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High risk and low prevalence diseases: Guillain-Barré syndrome

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ABSTRACT

Introduction: Guillain-Barré syndrome (GBS) is a rare but serious condition that carries with it a high rate of morbidity and mortality.
Objective: This review highlights the pearls and pitfalls of GBS, including presentation, diagnosis, and management in the emergency department (ED) based on current evidence.
Discussion: GBS is a rare immune-mediated neurologic disorder with peripheral nerve injury. It most commonly presents weeks after a bacterial or viral infection, though there are a variety of associated inciting events. The diagnosis is challenging and often subtle, as only 25–30% of patients are diagnosed on their initial healthcare visit. Clinicians should consider GBS in patients with progressive ascending weakness involving the lower extremities associated with hyporeflexia, but the cranial nerves, respiratory system, and autonomic system may be involved. While the ED diagnosis should be based on clinical assessment, further evaluation includes laboratory testing, cerebrospinal fluid (CSF) analysis, and potentially neuroimaging. Not all patients demonstrate albuminocytological dissociation on CSF testing. Several criteria exist to assist with diagnosis, including the National Institute of Neurological Disorders and Stroke criteria and the Brighton criteria. Management focuses first on assessment of the patient's hemodynamic and respiratory status, which may require emergent intervention. Significant fluctuations in heart rate and blood pressure may occur, and respiratory muscle weakness may result in the need for airway protection. Neurology consultation is recommended, and definitive treatment includes PLEX or IVIG.
Conclusions: An understanding of GBS can assist emergency clinicians in diagnosing and managing this potentially deadly disease.

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1. Introduction

This article series addresses high-risk and low-prevalence diseases encountered in the emergency department (ED). Much of the primary literature evaluating these conditions is not emergency medicine focused. By their very nature, many of these disease states and clinical presentations have little useful evidence available to guide the emergency physician in diagnosis and management. The format of each article defines the disease or clinical presentation to be reviewed, provides an overview of the extent of what we currently understand, and discusses pearls and pitfalls using a question-and-answer format. This article will discuss Guillain-Barré syndrome (GBS). This condition's low prevalence but high morbidity and mortality, variable atypical patient presentations, and challenging diagnosis make it a high-risk and low-prevalence disease.

1.1. Definition and pathophysiology

GBS is an immune-mediated peripheral nerve disease classically characterized by a symmetrical ascending weakness that can progress to paralysis with associated hyporeflexia or areflexia [1]. The mechanism behind GBS is not fully understood; however, molecular mimicry is the most common hypothesized mechanism [1]. The theorized pathophysiology is that an inciting infection or process creates antigens that resemble normal host cells or proteins (Schwann cells, gangliosides, etc.), which confuses the host's natural immune system. The body's immune system then creates antibodies to destroy the antigen, leading to normal host cells' death [2]. The target for these antibodies differs depending on the GBS variant. In acute inflammatory demyelinating polyneuropathy (AIDP), antibodies are directed against a component of Schwann cells. In contrast, in acute motor axonal neuropathy (AMAN), antibodies are directed against the axolemma and nodes of Ranvier [3]. In GBS, a trigger results in a cascade of immune responses that damage vital parts of peripheral nerves, leading to signaling

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dysfunction, which causes a sequela of symptoms such as weakness, paralysis, and hyporeflexia [3].

1.2. Epidemiology

Worldwide there are approximately 100,000 new cases of GBS annually [4]. The disease has the highest incidence in Bangladesh, with an incidence of 2.5 adult cases per 100,000 person-years and 3.25 cases per 100,000 person-years in pediatric patients, followed by Latin America (2.12 cases per 100,000 person-years), North America and Europe (0.81–1.91 cases per 100,000 person-years), and east Asia (0.44–0.67 per 100,000 person-years) [4-10]. The incidence appears to increase by 20% with every 10-year age increase; unlike many autoimmune diseases, males are more commonly affected [5]. There is a seasonal variation in the disease, with peaks in winter in Western countries, while China, India, Bangladesh, and Latin America appear to have a summer peak [11-13]. One study of over 900 patients with GBS found a median age of 51 years, with most patients between 50 and 69 years [5]. A national registry of pediatric GBS cases from Denmark found a median age of 8 and a peak incidence at 2 years [14]. The disease can be severe. Despite current immunotherapies, the mortality rate is close to 5%, and up to 20% cannot walk without assistance one year from the onset of the disease [15].

