



## Case Report

# Guillain-Barré Syndrome

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**Citation:** Palma DM, Cracchiolo AN, Zummo L, Lopez G, Lo Coco D, Turrisi R, Mazzola A, Palmeri M, Genco F, Ferruzza A, Piccoli T. (2022) Guillain-Barré Syndrome. Ann Case Report 7: 756. DOI: 10.29011/2574-7754.100756

**Received Date:** 17 January 2022; **Accepted Date:** 21 January, 2022; **Published Date:** 25 January 2022

### Abstract

**Background:** Guillain-Barré syndrome is a rare disorder in which our body's immune system attacks nerves determining weakness and tingling of extremities as first symptoms. It can also be associated to respiratory failure and require mechanical ventilation during hospitalization (up to 30% of patients). Nowadays patient's hyper-reactive immune responses benefits from immunotherapies such as intravenous immunoglobulin (IVIg), therapeutic plasma exchange (TPE) and new biological drugs.

**Case Report:** We report our experience with the case of a 64-year-old woman who presented a symmetric progressive flaccid paralysis after a week of mild cold symptoms. The respiratory and neurological symptoms worsened despite immunoglobulin infusions and intensive supportive care. She gradually improved with TPE, but we didn't respect schedules of the American Society for Apheresis (ASFA) and we decided to extend the number of TPE treatments to sixteen.

**Conclusions:** Although the first case of Guillain-Barré syndrome was described a century ago, there are still many dark sides about its etiology, pathogenesis, clinical variants and therapeutic strategies. Further studies are necessary to find answer to many still unanswered questions. The management of these patients must include a high index of clinical suspicion, a prompt diagnosis and adequate therapy without mistakes.

**Keywords:** Guillain-Barré syndrome; Acute inflammatory demyelinating polyneuropathy; Intravenous immunoglobulin; Plasma exchange

### Introduction

Guillain-Barré syndrome (GBS) is an acute, usually symmetrical, and typically ascending, paralyzing disorder caused by inflammation of the peripheral nerves. GBS has a mean age of onset of 40 years that affects slightly more males than females of all ages. GBS has an annual incidence of 0.81-1.89 cases (median, 1.11) per 100,000 persons worldwide [1]. GBS is usually preceded

by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots. Two-thirds of cases of GBS are associated with an antecedent infection, two to four weeks prior to the onset in most cases [2]. Almost two-thirds of GBS cases have a prodromal upper respiratory tract or gastrointestinal tract infection [3] without any specific organism identified. Molecular mimicry between microbial and nerve antigens is a major mechanism behind the development of the disorder, as suggested by the association with *Campylobacter jejuni* infection, and the increase of GBS incidence in regions with Zika virus outbreaks. However, how the immune

response is shifted towards unwanted auto-reactivity is still not well understood. Spontaneous recovery may occur; however, neurologic complications persist in up to 20% of patients, with half severely disabled at 1 year [4]. Given that up to 30% of GBS cases progress to respiratory failure, good supportive care is the most important element of intensive management. Failure to refer severely affected patients to a specialized neurological ICU may lead to higher mortality rates, implicating the importance of earlier referral of severe cases and providing neurocritical care. A multidisciplinary team is encouraged to provide supportive care for severe GBS cases in the ICU to avoid multiple comorbidities. The in-hospital mortality rate of GBS is approximately 2.6-2.8%, and risk factors include severity of weakness at entry, time to peak disability, mechanical ventilation (MV), old age, and pulmonary and cardiac complications [5].

## Case presentation

We report the case of a 66-year-old woman, who presented with a 72-hours history of increasing difficulty walking and acute fatigue; she had mild fever and cough 10 days earlier, with spontaneous resolution of fever after a few days. She also manifested a transient pruriginous dorsal rash but had no gastrointestinal symptoms nor relevant medical history, besides mild hypertension treated with beta-blockers. On examination, the patient was alert and conscious. Her vital signs revealed body temperature 36.5°C, blood pressure 155/85 mm Hg, respiratory rate 16 bpm, pulse rate 75 beats/min, and oxygen saturation 99%. The systemic examination was normal. First she was admitted to neurological departmental. On initial evaluation, she was paraparetic with a rapidly progressive symmetric weakness in the lower limbs, leading to falls and paraplegia. She denied any facial numbness, swallowing inability, and blurred vision but she subsequently developed distal weakness in the upper limbs and diffuse areflexia, without clear sensory deficits. She underwent lumbar puncture. The cerebrospinal fluid (CSF) puncture revealed normal glucose and cell count and 139 mg/dL protein. CSF viral serology and gram stain and culture were negative. Albumin-cytologic dissociation in the CSF is a clinical hallmark of GBS, which appears in up to 90% of all patients during the third week of the disease course [6]. Routine laboratory testing is unrevealing in GBS such as a mild and non-specific elevation of creatinekinase / or transaminases.

