No Results

Guillain-Barre Syndrome

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Practice Essentials

Guillain-Barré syndrome (GBS) can be described as a collection of clinical syndromes that manifests as an acute inflammatory polyradiculoneuropathy with resultant weakness and diminished reflexes.

Although the classic description of GBS is that of a demyelinating neuropathy with ascending weakness, many clinical variants have been well documented in the medical literature.

Signs and symptoms

The typical patient with GBS, which in most cases will be acute inflammatory demyelinating polyradiculoneuropathy (AIDP), presents 2-4 weeks following a relatively benign respiratory or gastrointestinal illness with complaints of finger dysesthesias and proximal muscle weakness of the lower extremities. The weakness may progress over hours to days to involve the arms, truncal muscles, cranial nerves, and muscles of respiration.

Common complaints associated with cranial nerve involvement in GBS include the following:

- Facial droop (may mimic Bell palsy)
- Diplopias
- Dysarthria
- Dysphagia
- Ophthalmoplegia
- Pupillary disturbances

Most patients complain of paresthesias, numbness, or similar sensory changes. Paresthesias generally begin in the toes and fingertips, progressing upward but generally not extending beyond the wrists or ankles.

Pain associated with GBS is most severe in the shoulder girdle, back, buttocks, and thighs and may occur with even the slightest movements. The pain is often described as aching or throbbing in nature.

Autonomic changes in GBS can include the following:

- Tachycardia
- Bradycardia
- Facial flushing
- Paroxysmal hypertension
- Orthostatic hypotension
- Anhidrosis and/or diaphoresis
- Urinary retention

Typical respiratory complaints in GBS include the following:

- Dyspnea on exertion
- Shortness of breath
- Difficulty swallowing
- Slurred speech

Ventilatory failure with required respiratory support occurs in up to one third of patients at some time during the course of their disease.

See Clinical Presentation for more detail.

Diagnosis

GBS is generally diagnosed on clinical grounds. A basic peripheral neuropathy workup is recommended in cases in which the diagnosis is uncertain. Biochemical screening can also be conducted and would include the following studies:

- Electrolyte levels
- Liver function tests (LFTs)
- Creatine phosphokinase (CPK) level
- Erythrocyte sedimentation rate (ESR)

Needle EMG and nerve conduction studies

Signs of demyelination can include the following:

- Nerve conduction slowing
- Prolongation of the distal latencies
- Prolongation of the F-waves [1, 2]
- Conduction block or dispersion of responses: Evidence frequently demonstrated at sites of natural nerve compression
- Weak muscles showing reduced recruitment: Demonstrated with needle examination (electromyography [EMG])

Pulmonary function

Maximal inspiratory pressures and vital capacities are measurements of neuromuscular respiratory function and predict diaphragmatic strength. Maximal expiratory pressures also reflect abdominal muscle strength. Negative inspiratory force (NIF) is a relatively easy bedside test to measure respiratory muscle function. Normal is usually greater than 60 cm water. If the NIF is dropping or nears 20 cm water, respiratory support needs to be available.

Cerebrospinal fluid studies

Most, but not all, patients with GBS have an elevated cerebrospinal fluid (CSF) protein level (>400 mg/L), with normal CSF cell counts. Elevated or rising protein levels on serial lumbar punctures and 10 or fewer mononuclear cells/mm^3 strongly support the diagnosis.

See Workup for more detail.

Management

Intensive care unit

Admission to the intensive care unit (ICU) should be considered for all patients with labile dysautonomia, a forced vital capacity of less than 20 mL/kg, or severe bulbar

palsy.[3, 4] Any patients exhibiting clinical signs of respiratory compromise to any degree also should be admitted to an ICU.[3]

Competent intensive care includes the following features:

- Respiratory therapy
- Cardiac monitoring
- Safe nutritional supplementation
- Monitoring for infectious complications (eg, pneumonia, urinary tract infections, septicemia)

Subcutaneous unfractionated or low–molecular-weight heparin (LMWH) and thromboguards are often used in the treatment of immobile patients to prevent lower-extremity deep venous thrombosis (DVT) and consequent pulmonary embolism (PE).

Immunomodulation

Immunomodulatory treatment in GBS has been used to hasten recovery. Intravenous immunoglobulin (IVIG) and plasma exchange have proved equally effective.