2. Discussion

2.1. Presentation

GBS can present along several phases, including an acute phase (within 2 weeks of symptom onset), a progressive phase (2–4 weeks after onset), and a plateau phase (> 4 weeks after onset) [16-18]. The pathognomonic clinical presentation of GBS is symmetrical ascending flaccid paralysis that starts in the lower extremities with decreased or absent reflexes [16-18]. Weakness is often preceded or accompanied by bilateral sensory changes such as paresthesias or pain [19]. Depending on the variant, patients may retain reflexes early in the disease course or even demonstrate hyperreflexia [20]. Patients may also present in various stages of respiratory distress due to diaphragmatic weakness or hemodynamic instability from dysautonomia [17,18].

The preceding event that results in GBS is most commonly an infection, such as an upper respiratory infection or gastroenteritis. Associated microbes include *Campylobacter jejuni*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, cytomegalovirus (CMV), Epstein-Barr virus (EBV), hepatitis E virus, influenza, and Zika virus [21]. Other antecedent events include vaccinations, checkpoint inhibitors, and surgery [5,22-27]. This antecedent event typically occurs up to 4–6 weeks before signs and symptoms of GBS develop [28]. Several studies have shown that symptom onset can vary, with subtle symptoms beginning 1 to 2 weeks after immune system excitation, with a slow progression to peak neurologic deficits occurring at 2 to 4 weeks, and sometimes in rare cases, up to 6 weeks [29-32]. The plateau phase can last for months and heavily depends upon the type of variant and time to treatment [31,33,34]. Recovery begins within a few months of symptom onset, with the most improvement in the first year; however, some patients may take multiple years to recover [31,33].

2.2. ED evaluation

GBS is a clinical diagnosis in the ED setting. However, the evaluation for GBS highly depends upon the clinician's suspicion and differential diagnosis. The ED evaluation focuses on excluding other organic causes of paralysis or weakness, such as acute ischemic stroke or acute spinal cord compression. Thus, a focused neurologic examination assessing the cranial nerves, motor and sensory system, reflexes, gait, and cerebellar function is necessary. Diagnosing GBS can be difficult, especially with atypical presentations. In one retrospective cohort of 69 patients ultimately diagnosed with GBS, the diagnosis was only considered in 30% of patients on the initial visit by the ED clinician, and the median number of ED visits before GBS was suspected was 2 (range 1 to 5) [35]. Another retrospective study of 20 patients diagnosed with GBS found that only 5 of 20 patients were diagnosed on their first ED visit [36]. Thirteen patients had at least 1 visit with a physician before their diagnosis, and 6 of the 20 had at least 2 visits [36].

There is currently no highly sensitive or specific laboratory assessment that can definitively diagnose GBS. However, laboratory assessments are recommended, including complete blood count, electrolytes, renal and liver function, and thyroid stimulating hormone to evaluate for other conditions [37-40]. In addition, lumbar puncture (LP) to obtain cerebrospinal fluid (CSF) can assist in excluding other causes of weakness and increase the clinical probability of GBS [33,40]. The classic finding on CSF analysis is albumino-cytological dissociation (elevated protein levels and normal cell counts) [33]. While imaging is not necessary to diagnose GBS, advanced imaging such as magnetic resonance imaging (MRI) may be necessary to evaluate for other causes of weakness and sensory changes [41].

2.3. ED management

The ED management of GBS focuses on stabilizing the patient's respiratory and hemodynamic status, particularly in the acute phase of the condition. Clinicians should first evaluate the patient's airway, respiratory, and hemodynamic status, as airway and respiratory compromise are among the main factors associated with mortality in GBS [42,43]. Up to 30% of patients with GBS require respiratory support, such as noninvasive positive pressure ventilation or endotracheal intubation with mechanical ventilation [44]. In addition, physicians should closely monitor the patient's hemodynamic status due to the risk of autonomic nervous system dysregulation, known as dysautonomia [45]. Severe dysautonomia may manifest as severe hypertension or hypotension and necessitate intensive care unit (ICU) admission for blood pressure management, discussed in detail later [45]. After stabilization, consultation with the neurology specialist and critical care specialist is recommended, as definitive care for GBS includes intravenous immunoglobulin (IVIG) or plasma exchange (PLEX) [46]. The prognosis can vary despite receiving definite treatment, depending on the patient's age, level of severity, and inciting event or infection [46]. Patients with GBS should be admitted for frequent neurological and cardiopulmonary monitoring secondary to their risk of decompensation with a center that has access to these therapies and neurology specialist consultation, which may necessitate transfer.