Our clinical suspect of GBS was endorsed by the demonstration of a typical albumin-cytological dissociation; subsequently we decided to confirm the diagnosis with electrophysiologic studies which were essential to exclude GBS's mimics. The differential of pure motor syndrome includes other diseases associated with quadriplegia/paralysis such as myasthenic crisis, acute presentation of the idiopathic inflammatory myopathies and the unusual motor neuron disease patient presenting with acute re-

spiratory failure. Associated clinical features are often helpful in distinguishing these from GBS. Although on the diagnosis of GBS prompted initiation of intra-venous immunoglobulin (IVIg, 0,4 g/kg for 5 days), her condition gradually deteriorated over the next few days, and she became quadriplegic despite the completion of immunoglobulin therapy. By this time, she had complete right-sided ptosis with a normal left eye. On hospital day 6, the illness evolved with autonomic features as the patient developed tachycardia and blood pressure instability. In addition, the patient developed bulbar involvement in a way she was unable to swallow, accompanied by severely slurred speech. Clearly, the woman did not benefit from early treatment with IVIg. Respiratory muscle weakness in our patient contributed to the loss of airway protection and ineffective cough. Progressively gas exchanges worsened with a sudden desaturation, requiring intubation and intensive care unit admission, where treatment started with therapeutic plasma exchange (TPE). GBS patients need to be admitted to the ICU when one or more of these criteria are met: (a) rapid progression of respiratory muscle weakness; (b) evolving respiratory distress; (c) severe dysautonomia or dysphagia; (d) Erasmus GBS respiratory insufficiency score (EGRIS) > 4 [7].

Recently, the Erasmus GBS outcome score was derived from data of 388 patients enrolled in two randomized controlled trials and one pilot study (17). This 1 to 7 score consists of three items: age (0=up to 40 years, 0.5=41–60 years or 1= for age > 60), preceding diarrhea (0 or 1), and modified GBS disability score at two weeks after entry (1 to 5). This score obtained at two weeks was validated in another GBS sample as a predictor of the probability of independent ambulation at six months. Predictions corresponding to these prognostic scores ranged from 1% to 83% for the inability to walk independently at six months with a very good discriminative ability (AUC 0.85) in both data sets. Of patients with an Erasmus GBS outcome score of 5 at two weeks, 27% are unable to walk independently at six months whereas a score of 5.5–7 markedly raises that proportion to 52%. Because a prolonged MV (>3 weeks) was predicted, we considered tracheostomy immediately and we performed it on the third day. Early tracheostomy potentially benefits GBS patients in several aspects: more comfort, earlier enteral nutrition, adequate oral hygiene, easier oral communication, and out-of-bed mobilization. Complications in the process of MV and ICU stay are essential parameters to predict the prognosis of GBS patients. Complications such as decubitus ulcers which may prolong ICU stay and worsen the prognosis, were prevented via frequent repositioning. She gradually improved with TPE. The first to improve was ptosis and autonomic feature, she returned to blood pressure stability on the sixth day (three TPE performed). Five days later her cough was turning to be effective and respiratory muscles were less weak; then we started weaning from mechanical ventilation, but she was still quadriplegic (six TPE performed). Her motility gradually

improved over the next week and lower limbs muscle strength slowly improved, upper limbs' weakness reduced few days later (eleven TPE performed). Respiratory weaning was very slow and difficult. She reached spontaneous breathing with tracheostomy 24 hours a day on the 25th day. Over the next four days we started oral feeding.

