THE GUILLAIN-BARRÉ SYNDROME

Guillain–Barré syndrome (GBS) is an acute onset of areflexic paralysis with recovery accompanied by acellular cerebrospinal fluid with an elevated protein.

Epidemiology

The reported incidence rates for GBS are 1–2 per 100,000 population. The lifetime likelihood of any individual acquiring GBS is 1:1000. The subtypes of GBS have different incidence rates in different parts of the world. Available Indian literature indicates a peak incidence between June–July and Sept–October. In western countries, GBS is common in the 5th decade, but in India it occurs more commonly at a younger age. GBS is equally common in men and women and can occur at any age. There is a male preponderance among the hospitalized patients.

Key Concepts

- Definition of Guillain–Barré Syndrome
- Epidemiology of Guillain–Barré Syndrome
- Pathogenesis of Guillain–Barré Syndrome
- Diagnosis of Guillain–Barré Syndrome
- Management options for Guillain–Barré Syndrome

Abstract

Guillain–Barré Syndrome is an acute onset of areflexic paralysis with recovery accompanied by acellular CSF with an elevated protein. It is a rare syndrome. Most often this is preceded by upper respiratory infection. The gold standard for diagnosis is by estimating proteins in CSF. The management is mainly supportive and immunotherapy. This is a disease with high mortality.

Key words: Guillain–Barré Syndrome, Demyelination, CSF pleocytosis, Immunoglobulins, Plasma exchange.
Pathogenesis
Strong evidence now exists that axonal subtypes of Guillain–Barré syndrome, acute motor axonal neuropathy (AMAN), and acute motor and sensory axonal neuropathy (AMSAN), are caused by antibodies to gangliosides on the axolemma that target macrophages to invade the axon at the node of Ranvier. About a quarter of patients with Guillain–Barré syndrome have had a recent C. jejuni infection, and axonal forms of the disease are especially common in these people. The lipo-oligosaccharide from the C. jejuni bacterial wall contains ganglioside-like structures and its injection into rabbits induces a neuropathy that resembles acute motor axonal neuropathy. Antibodies to GM1, GM1b, GD1a, and GalNac-GD1a are in particular implicated in acute motor axonal neuropathy.

Clinical Features
Most often an unremarkable infection, such as upper respiratory infection, often predates the onset of GBS by 14 days. Many antecedent infections have been identified, including Campylobacter jejuni, cytomegalovirus (CMV), Mycoplasma pneumonia, Epstein–Barr virus, influenza virus, JEV. Surgery, immunization, and parturition have also been associated with GBS. GBS usually begins abruptly with distal, relatively symmetrical onset of paraesthesias and quickly followed by progressive limb weakness. Progression is rapid, with 50% of patients reaching clinical nadir by 2 weeks and more than 90% by 4 weeks. The current diagnostic criteria include <4 weeks of progression to clinical nadir. Approximately 80%–90% of patients with GBS become nonambulatory during the illness. Pain is prominent in 50% of patients. Neurological examination is characterized by distal and often proximal, relatively symmetrical, weakness. Although GBS is essentially a motor neuropathy, sensory dysfunction is seen in a few patients. It is seen more in a demyelinating form of GBS. Sensory examination is often normal in the early phase of disease. Facial or pharyngeal weakness is commonly seen in GBS. Diaphragmatic weakness due to phrenic nerve involvement is also common. Approximately one third of hospitalized GBS patients require mechanical ventilation due to respiratory muscle or oropharyngeal weakness. Tachycardia is common but more serious autonomic nervous system dysfunction may occur, including life-threatening arrhythmias, hypotension, hypertension, and gastrointestinal dysmotility. The incidence is between 27% and 55% and is more common in demyelinating than axonal form.

Diagnosis
Progressive weakness in both upper and lower extremities within 4 weeks along with areflexia is essential requirement for the diagnosis. Supportive ancillary testing for GBS includes CSF analysis and electrodiagnostic testing, both of which may be normal in the early phase of GBS. The limitations of ancillary testing in the early phase combined with the importance of prompt treatment of GBS mandates that the clinician at times make the diagnosis based solely on history and examination. An elevated CSF protein concentration (with
normal cell count) is only found on initial CSF analysis in 50% of patients; elevated CSF protein concentration occurs in more than 90% of patients at the peak of the disease. CSF pleocytosis is an important red flag, which raises the question of infectious (HIV, CMV, Lyme, sarcoid), carcinomatous, or lymphomatous polyradiculoneuropathy.

Management

i) Supportive

There are no studies specifically addressing thromboprophylaxis in GBS, however this is an important aspect of supportive care.

Dysautonomia - which includes paralytic ileus and bronchial dysfunction as well as instability of pulse and blood pressure - occurs in 20% of patients with GBS. Wide blood pressure swings may augur severe bradycardia, which can precede asystole. These complications occur mostly in severely affected patients with generalised weakness and respiratory failure.

Neuromuscular respiratory insufficiency ensues in 17-30% of patients with GBS. Accumulating secretions secondary to bulbar and bronchial mucosal dysfunction may further compromise gas-exchange. Rapid progression and pattern of involvement signal risk of respiratory compromise.

Pain - occurs in 90% of patients with GBS and at least six types of pain have been identified. Commonly, sensory symptoms exceed the signs. Neurogenic pain may arise from the loss of inhibition of the substantia gelatinosa by larger myelinated fibres and from small unmyelinated C fibres. Radicular pain and meningeal irritation may be secondary to inflammation of spinal nerve roots. Weakness of paraspinal muscles may result in mechanical back pain. Rate related cardiac ischaemic pain and discomfort from constipation and urinary retention could be mis-interpreted as radicular pains. Both carbamazepine and gabapentin are effective in reducing pain scores and requirement for opioid analgesia in GBS patients. Gabapentin seems to have a quicker onset and be most effective. Amitriptyline is also frequently used.

ii) Immunotherapy

When given to non-ambulant patients within four weeks of presentation, intravenous immunoglobulin (IVIg) and plasma exchange (PE) have a similar efficacy both in terms of disability measured one month after treatment and long term outcome. IVIg is usually used (0.4g/Kg body weight/day for five days) because of convenience despite the theoretical risk of transmission of virus or prion. IVIg may work by multiple mechanisms, including blocking Fc receptors, provision of anti-ideotypic antibodies, interference with complement activation and T-cell regulation. Monoclonal antibodies show promise as future treatments. Eculizimab disrupts the complement cascade, protecting terminal motor nerves from anti-GQ1b antibody induced injury.

Prognosis

GBS has a serious long-term impact on the patients' work and private life, even 3–6 years after the onset of illness. Recovery can be slow and take years. Persistent disability is seen in 20%–30% of adult patients but is
less common in children. Severe fatigue is a sequel of GBS in two thirds of adult patients. In an RCT of amantidine, it was not superior to placebo. Twelve weeks bicycle extensive training program had positive effects on fatigue, anxiety, depression, and functional outcome.

Conclusions
GBS is a monophasic immune-mediated neuropathy characterized by acute onset of predominantly motor weakness and is a common cause of respiratory paralysis. There are many variants described with different prognosis and manifestations. Electrodiagnosis aids in the diagnosis. Immunotherapy definitely makes a difference in the recovery of GBS patients and both PE and IVIg are equally effective. IVIg may be preferred because of its low side-effect profile and ease of administration. However, small volume PE can be used with equal efficacy due to cost constraints. Attentive anticipatory supportive treatment is equally important in reducing the morbidity and mortality in GBS.

References