3. Pearls and pitfalls

3.1. What are the 'must-know' risk factors for GBS for the emergency clinician?

Various factors are associated with developing GBS, including bacterial infections, viral infections, vaccinations, and surgeries (Table 1). An antecedent event is reported in up to 76% of cases, most often some

Table 1
Events associated with GBS.

Association/Antecedent Event	Examples
Viral Infection	CMV, SARS-CoV-2, Zika, EBV, Dengue, Measles, Influenza, Enterovirus
Bacterial Infection	*Campylobacter jejuni, Mycoplasma pneumonia, Escherichia coli, Haemophilus influenzae*
Vaccinations	Influenza, Measles-Mumps-Rubella, COVID-19
Medications	Ipilimumab, nivolumab, pembrolizumab, atezolizumab, durvalumab
Medical Conditions	Recent surgery, pregnancy, myocardial infarction

form of infection [5]. A large observational study evaluated the presence of recently confirmed infection among GBS patients and found that 30% were infected by *C. jejuni*, 10% by *M. pneumonia*, 3% by hepatitis E, 4% by CMV, and 1% by EBV [47]. A case-control study of GBS during a Zika outbreak found that all 42 patients with GBS had evidence of prior infection with Zika, compared to 55% of a selected control group of patients [48]. From 2013 to 2016, the Zika virus impacted multiple countries in the Americas and the Pacific, subsequently accompanied by a rise in GBS cases [49]. GBS has also been reported after COVID-19 infection [50]. One retrospective study suggested recent surgery was the suspected trigger for GBS in 9.5% of patients, with an estimated attributable risk of GBS of 4.1 per 100,000 surgeries [51]. There are case reports of GBS occurring after myocardial infarction, during pregnancy, and as the presenting symptom of cancer [52-54]. The relationship between receiving a vaccine and the development of GBS has been intensely explored since an earlier version of the influenza vaccination seemed to be associated with a rise in cases of GBS [55]. Although beyond the scope of this article for emergency clinicians, there may be a rare but increased risk of GBS after the influenza, measles-mumps-rubella, and meningococcal vaccines [55]. There have also been case reports of GBS after immunization with the Pfizer, Oxford-AstraZeneca, and Johnson&Johnson COVID-19 vaccines [56]. Some medications have been associated with GBS, particularly immune checkpoint inhibitors such as ipilimumab, nivolumab, and pembrolizumab [57]. Importantly, although there are many case reports of GBS and observational studies suggesting an association with infection, medical illness, medication, surgery, vaccination, or other entity, these do not prove causation. Thus, while knowing these common risk factors can assist, not all patients with these risk factors will develop GBS.

3.2. What are high yield factors of the history and examination that suggest GBS?

GBS patients classically present with ascending bilateral symmetric weakness and hypo- or areflexia after some infectious process. However, the signs and symptoms are more complex with various presentations. Two findings have been required since 1978, the creation of the diagnostic criteria of GBS, to diagnose the disease: progressive motor weakness in greater than one limb and areflexia [29]. However, these criteria include supporting features as well (discussed in section 3.3). In one cohort study of 344 patients with GBS, the most common finding was limb weakness, with >99% of the patients having limb weakness and 98% having hypotonia [58]. The severity of the weakness varied, with lower limb weakness more severe than upper limb deficits [58]. However, GBS has multiple variants with various presentations (Table 2). The neuronal targets of autoantibodies distinguish the variants AIDP, AMAN, and acute motor sensory axonal neuropathy (AMSAN) and have different electromyographic characteristics less relevant to the emergency clinician [59]. Other variants such as the Miller Fisher Syndrome (MFS), Cervico-Brachial-Pharyngeal variant, sensory variant, and acute pandysautonomia variant differ in the localization of affected nerve types and thus have different clinical presentations [59]. AIDP is the most common form of GBS and presents with classic signs of ascending weakness and decreased reflexes [59]. AMAN and AMSAN can present similarly to the AIDP variant, although AMAN has a more rapid progression [60]. In one observational study of patients with GBS, patients with the AMAN variant had more significant extremity weakness than patients with the AIDP variant, and they also tended to have lower recovery rates at three months [61]. The MFS variant is characterized by ophthalmoplegia, ataxia, and areflexia without weakness [62]. The Cervico-Brachial-Pharyngeal variant can mimic botulism, with ptosis, difficulty swallowing, weakness in the upper extremities, and preserved sensation and lower extremity strength [60]. The sensory ataxia variant is characterized by sensory loss without motor weakness [63]. Finally, the acute pandysautonomia variant is characterized by orthostatic hypotension, ileus, urinary retention, areflexia, and ataxia without motor weakness [64]. Although ascending weakness is considered a classic symptom of GBS, leg weakness is not always present at the initial visit, with some studies reporting it in only 32–50.7% of patients, thus leading to delays in diagnosis [40,60,61]. Decreased sensation may be preceded by neuropathic pain and is often not in the distribution of a specific spinal cord level [60]. Patients may also present with dysautonomia, which is dysregulation of the autonomic nervous system that causes sympathetic and parasympathetic system alterations. Dysautonomia may develop in up to 66% of patients with GBS [65]. These alterations can manifest as heart rate and blood pressure changes, gastrointestinal motility, and body temperature [66]. In a study of factors associated with delay in diagnosis of GBS, intact deep tendon reflexes had an odds ratio (OR) of 0.07 (95% confidence interval [CI] 0.01–0.35) for failure to consider GBS on a differential [40]. A descending or asymmetric pattern of weakness was also associated with a failure to consider GBS as a diagnosis with an OR of 0.25 (95% CI 0.09–0.74) [40]. Respiratory fatigue may lead to respiratory failure, necessitating airway intervention. Up to 30% of patients with GBS experience respiratory failure requiring airway intervention and mechanical ventilation [17,33]. In one observational study of patients with GBS, cranial nerve involvement was associated with a need for mechanical ventilation (OR 3.8, 95% CI 1.3–10.5) [67].