TPE is performed only at specialized centers and involves removing 3–6 liters of plasma over several hours and replacing it with preferably albumin or in some cases fresh frozen plasma. Limitations include IV access as it requires large double-lumen catheter through subclavian, internal jugular or femoral venous access. No complications occurred (pneumothorax, hypotension, sepsis, pulmonary embolism, hemorrhage from vein puncture, low platelets, prolonged clotting parameters, hypocalcemia, citrate toxicity and anemia). For our patient the total exchange volume was approximately 15,000 cc. During TPE, we monitored blood pressure, pulse, and amount of fluids intake and output. We obtained daily platelets, calcium, PT, PTT and INR and hold apheresis one to two days if coagulation parameters became abnormal. Prolonged ICU stay (>3 weeks) may breed complex complications and increase mortality. Nosocomial complications including hospital-acquired pneumonia (HAP), ventilator acquired pneumonia (VAP), hyponatremia were considerable factors in causing death, prolonged MV (>21 days) and long hospitalization (>36 days). Blessedly our patient didn't have any nosocomial complications and she was transferred to rehabilitation department where stayed over several months.

## Discussion

The most common initial symptom of GBS is acroparesthesia with little objective sensory loss [2]. Most patients with GBS are clinically characterized by acute flaccid paralysis and/or sensory/autonomous nerve dysfunction [9]. Severe radicular back pain or neuropathic pain affects most cases. Within a few days, weakness ensues commonly in a symmetric “ascending pattern”. Most patients present initially with leg weakness and arm weakness (32%) or selective proximal and distal leg weakness (56%) often spreading to the arm while some have onset of weakness in the arms (12%). Besides prominent weakness, patients are hypo- or areflexic within the first few days but this may be delayed by up to a week. Weakness can be somewhat asymmetric, and sensory loss can also be variable. Facial nerve involvement occurs in up to 70% of cases, dysphagia in 40%, and rarely (5%) patients may develop ophthalmoplegia, ptosis, or both suggesting botulism or myasthenia gravis [3]. Nadir of weakness is reached within two weeks in half of cases and 90% by four weeks [3]. Some patients progress rapidly to become ventilator dependent within hours or days, while others will have very mild progression for several weeks and never lose ambulation. Weakness ranges from mild to severe flaccid quadriplegia and in up to 30% respiratory failure

within a few days of onset.

### Poor Prognostic Factors in GBS

- Older age (>50–60)
- Rapid onset prior to presentation (<7 days)
- Ventilator dependency
- Preceding infection with CMV
- Preceding diarrheal illness / C. Jejuni

The revised diagnostic criteria have been published (Table 1) several years ago and are well established. These include clinical, cerebrospinal fluid and electrophysiologic criteria (see Electrophysiologic Features section below).

**Table 1:** Diagnostic Criteria of Guillain-Barré Syndrome (adapted and modified from reference 4).

Required	Supportive	Exclusionary
Progressive symmetric weakness of > 1 limb	Sensory symptoms or signs	Other causes excluded (toxins, botulism, porphyria, diphtheria)
Hyporeflexia or areflexia	Cranial nerve involvement especially bilateral VII	
Progression <4 weeks	Autonomic dysfunction	
Symmetric weakness	CSF cell count < 10/mm <sup>3</sup>	
	CSF protein elevation	
	Electrophysiologic features of demyelination	
	Recovery	

TPE is the extracorporeal technique performed in an apheresis device where patient's plasma is separated from whole blood and removed, while the cellular blood components are returned to the patient together with a replacement fluid. By the extracorporeal removal of pathological substances and the replacement of deficient plasma components, it constitutes an important tool for the management of several disorders and it is a well-known and established treatment for numerous diseases. Additionally, overall available data confirm the safety and efficacy of TPE. Currently, to assist the requesting and/or apheresis physicians in evaluating the utility of apheresis as a treatment modality, the American Society for Apheresis (ASFA) regularly publishes updated evidence-based treatment guidelines, with the most recent edition being published

in 2019. The role of TPE in the treatment of diseases and indications in the Guidelines are categorized in accordance with the ASFA categories (Table 2).

**Table 2:** ASFA category indications

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment
III	Optimal role of apheresis therapy is not established. Decision making should be individualized
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken

Additionally, a recommendation grade based on the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) system (Table 3) is also provided along with the ASFA category for each TPE indication.