Physical, occupational, and speech therapy

Addressing upright tolerance and endurance may be a significant issue during the early part of physical rehabilitation. Active muscle strengthening can then be slowly introduced and may include isometric, isotonic, isokinetic, or progressive resistive exercises.

Occupational therapy professionals should be involved early in the rehabilitation program to promote positioning, posture, upper body strengthening, range of motion (ROM), and activities that aid functional self care.

Speech therapy is aimed at promoting speech and safe swallowing skills for patients who have significant oropharyngeal weakness with resultant dysphagia and dysarthria.

See Treatment and Medication for more detail.

Background

Guillain-Barré syndrome (GBS) can be described as a collection of clinical syndromes that manifests as an acute inflammatory polyradiculoneuropathy with resultant weakness and diminished reflexes. With poliomyelitis under control in developed countries, GBS is now the most important cause of acute flaccid paralysis. (See Clinical Presentation.)

Although the classic description of GBS is that of a demyelinating neuropathy with ascending weakness, many clinical variants have been well documented in the medical literature, and variants involving the cranial nerves or pure motor involvement and axonal injury are not uncommon. (See Pathophysiology.)

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most widely recognized form of GBS in Western countries, but the variants known as acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and Miller-Fisher syndrome also are well recognized.

Based on a clinical spectrum of symptoms and findings, it is widely believed that strictly defined subgroups of GBS exist. However, these subgroups are not easily distinguished.

GBS remains a diagnosis made primarily through the assessment of clinical history and findings (see Clinical Presentation). Serum autoantibodies are not measured routinely in the workup of GBS, but results may be helpful in patients with a questionable diagnosis or a variant of GBS (see Workup).

Approximately one third of patients require admission to an intensive care unit (ICU), primarily because of respiratory failure. After medical stabilization, patients can be treated on a general medical/neurologic floor, but continued vigilance remains important in preventing respiratory, cardiovascular, and other medical complications. Treatment with intravenous immunoglobulin (IVIG) or plasma exchange may hasten recovery. After discharge, outpatient physical therapy and occupational therapy may be beneficial in helping patients with GBS to regain their baseline functional status. (See Treatment and Medication.)[5, 3, 6, 7]

Historical background

In 1859, Landry published a report on 10 patients with an ascending paralysis.[8] Subsequently, in 1916, 3 French physicians (Guillain, Barré, and Strohl) described 2 French soldiers with motor weakness, areflexia, cerebrospinal fluid (CSF) albuminocytologic dissociation, and diminished deep tendon reflexes.[1] The identified syndrome was later named Guillain-Barré syndrome. Historically, GBS was a single disorder; however, current practice acknowledges several variant forms.

Pathophysiology

GBS is a postinfectious, immune-mediated disease. Cellular and humoral immune mechanisms probably play a role in its development. Most patients report an infectious illness in the weeks prior to the onset of GBS. Many of the identified infectious agents are thought to induce production of antibodies that cross-react with specific gangliosides and glycolipids, such as GM1 and GD1b, that are distributed

throughout the myelin in the peripheral nervous system.[9]

The pathophysiologic mechanism of an antecedent illness and of GBS can be typified by *Campylobacter jejuni* infections.[10, 11] The virulence of *C jejuni* is thought to be based on the presence of specific antigens in its capsule that are shared with nerves.

Immune responses directed against lipopolysaccharide antigens in the capsule of *C jejuni* result in antibodies that cross-react with ganglioside GM1 in myelin, resulting in immunologic damage to the peripheral nervous system. This process has been termed molecular mimicry.[12, 13]

Pathologic findings in GBS include lymphocytic infiltration of spinal roots and peripheral nerves (cranial nerves may be involved as well), followed by macrophage-mediated, multifocal stripping of myelin. This phenomenon results in defects in the propagation of electrical nerve impulses, with eventual absence or profound delay in conduction, causing flaccid paralysis. Recovery is typically associated with remyelination.

In some patients with severe disease, a secondary consequence of the severe inflammation is axonal disruption and loss. A subgroup of patients may have a primary immune attack directly against nerve axons, with sparing of myelin. The clinical presentation in these patients is similar to that of the principal type.

Subtypes of Guillain-Barré syndrome

Several variants of GBS are recognized. These disorders share similar patterns of evolution, symptom overlap, and probable immune-mediated pathogenesis. Recovery from them varies.

