Guillain-Barré Syndrome: A Common Neurological Entity with Myriad Manifestations

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Guillain-Barré syndrome (GBS) is a heterogeneous condition with several variant forms. These acute immune-mediated polyneuropathies are classified under as Guillain-Barré syndrome. Typically, GBS presents as an acute monophasic paralyzing illness preceded by an infection.

Typical clinical features of Guillain-Barré syndrome (GBS) are progressive, symmetric muscle weakness associated with absent or depressed deep tendon reflexes. Patients usually present within a few days after onset of symptoms which is most commonly the weakness of lower limbs. GBS usually progresses over a period of about two weeks at times up to 4 weeks by which time patients usually reach the maximum neurological deficit. If the disease progresses beyond 8 weeks the diagnosis is chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The weakness is very variable ranging from mild difficulty in walking to complete paralysis of all four extremities, motor cranial weakness to life-threatening respiratory muscle weakness. The latter develops in 10 to 25% of patients necessitating ventilatory support.1

Facial weakness can occur in up to 50 percent and of these 50% may develop oropharyngeal weakness. Oculomotor weakness occurs in about 15 percent of patients. Albeit predominantly a motor disease, paresthesias can occur in the hands and feet in up to 80 percent of patients; however, sensory abnormalities on examination are frequently mild.

GBS also affects autonomic nervous system and dysautonomia may occur in 70% of patients and may manifest as tachycardia, bradycardia, hypertension alternating with hypotension, orthostatic hypotension, urinary retention, and loss of sweating. Dysautonomia may be poor prognostic indicator as severe autonomic dysfunction may result in sudden death.2 Severe cardiac arrhythmias, including bradycardia and asystole, occur in about 4 percent of patients with GBS. Other arrhythmias and electrocardiogram (ECG) changes have also been described; these include atrial fibrillation, atrial flutter, paroxysmal tachycardia, ventricular tachycardia, ST-T changes, Q-T interval prolongation, axis deviation, and various conduction blocks.

Some of the atypical features of GBS include papilledema, facial myokymia, meningeal signs, vocal cord paralysis, and even mental status changes. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) has also been reported in association with GBS.3

GBS is a heterogeneous syndrome with several variant forms. Each form of GBS has distinguishing clinical, pathophysiologic, and pathologic features; acute immune-mediated polyneuropathy (AIDP) being the most common form which occurs in almost 85 to 90 percent of cases. The clinical variant Miller Fisher syndrome (MFS), characterized by ophthalmoplegia, ataxia, and areflexia, occurs in 5% of cases. Acute motor axonal neuropathy (AMAN) and acute sensorimotor axonal neuropathy (AMSAN) are primary axonal forms of GBS which are rare in less than 5% of cases. Most cases of AMAN are preceded by Campylobacter jejuni infection. Deep tendon reflexes are occasionally preserved in patients with AMAN and sensory nerves are not affected. The presenting clinical features and recovery of AMAN are almost similar to those of AIDP. AMSAN is a more severe form of AMAN wherein both sensory and motor fibers are affected with marked axonal degeneration, and therefore, ASMAN has delayed and incomplete recovery.4

Other uncommon variants include pharyngeal-cervical-brachial paralysis, paraparesis, acute pandysautonomia, pure sensory GBS, facial diplegia and distal limb paresthesias, sixth nerve palsy and distal paresthesias, bilateral lumbar radiculopathy. Bickerstaff encephalitis is brainstem encephalitis with features of MFS associated with an encephalopathy and hyperreflexia.5

There are different antibodies associated with pathogenesis of GBS. Peripheral nerve myelin is the target of immune attack in AIDP. Glycolipid antibodies may be associated with different forms or aspects of GBS. Antibodies against GQ1b (a ganglioside component of nerve) are found in 85 to 90% of patients with the Miller Fisher syndrome. Antibodies to GM1, GD1a, GalNac-GD1a, and GD1b are mostly associated with axonal variants of GBS viz. AMAN and AMSAN. Antibodies to GT1a are associated with swallowing dysfunction whereas antibodies to GD1b are associated with pure sensory GBS.6

Peripheral nerve remyelination occurs relatively rapidly over several weeks to months resulting in good recovery. However, in a small percentage of patients where there is superimposed significant axonal degeneration the recovery is markedly delayed and incomplete.

Diagnosis of GBS is usually clinical. Nerve conduction studies when available should be performed to confirm diagnosis. Neurophysiology studies (electromyography and nerve conduction studies) show evidence of an acute polyneuropathy with predominantly demyelinating features in acute inflammatory demyelinating polyradiculoneuropathy (AIDP). Nerve conduction studies (NCS) and electromyography (EMG) are valuable not only for confirming the diagnosis of GBS but also for providing information regarding prognosis. The typical finding in cerebrospinal fluid (CSF) is albuminocytologic dissociation with an elevated protein with a normal white blood cell (WBC) count in CSF and is present in 80 to 90 percent of patients with GBS at one week after onset of symptoms. In clinical practice, commercially available testing for serum IgG antibodies to GQ1b is useful for the diagnosis of MFS. Currently, laboratory testing for antibodies to glycolipids other than GQ1b is not performed routinely because of limited clinical utility. Diagnostic criteria for GBS from the National Institute of Neurological Disorders and Stroke (NINDS)7 have an important role in research and are widely used in clinical practice.

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One proposed mechanism for Guillain-Barré syndrome (GBS) is molecular mimicry. An antecedent infection evokes an immune response, which in turn cross-reacts with peripheral nerve components because of the sharing of cross-reactive epitopes. This immune response can be directed towards the myelin or the axon of peripheral nerve resulting in an acute polyneuropathy. Approximately two-thirds of patients give a history of an antecedent respiratory tract or gastrointestinal infection. A variety of infections are known to be associated with GBS which include Campylobacter species, cytomegalovirus, Epstein-Barr virus, Mycoplasma pneumoniae, varicella-zoster virus, herpes simplex virus, hepatitis A, B, and C virus, influenza virus, and the bacteria Haemophilus influenzae and Escherichia coli. GBS is now being associated commonly with human immunodeficiency virus (HIV) infection, predominantly in those who are not profoundly immunocompromised although it can occur in any stage of HIV infection. GBS is known to occur after acute HIV seroconversion and also following immune reconstitution from highly-active antiretroviral therapy.

Today, two therapeutic options available include plasmapheresis and intravenous immune globulin (IVIG). Plasmapheresis is thought to remove circulating antibodies, complement, and soluble biological response modifiers; whereas the precise mechanism of action for intravenous immune globulin (IVIG) in GBS is unknown. IVIG may act by providing anti-idiotypic antibodies, modulating expression and function of Fc receptors, interfering with activation of complement and production of cytokines, and interfering with activation and effector functions of T and B cells. Intravenous immune globulin (IVIG) is as effective as plasma exchange for the treatment of GBS. Patients with more severe clinical disease may benefit from longer duration of IVIG treatment. Glucocorticoids which have been used for long time have not been shown to be beneficial and no longer have a role in treatment of GBS. Disease-modifying therapy with plasma exchange or IVIG is recommended for nonambulatory patients with GBS who present within four weeks of onset of GBS. Patients recover sooner and better when treated early. Approximately 80 and 84 percent patients with GBS walk independently at six months and one year after diagnosis, respectively. At one year, full recovery of motor strength occurs in about 60 percent of patients, while severe motor deficit may persist in about 14 percent.

In this issue of JAPI, Dhadke et al have made a good attempt to generate some data, however, we need to have more data as in our set up as offending pathogens are different and outcomes may vary from Western countries.

**References**