**Table 3:** Grading Recommendations

Reccomandation grade	Description	Methodological quality of supporting evidence	Implications
1 A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1 B	Strong recommendation, moderate-quality evidence	RCTs with important limitations or exceptional strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1 C	Strong recommendation, low-quality evidence	Observational studies or case series	Strong recommendation, but may change when higher quality evidence becomes available
2 A	Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances
2 B	Weak recommendation, moderate-quality evidence	RCTs with important limitations or exceptional strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances
2 C	Weak recommendation, low-quality evidence	Observational studies or case series	Very weak recommendation; other alternatives may be equally reasonable

TPE (therapeutic plasma exchange) for GBS is primary treatment, category I, GRADE I A. TPE is an effective treatment of GBS and should be initiated within 7 days of disease onset [10]. It was further concluded that TPE has beneficial effect in severely and mildly affected individuals; with significantly increased proportion of patients able to walk after 4 weeks. The typical TPE strategy is to exchange 1-1.5 plasma volumes 5-6 times over 10-14 days, some patients may need additional treatments. The management of the severe GBS patient who don't improve 10-14 days after PE or IVIg is problematic. Our patient didn't improve in standard time, so we decided to extend the number of TPE treatments to 16. We didn't use corticosteroids because they are not beneficial in the disorder. Dramatic improvement within days

of beginning treatment is not the rule and if this occurs, it may have happened regardless of treatment.

Since autonomic dysfunction may be present, affected patients may be more susceptible to intravascular volume shifts during apheresis treatments and should be monitored carefully. Relapses may occur in up to 5-10% of patients 2-3 weeks following either treatment with TPE or IVIG. TPE directly removes humoral factors such as autoantibodies, immune complexes, complement, cytokines and other nonspecific inflammatory mediators and was the first treatment shown in randomized controlled trials to be effective in GBS [11,12]. In both studies, TPE performed within two weeks from symptom onset consistently demonstrated a



statistically significant reduction in the time to weaning from the ventilator by 13 to 14 days and time to walk unaided by 32 to 41 days. IVIg is a plasma product that contains a broad spectrum of different antibodies. IVIg has pleiotropic immunomodulatory effects, which include inhibiting Fc-mediated activation of macrophages, preventing the binding of antibodies to neural targets, and preventing complement activation which would otherwise trigger further nerve damage [13]. Meanwhile, high-dose IVIg [ranging from 1000 to 3000 mg/kg body weight (BW)] results in immunosuppressive and anti-inflammatory phenotypes, which is universally employed to treat autoimmune diseases like GBS. Unless contraindicated, patients unable to walk without assistance are routinely treated with a standard IVIg regimen (0.4 g/kg BW per day, for five consecutive days, or 1 g/kg BW per day, for two consecutive days). Not only is IVIg easier to administer but it also efficiently hastens recovery [2]. The benefit of a second course of IVIg has yet to be corroborated [13].

The postulated mechanisms of action of IVIg in neuromuscular disorders include interference with costimulatory molecules involved in antigen presentation and modulation of autoantibodies, cytokines and adhesion molecules production as well as macrophage Fc receptor. It also disrupts complement activation and membrane attack complex formation [14]. We closely monitor patients with the first infusion, starting at a very slow rate of 25 to 50 cc/hr for 30 minutes and increasing it progressively by 50 cc/hr every 15 to 20 minutes up to 150 to 200 cc/per hour. Mild reactions (headache, nausea, chills, myalgia, chest discomfort, back pain) occur in 10% and are improved with slowing the infusion rate and are preventable with pre-medication with acetaminophen and if need be IV methylprednisolone. Moderate rare reactions include chemical meningitis neutropenia and delayed red, macular skin reaction of the palms, soles and trunk with desquamation. Acute renal failure is uncommon and related to patient dehydration and the prior use of sucrose or maltose diluents [15]. Other therapeutic modalities studied include cerebrospinal fluid filtration, double filtration plasmapheresis, and drug targeting of complement activation. Since IVIG is readily available and a more convenient form of immunomodulatory treatment, it is frequently used as initial therapy; the typical dose is 0.4 g/kg for 5 consecutive days. The favored pathogenesis of GBS is autoimmune antibody-mediated damage to peripheral nerve myelin. The results of several CTs comparing TPE to supportive care alone indicate that TPE can accelerate motor recovery, decrease time on the ventilator, and decrease time to attainment of other clinical milestones. TPE has beneficial effect in severely and mildly affected individuals; with significantly increased proportion of patients able to walk after 4 weeks. A priori combining of TPE and IVIG in sequential order is not advantageous and is not recommended. There are insufficient data to conclude on the efficacy of TPE after IVIG failure. Treatment decisions must be

made on a case-by-case basis [16]. Consistently, administration of IVIg combined with TPE could reduce GBS mortality, shorten hospitalization, and promote earlier weaning from MV in pediatric cases [17]. Nonetheless, the combination of IVIg and TPE confers an insignificant advantage in adults [16].