Acute inflammatory demyelinating polyneuropathy

The acute inflammatory demyelinating polyneuropathy (AIDP) subtype is the most commonly identified form in the United States. It is generally preceded by a bacterial or viral infection. Nearly 40% of patients with AIDP are seropositive for *C jejuni.* Lymphocytic infiltration and macrophage-mediated peripheral nerve demyelination is present. Symptoms generally resolve with remyelination.

Acute motor axonal neuropathy

The acute motor axonal neuropathy (AMAN) subtype is a purely motor disorder that is more prevalent in pediatric age groups.[14] AMAN is generally characterized by rapidly progressive symmetrical weakness and ensuing respiratory failure.

Nearly 70-75% of patients with AMAN are seropositive for *Campylobacter*, with the majority of cases of AMAN being associated with preceding *C jejuni* diarrhea. Patients typically have high titers of antibodies to gangliosides (ie, GM1, GD1a, GD1b). Inflammation of the spinal anterior roots may lead to disruption of the blood-CNS barrier.[12] Biopsies show wallerianlike degeneration without significant lymphocytic inflammation.

Many cases have been reported in rural areas of China, especially in children and young adults during the summer months.[15] Pure axonal cases may occur more frequently outside of Europe and North America. AMAN cases may also be different from cases of axonal GBS described in the West.

Prognosis is often quite favorable. Although recovery for many is rapid, severely disabled patients with AMAN may show improvement over a period of years.[16]

One third of patients with AMAN may actually be hyperreflexic. Although the mechanism for this hyperreflexia is unclear, dysfunction of the inhibitory system via spinal interneurons may increase motor neuron excitability. Hyperreflexia is significantly associated with the presence of anti-GM1 antibodies.[8]

Acute motor-sensory axonal neuropathy

Acute motor-sensory axonal neuropathy (AMSAN) is a severe acute illness differing from AMAN in that it also affects sensory nerves and roots.[17] Patients are typically adults. AMSAN often presents as rapid and severe motor and sensory dysfunction. Marked muscle wasting is characteristic, and recovery is poorer than it is from electrophysiologically similar cases of AMAN.

As with AMAN, AMSAN is often associated with preceding *C jejuni* diarrhea. Pathologic findings show severe axonal degeneration of motor and sensory nerve fibers with little demyelination.[18]

Miller-Fisher syndrome

Miller-Fisher syndrome (MFS), which is observed in about 5% of all cases of GBS, classically presents as a triad of ataxia, areflexia, and ophthalmoplegia.[19] Acute onset of external ophthalmoplegia is a cardinal feature.[12] Ataxia tends to be out of proportion to the degree of sensory loss. Patients may also have mild limb weakness, ptosis, facial palsy, or bulbar palsy. Patients have reduced or absent sensory nerve action potentials and absent tibial H reflex.[20]

Anti-GQ1b antibodies are prominent in MFS, and have a relatively high specificity and sensitivity for the disease.[21] Dense concentrations of GQ1b ganglioside are found in the oculomotor, trochlear, and abducens nerves, which may explain the relationship between anti-GQ1b antibodies and ophthalmoplegia. Patients with acute oropharyngeal palsy carry anti-GQ1b/GT1a IgG antibodies.[12] Recovery generally occurs within 1-3 months.

Acute panautonomic neuropathy

Acute panautonomic neuropathy, the rarest GBS variant, involves the sympathetic and parasympathetic nervous systems. Patients have severe postural hypotension, bowel and bladder retention, anhidrosis, decreased salivation and lacrimation, and pupillary abnormalities. Cardiovascular involvement is common, and dysrhythmias are a significant source of mortality. Significant motor or sensory involvement is lacking. Recovery is gradual and often incomplete.

Pure sensory GBS

A pure sensory variant of GBS has been described in the literature. It is typified by a rapid onset of sensory loss, sensory ataxia, and areflexia in a symmetrical and widespread pattern. Lumbar puncture studies show albuminocytologic dissociation in the CSF, and results from electromyography (EMG) show characteristic signs of a demyelinating process in the peripheral nerves.

The prognosis in pure GBS is generally good. Immunotherapies, such as plasma exchange and the administration of IVIGs, can be tried in patients with severe disease or slow recovery.

Other variants

The pharyngeal-cervical-brachial variant of GBS is distinguished by isolated facial, oropharyngeal, cervical, and upper limb weakness without lower limb involvement. There can be combinations of any of the above subtypes, and virtually any combination of nerve injury. There are likely mild cases that cause temporary symptoms, improve spontaneously, and never get definitively diagnosed.