Table 2
GBS variants.

GBS Variant	Description
Acute Motor Axonal Neuropathy (AMAN)	The motor variant is rapidly progressive; antibodies targeted against axolemma and nodes of Ranvier
Acute Inflammatory Demyelinating Polyradiculopathy (AIDP)	The most common form of GBS presents with classic ascending paralysis and decreased reflexes
Acute Motor Sensory Axonal Neuropathy (AMSAN)	Motor and sensory variant can present similarly to AIDP
Miller-Fisher Syndrome (MFS)	Characterized by ophthalmoplegia, ataxia, and areflexia without any weakness
Cervico-Brachial-Pharyngeal	Can present with ptosis, difficulty swallowing, weakness in the upper extremities, and preserved sensation and lower extremity strength
Acute Pseudodysautonomia	A rare variant characterized by orthostatic hypotension, ileus, urinary retention, areflexia, and ataxia without motor weakness

3.3. What diagnostic criteria are available?

GBS is a rare but deadly disorder that is complicated to diagnose. Two well-recognized criteria initially created for epidemiologic studies have been utilized for diagnosis: The National Institute of Neurological Disorders and Stroke (NINDS) and The Brighton Criteria (Tables 3 and 4) [29,68-70]. The criteria were based on expert opinions and prior scientific knowledge, hoping to assist physicians in ruling out other pathologies [68]. A study published in 1999 found that the NINDS criteria missed up to 15% of GBS cases, mostly GBS variants [69]. The Brighton Criteria were published due to recent associations between Swine flu and GBS to classify suspected GBS patients by a level of certainty [70]. The criteria were later adapted to aid clinicians in diagnosing GBS, with various validation studies showing high sensitivity. One such study in Rotterdam analyzed 46 children, revealing 72%, 96%, and 98% sensitivity rates for diagnostic certainty levels one, two, and three, respectively [71]. The sensitivities found in these validation studies suggest that the Brighton criteria could assist in the early evaluation of patients with suspected GBS, further augmenting the suspicion of the diagnosis, especially in resource-limited countries. However, these criteria do not display 100% accuracy, do not account for atypical presentations or various GBS variants, and were made as screening tools rather than diagnostic tools. Lastly, data evaluating the Brighton Criteria

Table 3
The national institute of neurological disorders and stroke.

The NINDS Criteria
Required features include:
• Progressive weakness of the arms and/or legs, ranging from minimal weakness of the legs to total paralysis of all four limbs, and including the trunk, bulbar and facial muscles, and external ophthalmoplegia.
• Areflexia or decreased deep tendon reflexes in weak limbs.
Supportive features include:
• Symptom progression over days to four weeks
• Relatively symmetric, bilateral symptoms
• Pain in the trunk or limbs
• Cranial nerve symptoms or signs
• Autonomic dysfunction
• Sensory dysfunction that is mild
• No fever at symptom onset
• CSF with elevated protein and normal to mildly elevated leukocyte count (usually <5 cells/mm3)
• Electrodiagnostic abnormalities consistent with GBS
• Recovery starting two to four weeks after progression halts
Features that argue against the diagnosis:
• CSF cell count with >50 cells/ microgram of fluid
• Severe Asymmetrical weakness that is constant
• Urinary or Intestinal dysregulation at initial onset or continuing throughout the disease
• Respiratory distress and extremity weakness at the initial onset
• Sensory changes with limited weakness at the initial onset
• Fever at initial presentation
• Reaching disease Nadir <24 h
• Well-demarcated sensory level increasing concern for spinal cord pathology
• Presence of clonus or Hyperreflexia
• Babinski Sign
• Gastrointestinal pain
• Slow progression with limited weakness without respiratory involvement
• Symptoms progressing beyond four weeks after the initial onset
• Altered mental status, not including Bickerstaff brainstem encephalitis