## Conclusions

GBS patients are mostly admitted to the neurological intensive care unit or an intermediary care telemetry unit to allow for close and frequent monitoring of respiratory, bulbar and autonomic function. A rapid decline of the expiratory forced vital capacities to less than 15cc/kg of ideal body weight (adjusted for age) or of the negative inspiratory force to below 60 cm H<sub>2</sub>O each indicate the need for urgent intubation and mechanical ventilation before hypoxemia supervenes [2]. This is associated with marked weakness of neck muscles and inability to count out loud till 20. Patients with severe dysphagia may require nasogastric or feeding tubes. Intubation should also be considered for patients who cannot handle their secretions or who have an ineffective cough. After two weeks of intubation, tracheostomy should be considered in those without improved pulmonary mechanics. In those intubated but with improved pulmonary parameters at two weeks, an additional week of intubation may be judicious to allow for successful weaning from the ventilator [5].

It is important when managing autonomic instability to be conservative and avoid aggressively treating blood pressure fluctuations since patients are sensitive to medications and use of long-acting antihypertensives is contraindicated. For those with marked radicular back pain or neuropathic pain refractory to acetaminophen or NSAIDS, treatment with pain modulating drugs such as antidepressants, gabapentin, pregabalin, carbamazepine, tramadol is indicated [5]. Bed-ridden patients should have deep venous thrombosis prophylaxis with compressive hose and/or anticoagulants in the form of subcutaneous heparin. Bedside passive range of motion can help prevent muscle contractures in paralyzed patients but it is also important to be mindful that these patients are most often alert and cognitively intact. A multispecialty team is needed for the decision-making of MV in patients with respiratory failure. In practice, MV needs to be considered when one or two of following criteria are met: (a) vital capacity <15 ml/kg BW, (b) hypoxemia (PaO<sub>2</sub> < 7.5 kPa), (c) hypercarbia (PaCO<sub>2</sub> > 6.4 kPa), and (d) intolerable respiratory distress [18]. Immunotherapies, mechanical ventilation, supportive care, and complication management during the intensive care unit (ICU) stay are equally emphasized. Immunotherapies were originally postulated from the immune-related pathogenesis in GBS: IVIg dimerizes pathogenic autoimmune antibodies [13]; TPE scavenges pathogenic inflammatory mediators [10]. IVIg and TPE have been the mainstay for the treatment of GBS [10]. Currently, IVIg and TPE are used to treat up to 92% of GBS patients in the

United States [13]. However, little evidence supports their use in patients with mild GBS, treatment failure, and treatment-related fluctuation [13]. The efficacy of intravenous immunoglobulin (IVIg) and plasma exchange (TPE) in the treatment of GBS has been validated by extensive investigations [15]. Notwithstanding, these immunotherapies for GBS are still incurring controversies due to its high cost, potential adverse events, and incompletely known mechanisms, among others [15]. Currently, TPE is used as an effective therapy to promote recovery of GBS patients [19]. TPE was administered in around 4% GBS patients worldwide, except in several countries (i.e., the United States. 15%, Malaysia 33%, and Italy 30%) [13].