Other unusual clinical variants with restricted patterns of weakness are observed only in rare cases.

Etiology

GBS is considered to be a postinfectious, immune-mediated disease targeting peripheral nerves. Up to two thirds of patients report an antecedent bacterial or viral illness prior to the onset of neurologic symptoms.[22, 23] Respiratory infections are most frequently reported, followed by gastrointestinal infections.[24] Administration of certain vaccinations and other systemic illnesses have also been associated with GBS. Case reports exist regarding numerous medications and procedures; however, whether any causal link exists is unclear.

C jejuni

In several studies, *C jejuni* was the most commonly isolated pathogen in GBS. Serology studies in a Dutch GBS trial identified 32% of patients as having had a recent *C jejuni* infection, while studies in northern China documented infection rates as high as 60%.[15, 25, 26]

Gastrointestinal and upper respiratory tract symptoms can be observed with *C jejuni* infections. *C jejuni* infections can also have a subclinical course, resulting in patients with no reported infectious symptoms prior to the development of GBS. Patients who develop GBS following an antecedent *C jejuni* infection often have a more severe course, with rapid progression and a prolonged, incomplete recovery. A strong clinical association has been noted between *C jejuni* infections and the pure motor and axonal forms of GBS.

The virulence of *C jejuni* is thought to result from the presence of specific antigens in its capsule that are shared with nerves. Immune responses directed against capsular lipopolysaccharides produce antibodies that cross-react with myelin to cause demyelination.

C jejuni infections also generate anti-ganglioside antibodies—including to the gangliosides GM1, GD1a, GalNac-GD1a, and GD1b—that are commonly found in patients with AMAN and AMSAN, the axonal subtypes of GBS. (Patients with *C. jejuni* enteritis not complicated by GBS, however, do not produce the specific anti-ganglioside antibodies.)

Even in the subgroup of patients with GM1 antibodies, however, the clinical manifestations vary. Host susceptibility is probably one determinant in the development of GBS after infectious illness.[25, 27]

Although GM1 antibodies can also be found in patients with demyelinating GBS, they are much less common in these cases. *C. jejuni* infection can also generate antibodies to the ganglioside GQ1b, a component of oculomotor nerve myelin; these are associated with MFS.

CMV

Cytomegalovirus (CMV) infections are the second most commonly reported infections preceding GBS, with CMV being the most common viral trigger of GBS. The aforementioned Dutch GBS study found CMV to be present in 13% of patients.[28]

CMV infections present as upper respiratory tract infections, pneumonias, and nonspecific, flulike illnesses. GBS patients with preceding CMV infections often have prominent involvement of the sensory and cranial nerves. CMV infections are significantly associated with antibodies against the ganglioside GM2.

Other infections

Other significant, although less frequently identified, infectious agents in GBS patients include Epstein-Barr virus (EBV), *Mycoplasma pneumoniae*, and varicella-

zoster virus.[29] An association between GBS and acute human immunodeficiency virus (HIV) infection also is well recognized.[8, 30, 31, 32, 33, 34]

Infections with *Haemophilus influenzae*, *Borrelia burgdorferi*, para-influenza virus type 1, influenza A virus, influenza B virus, adenovirus, and herpes simplex virus have been demonstrated in patients with GBS, although not more frequently than they have in controls.[35]

There has been speculation that the Zika virus can cause GBS. Reported cases of the syndrome began to increase in Brazil during the Zika virus outbreak that was identified there in 2015, with hundreds of cases of GBS reported that year.[36, 37] In July 2015, for example, out of 76 patients in the state of Bahia identified with neurologic syndromes, 42 were confirmed as having GBS, with the symptom history of 26 of these confirmed cases having been consistent with Zika virus infection.[38]

Other Latin American countries to which the Zika outbreak spread, including Colombia, Venezuela, and El Salvador, also reported increases in GBS cases.[37] In El Salvador, where an average of 14 cases of GBS are reported per month, 46 cases were reported between December 1, 2015 and January 6, 2016.[38]

However, additional research will be required to resolve speculation about the Zika-GBS link. The reliability of Zika virus diagnoses outside of the United States is not known. In the United States, the only infectious disease laboratories capable of making this diagnosis are at the US Centers for Disease Control and Prevention (CDC) and a few state or local health departments. There is currently no commercially available test for Zika virus.[39]

