus antibody assays. In 18 of 42 patients (43%) with GBS who has underwent laboratory testing, the presence of ZIKV infection was supported by clinical and immunologic findings. In 20 of these 42 patients (48%), the GBS had a parainfectious onset. They concluded that RT-PCR test results evidences the role of infection in development of GBS.

CONCLUSION

Guillain Barre Syndrome is characterized as a rare nervous disorder, where the body's immune system launches an attack on the nervous system, causing symptoms ranging from muscle weakness to even paralysis. The cause of GBS is unknown. It is triggered by infectious illness, like gastroenteritis, lung infection. The most common risk factor for GBS is *Campylobacter jejuni infection.* There is no cure for GBS, but treatment can help reduce the severity of symptoms and shorten the duration of the illness. eyes, face, talking, chewing, swallowing, lower back pain, fast heart rate, paralysis etc. Guillain-Barre Syndrome is difficult to diagnose at first. Spinal Tap, EMG, Nerve conduction studies are used for diagnosing GBS. As it is an autoimmune inflammatory process, it will resolve on its own. Treatments are plasmapheresis, IV immunoglobulin(IVIG). Other treatments include pain reliever, drugs to prevent clotting, occupational, physical therapy.

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