In practice, TPE is strongly recommended for GBS patients in the acute phase with impaired independent walking capacity or requiring MV assistance, whereas contraindicated in patients who cannot tolerate central line placement or with unstable haemodynamics or allergic to frozen plasma/albumin. TPE mainly functions via scavenging pathogens and autoimmune antibodies in patients' peripheral blood [10]. Patients with GBS routinely benefit from a standard TPE schedule (5 sessions with 40–50 ml plasma/kg per session within 7–14 days) [10]. Usually, TPE is performed every other day to allow the redistribution of pathogenic agents in both extravascular and intravascular compartments [20]. Efficacy of TPE is closely dependent on the speed of production and clearance of pathogenic agents; as such, immunosuppressive treatments are regularly considered as adjuvants for TPE [20]. Moderate-quality evidence shows higher efficacy of TPE than supportive care alone in adults with GBS, without an significant increase in serious adverse events [10]. Optimization of the procedure of TPE is intriguing. For instance, the appropriate frequency of TPE is set as four sessions for moderate to severe GBS cases, while two sessions for those with mild GBS [11]. TPE can also be conducted with albumin and gelatin, instead of fresh frozen plasma [11]. However, when albumin or gelatin is used to replace patients' serum, dilution of the anti-infectious immunoglobulins needs caution [10]. Between individual sessions, TPE is suggested to be performed with continuous flow machines, instead of the intermittent version. However, the benefits of continuous flow machines in TPE remain controversial [11].

Treatment with plasmapheresis or IVIG is indicated for patients with weakness impairing function or any respiratory involvement. Before initiating any of these therapies, patients and their families should be educated about the fact that it takes on average two to three months for patients to walk without aids no matter what therapy is used. Noticeably, although hypotension, coagulation disorders, or allergic reactions may occasionally occur, most adverse effects are unpredictable and TPE is generally

safe for patients in the ICU setting. As the incidence of GBS is low and the disease is clinically heterogeneous, most of the documented investigations have a relatively small sample size. In contrast with immunotherapies, care and treatment of GBS in the ICU setting are largely empirical. As a consequence, observational data are occasionally used to guide clinical practice. Managements of severe GBS in the ICU setting are usually multidisciplinary and even more complex in continuously evolving conditions. The intensive care and treatment is better provided by neurointensivists so as to precisely monitor the progression of GBS. Currently, TPE and IVIg remain the mainstay of GBS treatment. Despite research displaying the superiority of IVIg to TPE in MV-dependent GBS patients [21], the evidence quality is very low. No evidence supports the combinational use of IVIg and TPE for severe GBS patients as well. As such, neurointensivists still need to weigh the cost-effectiveness ratio and the reward-to-risk ratio of IVIg or TPE or a combination of the two, especially in the ICU setting. Future large sample size RCTs are needed to address treatment dilemmas like mild cases, variant forms of GBS, when the onset of weakness was more than 2 weeks ago, or when patients do not improve or even progress after initial treatment. Efficacy of small-volume TPE, double filtration plasmapheresis, a second dose of IVIg, and very early use of steroids merits further investigation. A multidisciplinary team is needed to assist intensive care for severe GBS cases to avert life-threatening complications. Moreover, rehabilitation and psychological support are also emphasized in both ICU-recruited and discharged patients.

### **Conflict of interest**

The authors have no relevant financial or non-financial interests to disclose.

### **Compliance with Ethical Standards**

No Human Participants and/or Animals have been involved. No informed consent was necessary

### **Statements and Declarations**

The authors did not receive support from any organization for the submitted work

### **Author contributions**

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Daniela Maria Palma], [Andrea Neville Cracchiolo], [Leila Zummo], [Gianluca Lopez], [Daniele Lo Coco], [Alfredo Mazzola], [Rosa Turrisi] [Marco Palmeri] [Fabio Genco] [Angela Ferruzza] [Tommaso Piccoli]. All authors read and approved the final manuscript

## Key Points

- Besides the classic presentation of ascending paralysis in demyelinating Guillain Barré Syndrome, clinical variants are based on the types of nerve fibers involved (motor, sensory, sensory and motor, cranial or autonomic), predominant mode of fiber injury (demyelinating versus axonal), and the presence of alteration in consciousness.
- Treatment should not be delayed when electrophysiology is not confirmatory of Guillain Barré Syndrome.
- All patients should be treated with either Plasma Exchange or IVIG, even if the disease is mild.
- Although therapy should be initiated within 2 weeks of onset, it is still appropriate to treat patients after 2 weeks, particularly if they are still progressing.
- Both Plasma Exchange and IVIg are equally effective in shortening the time to independent ambulation but the combination is no more effective.
- While Plasma Exchange is available at specialized centers, IVIG is more readily available in most hospitals.
- In hemodynamically unstable patients, Plasma Exchange is contraindicated. Caution with administering IVIg is advised in patients with hypercoagulability or renal insufficiency.
- There is no justification to use recurrent courses of IVIG or Plasma Exchange unless the patient has recurrent disease.
- Prognosis is overall good as eighty percent of GBS cases have slow but “complete” recovery within 6 months.
- However, sixty-five percent have mild to moderate residual symptoms or signs and persistent major residual neurologic deficits affect 10–15% of patients despite appropriate therapy.
- Newer prognostic tools are helpful in identifying in the first 2 weeks those at higher risk of poor recovery at 6 months