Vaccines

Vaccinations have been linked to GBS[40] by temporal association. For example, a study reviewing GBS cases during the 1992-1993 and 1993-1994 influenza seasons found an adjusted relative risk of 1.7 cases per 1 million influenza vaccinations.[41]

In most cases, however, no definite causal relation has been established between vaccines and GBS, with the exception of rabies vaccine prepared from infected brain tissue and the 1976 swine flu vaccine.[35, 42] (The increased risk of GBS after the swine flu vaccination, however, was just one extra case per 100,000 vaccinations.[43])

Moreover, a review of all postvaccination cases of GBS from 1990-2005 did not reveal an increase in mortality with postvaccination cases of GBS compared with cases resulting from other causes.[40]

In addition, some studies have called the GBS/vaccine link into question, finding no evidence of an increased risk of GBS after seasonal influenza vaccine or after the 2009 H1N1 mass vaccination program.[44, 45, 46]

For example, a study by Kawai et al that monitored adverse events following administration of the 2012-13 influenza vaccines found no association between the vaccines and GBS. Results were based on 3.6 million first doses of inactivated influenza vaccine in patients aged 6 months and older and 250,000 first doses of live attenuated vaccine in patients aged 2-49 years.[47]

A study by Dieleman et al researched the association between the pandemic influenza A (H1N1) 2009 vaccine and GBS in 104 patients in 5 European countries. Adjusting for the effects of influenzalike illness/upper respiratory tract infection, seasonal influenza vaccination, and calendar time, the authors concluded that there was no increased risk of occurrence of GBS after receiving the pandemic influenza vaccine.[48]

Similarly, a study conducted by the Chinese Centers for Disease Control found no evidence of increased risk of GBS from administration of the H1N1 vaccine, following the administration of 89.6 million doses of the vaccine between September 21, 2009 and March 21, 2010.[49]

Epidemiologic studies from Finland and southern California failed to validate an earlier retrospective study from Finland that suggested a cause-effect relationship between oral polio vaccination and GBS.[50, 51] In contrast, a Brazilian study suggested that, based on a temporal association between the vaccine and the onset of GBS, the vaccine may rarely correlate with the syndrome.[52]

Results from studies into the association between GBS and other vaccines include the following:

- Data from a large-scale epidemiologic study reported a decreased GBS incidence following administration of tetanus toxoid containing vaccinations when compared with the baseline population [53]
- An epidemiologic study failed to show any conclusive epidemiologic association between GBS and the hepatitis B vaccine [54]
- A large Latin American study of more than 2000 children with GBS following a mass measles vaccination program in 1992-1993 failed to establish a statistically significant causal relationship between administration of the measles vaccine and GBS [55]
- A report from the CDC suggests that recipients of the Menactra meningococcal conjugate vaccine may be at increased risk of GBS [56]
- Case reports exist regarding group A streptococcal vaccines and the rabies vaccine; however, conclusive, statistically significant evidence is lacking

Medications

In a case-controlled study, patients with GBS reported more frequent penicillin and antimotility drug use and less frequent oral contraceptive use. However, no definite cause-effect relationships have been established.[57]

Case reports exist in the setting of tumor necrosis factor antagonist agents used in rheumatoid arthritis.[58, 59, 60, 61] Case reports also exist regarding streptokinase, isotretinoin, danazol, captopril, gold, and heroin, among others.

A study by Ali indicated that antibiotic therapy with fluoroquinolones also is associated with the development of GBS. Using cases reported between 1997 and 2012 to the US Food and Drug Administration (FDA) Adverse Reporting System, he determined that of 539 reports of peripheral neuropathy associated with fluoroquinolone treatment, 9% were for patients with GBS.[62]

Other associations

Various events, such as surgery, trauma, and pregnancy, have been reported as possible triggers of GBS, but these associations remain mostly anecdotal.

Case reports cite associations between bariatric and other gastric surgeries, renal transplantation, and epidural anesthesia.[63]

Anecdotal associations include systemic lupus erythematosus, sarcoidosis, lymphoma, and snakebite.

Tumor necrosis factor–alpha polymorphisms with increased expression are associated with many autoimmune and inflammatory diseases, and may increase susceptibility to axonal GBS subtypes. However, the role of these polymorphisms in GBS remains unclear and warrants further investigation.[64]

Epidemiology

Occurrence in the United States

The annual US incidence of GBS is 1.2-3 per 100,000 inhabitants, making GBS the most common cause of acute flaccid paralysis in the United States.[8, 1, 30, 65] In comparing age groups, the annual mean rate of hospitalizations in the United States related to GBS increases with age, being 1.5 cases per 100,000 population in persons aged less than 15 years and peaking at 8.6 cases per 100,000 population in persons aged 70-79 years.[66]

US military personnel are at slightly increased risk of GBS compared with the general population. An antecedent episode of infectious gastroenteritis was a significant risk factor for the development of GBS among military personnel.[24]

International occurrence

GBS has been reported throughout the world.[67, 68] Most studies show annual incidence figures similar to those in the United States, without geographical clustering. AMAN and AMSAN occur mainly in northern China, Japan, and Mexico, making up only 5-10% percent of GBS cases in the United States.[69] AIDP accounts for up to 90% of cases in Europe, North America, and the developed world.

Epidemiologic studies from Japan indicate that in this region, in comparison with North America and Europe, a greater percentage of GBS cases are associated with antecedent *C jejuni* infections and a lesser number are related to antecedent CMV infections. Similarly, it has been reported that 69% of GBS cases in Dhaka, Bangladesh, have clinical evidence of antecedent *C jejuni* infection.[31]

Race-related demographics

GBS has been reported throughout the international community; no racial preponderance exists. In North America, Western Europe, and Australia, most patients with GBS meet electrophysiologic criteria for demyelinating polyneuropathy. In northern China, up to 65% of patients with GBS have axonal pathology.[15]

Sex-related demographics

GBS has a male-to-female ratio of 1.5:1; male preponderance is especially seen in older patients. However, a Swedish epidemiologic study reported that GBS rates decrease during pregnancy and increase in the months immediately following delivery.[70]

Age-related differences in incidence

GBS has been reported in all age groups, with the syndrome occurring at any time between infancy and old age. In the United States, the syndrome's age distribution seems to be bimodal, with a first peak in young adulthood (ages 15-35 y) and a second, higher one in middle-aged and elderly persons (ages 50-75 y). Infants appear to have the lowest risk of developing GBS.[71]

Prognosis

Short of death, the worst-case scenario in GBS is tetraplegia within 24 hours, with incomplete recovery after 18 months or longer. The best-case scenario is mild difficulty walking, with recovery within weeks. The usual scenario, however, is peak weakness in 10-14 days, with recovery in weeks to months. Average time on a ventilator (without treatment) is 50 days. There are likely many mild cases of GBS that are never definitively diagnosed, and patients make full recovery without

treatment. The spectrum of milder disease has not been well studied nor clarified.

Approximately 80% patients with GBS walk independently at 6 months, and about 60% of patients attain full recovery of motor strength by 1 year. Recovery in approximately 5-10% of patients with GBS is prolonged, with several months of ventilator dependency and a very delayed, incomplete recovery.

Mortality

A 2008 epidemiologic study reported a 2-12% mortality rate despite ICU management,[65] although the rate may be less than 5% in tertiary care centers with a team of medical professionals who are familiar with GBS management.

Causes of GBS-related death include acute respiratory distress syndrome (ARDS), sepsis, pneumonia, venous thromboembolic disease, and cardiac arrest. Most cases of mortality are due to severe autonomic instability or from the complications of prolonged intubation and paralysis.[72, 73, 74, 75] The leading cause of death in elderly patients with GBS is arrhythmia.

GBS-associated mortality rates increase markedly with age. In the United States, the case-fatality ratio ranges from 0.7% in persons younger than 15 years to 8.6% in individuals older than 65 years. Survey data has shown that in patients aged 60 years or older, the risk of death is 6-fold that of persons aged 40-59 years and is 157-fold that of patients younger than 15 years. Although the death rate increases with age in males and females, after age 40 years males have a death rate that is 1.3 times greater than that of females.

GBS-related deaths usually occur in ventilator-dependent patients, resulting from such complications as pneumonia, sepsis, acute respiratory distress syndrome, and, less frequently, autonomic dysfunction.[76] Underlying pulmonary disease and the need for mechanical ventilation increase the risk of death, especially in elderly patients.

Morbidity

A significant percentage of survivors of GBS have persistent motor sequelae. Estimates indicate that 15-20% of patients have moderate residual deficits from GBS and that 1-10% are left severely disabled. Although the exact prevalence is uncertain, up to 25,000-50,000 persons in the United States may have long-term functional deficits from GBS.