## References

1. Benedetti L, Briani C, Beronio A, Massa F, Giorli E, et al. (2019) Increased incidence of axonal Guillain-Barré syndrome in La Spezia area of Italy: A 13-year follow-up study *J Peripher Nerv Syst*. 24: 80-86.
2. Hughes RA, Cornblath DR. (2005) Guillain-Barré syndrome. *Lancet*. 366: 1653-1666.
3. Wakerley BR, Yuki N. (2013) Infectious and noninfectious triggers in Guillain-Barré syndrome. *Expert Rev Clin Immunol*. 9: 627-639.
4. Barohn RJ, Saperstein DS. (1998) Guillain-Barré syndrome and chronic inflammatorydemyelinating polyneuropathy. *Semin Neurol*. 18: 49-61.
5. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. (2014) Diagnosis of Guillain Barré syndrome and validation of Brighton criteria *Brain*. 137: 33-43.
6. Dimachkie MM, Barohn RJ. (2013) Guillain-Barré syndrome and variants *Neurol Clin*. 31: 491-510.
7. Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, et al. (2019) Diagnosis and management of Guillain-Barré syndrome in ten steps *Nat Rev Neurol*. 15: 671-683.
8. Pei shang, Jiachun Feng, Wei Wu and Hong-Liang Zhang. (2021) Intensive Care and Treatment of Severe Guillain-Barré Syndrome *Front Pharmacol* 12: 608130
9. Sejvar JJ, Baughman AL, Wise M, Morgan OW. (2011) Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. *Neuroepidemiology*. 36: 123-33.
10. Chevret S, Hughes RA, Annane D. (2017) Plasma exchange for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2: CD001798.
11. French Cooperative Group on Plasma Exchange in Guillain-Barré syndrome. Appropriate number of plasma exchanges in Guillain-Barré syndrome. *Ann Neurol*. 41: 298-306.
12. Dalakas MC. (2004) Intravenous immunoglobulin in autoimmune neuromuscular diseases. *JAMA*. 291: 2367–2375.
13. Verboon C, van Doorn PA, Jacobs BC. (2017) Treatment dilemmas in Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry*. 88: 346-352.
14. Van der Meché FG, Schmitz PI the Dutch Guillain-Barré Study Group. (1991) A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barré syndrome. *N Engl J Med*. 326: 1123-1129.
15. Hughes RA, Wijdicks EF, Barohn R, Benson E, Cornblath DR, et al. (2003) Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 61: 736-740.
16. Plasma Exchange Sandoglobulin Guillain-Barré Syndrome Trial Group. Randomized trial of plasma exchange, intravenous immunoglobulin and combined treatments in Guillain-Barré syndrome. *Lancet*. 349: 225-230.
17. Kesici S, Tanyıldız M, Yetimakman F, Bayrakci B. (2019) A Novel Treatment Strategy for Severe Guillain-Barré Syndrome: Zipper Method *J Child Neurol*. 34: 277-283.
18. Burakgazi AZ, Höke A. (2010) Respiratory muscle weakness in peripheral neuropathies. *J Peripher Nerv Syst*. 15: 307-313.
19. El-Bayoumi MA, El-Refaey AM, Abdelkader AM, El-Assmy MM, Alwakeel AA, et al. (2011) Comparison of intravenous immunoglobulin and plasma exchange in treatment of mechanically ventilated children with Guillain Barré syndrome: a randomized study. *Crit Care*. 15: R164.
20. Fernández-Zarzoso M, Gómez-Seguí I, de la Rubia. (2019) Therapeutic plasma exchange: Review of current indications. *J. Transfus Apher Sci*. 58: 247-253.
21. Charra B, Hachimi A, Benslama A, Motaouakkil S. (2014) Intravenous immunoglobulin vs plasma exchange in treatment of mechanically ventilated adults with Guillain-Barré syndrome. *Pan Afr Med J*. 18: 35.