The speed of recovery varies. Recovery often takes place within a few weeks or months; however, if axonal degeneration has occurred, recovery can be expected to progress slowly over many months, because regeneration may require 6-18 months. Length of hospital stay increases with advancing age, because of disease severity and associated medical complications.

Patients may experience persistent weakness, areflexia, imbalance, or sensory loss. Approximately 7-15% of patients have permanent neurologic sequelae (although figures of as high as 40% have been estimated), including bilateral footdrop, intrinsic hand muscle wasting, sensory ataxia, and dysesthesia. Patients may also exhibit long-term differences in pain intensity, fatigability, and functional impairment compared with healthy controls.[77, 78] In extremely rare cases, patients may experience recurrent GBS.[79, 80]

Numerous papers have addressed the issue of persistent fatigue after recovery from GBS.[81, 82, 83] Studies have suggested that a large percentage of patients continue to have fatigue-related problems, subsequently limiting their function at home and at work, as well as during leisure activities. Treatment suggestions range from gentle exercise to improvement in sleep patterns to relief of pain or depression, if present.

GBS can produce long-lasting changes in the psychosocial status of patients and their families.[84, 85, 86] Changes in work and leisure activities can be observed in just over one third of these patients, and psychosocial functional health status can be impaired even years after the GBS event.

Interestingly, psychosocial performance does not seem to correlate with the severity of residual problems with physical function. Poor conditioning and easy fatigability may be contributory factors.

Rudolph et al determined that patients who have had GBS seem overall to have a reduced quality of life and physical functioning. Their findings were based on a study of 42 GBS patients who were examined after a median of 6 years post–disease onset using a variety of measures, including the visual analogue scale (VAS) for pain, the disability rating index (DRI), and the Medical Outcome Study 36-item short-form health status scale (SF-36).[78]

Prognostic factors

The following factors have been associated with adverse effect on outcomes in GBS[6, 87, 88]:

- Preceding gastrointestinal infection or diarrheal illness
- Older age (57 years or older)
- Poor upper extremity muscle strength
- Acute hospital stay of longer than 11 days
- ICU requirement
- Need for mechanical ventilation
- Medical Research Council (MRC) score below 40
- Discharge to rehabilitation

A rapidly progressing onset of weakness also has been associated with less favorable outcomes in many studies, although in other reports, delayed time to peak disability has been shown to be an independent predictor of poor outcome at 1 year.

Mean compound muscle action potential (CMAP) amplitudes of less than 20% of the lower limit of normal or the presence of inexcitable nerves on initial electrophysiologic studies are other predictors of poorer functional outcomes. Later tests (>1 mo after onset) showing persistence of a low mean CMAP have an even higher sensitivity and specificity than do initial tests showing low amplitude.

A prospective, multicenter study by Petzold et al suggested that CSF levels of high–molecular weight neurofilament (NfH) protein, an axonal protein, are prognostic indicators in GBS.[89] The investigators found that among patients with GBS who suffered a poor outcome (defined as an inability to walk independently), the median NfH level was 1.78 ng/mL; in patients with GBS who had a good outcome, the median level was 0.03 ng/mL.

Increased CSF levels of neuron-specific enolase and S-100b protein are also associated with longer duration of illness.[8] Serologically, a longer-lasting increase in immunoglobulin M (IgM) anti-GM1 predicts slow recovery.[8]

The presence of underlying pulmonary disease or manifestation of dysautonomia has no prognostic significance in GBS.

Relapse

In a small percentage (~10%) of patients, an acute relapse occurs after initial improvement or stabilization after treatment. Some patients also demonstrate treatment fluctuations during their clinical course. Recurrence of Guillain-Barré syndrome is rare but has been reported in 2-5% of patients.[79, 80]

There is no convincing evidence that IVIG treatment or plasma exchange has a significant effect on the rate of treatment failure or of acute relapse.[90] The risk of relapse does, however, appear to be higher in patients in whom there has been a later onset of treatment, a more protracted disease course, and more associated medical conditions. Additional plasma exchange or IVIG treatments often result in further improvement.[91]

Patient Education

Patients with GBS and their families should be educated on the illness, the disease process, and the anticipated course. GBS is a life event with a potentially long-lasting influence on patients' physical and psychosocial well-being.[84, 85, 86] Family education and training also is recommended to prevent complications during the early stages of the disease and to assist in the recovery of function during the rehabilitation stages.

For patient education information, see the Brain and Nervous System Center, as well as Guillain-Barré Syndrome.

Clinical Presentation

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