in the ED setting are limited; the studies previously discussed only included patients with complete data sets in their analysis, which may not be available during the patient's evaluation in the ED.

3.4. What are the essential laboratory and imaging tests in GBS, and what are pearls and pitfalls concerning testing?

While the diagnosis of GBS is primarily clinical, diagnostic testing is helpful in the ED setting to assist with diagnosing and managing GBS and exclude alternative causes (Table 5). A basic metabolic panel, magnesium, and phosphate should be ordered in a patient presenting with weakness to assess for electrolyte causes of weakness, such as hypokalemia or hypophosphatemia [72]. Cytoalbuminologic dissociation on CSF testing, defined as elevated CSF protein and a cell count of fewer than 50 cells/microgram of fluid, suggests GBS [70]. One study of patients with GBS undergoing LP found 64% displayed cytoalbuminologic dissociation on CSF testing [33]. This relatively low rate was likely due to the timing of when the LP was performed and the onset of weakness. When patients had an LP performed between 0 and 1 days after the onset of weakness, only 49% had cytoalbuminologic dissociation.

Table 5
Differential diagnosis for GBS.

• Amyotrophic lateral sclerosis
• Botulism
• Dermatomyositis
• Electrolyte abnormality (e.g., hypokalemia)
• Lambert-Eaton myasthenic syndrome
• Multiple sclerosis
• Myasthenia gravis
• Rhabdomyolysis
• Spinal cord compression or infarction
• Tick paralysis
• Transverse myelitis

However, this finding was present in 88% of patients with an LP performed three weeks after the onset of weakness [33]. Additionally, as patients age, there can be a gradual increase in CSF protein concentration, which can alter the sensitivity and specificity of CSF analysis for diagnosing GBS [73-75]. In summation, physicians should not rely on cytoalbuminologic dissociation for diagnosing GBS, as the accuracy of the results can be skewed or not present depending on the timing of the procedure and the patient's age [33].

Most patients will undergo neuroimaging in the ED. While imaging is not necessary for the diagnosis of GBS, it can assist in excluding other pathologies. Patients with GBS typically demonstrate nonspecific findings on imaging. One case report described a patient who presented with right facial and bilateral lower extremity weakness one week after a mild upper respiratory infection [76]. Although CSF and EMG testing were consistent with GBS, MRI demonstrated enhancement of various segments of the facial nerves, abducens nerve bilaterally, and the vagus and glossopharyngeal nerves [76]. In another case report, MRI in a patient with bilateral lower extremity weakness and suspected GBS demonstrated enhancement of the anterior and posterior nerve roots of the conus medullaris and cauda equina [77]. Both patients underwent plasmapheresis with subsequent complete to near-complete resolution of their symptoms at eight and six weeks, further strengthening their likelihood of GBS [76,77]. Thus, the presence of abnormalities in neuroimaging could enhance the likelihood of the diagnosis of GBS.

3.5. What are the key components of ED management?

The critical components of ED management involve stabilizing the patient, providing supportive care and airway/respiratory intervention if necessary. A potentially significant neurologic deficit is bulbar dysfunction, which leads to patients experiencing difficulty handling secretions or dysphagia, increasing the risk for aspiration [78]. Furthermore, as the ascending paralysis progresses, the abdominal muscles, diaphragm, and intercostals can become involved leading to respiratory weakness. This may lead to poor ventilation, resulting in hypercarbia and ultimately hypoxia [78]. Patients with severe respiratory compromise resulting in respiratory distress or failure need intubation and mechanical ventilation (Table 6). Several bedside tools can assist in predicting the degree of respiratory involvement. An objective data

Table 4
Brighton criteria for GBS.

Criteria	Levels of Diagnostic Certainty			
History/symptoms/findings	1	2	3	4
Bilateral and flaccid weakness of limbs	+	+	+	+/−
Hyporeflexia or areflexia in weak limbs	+	+	+	+/−
Monophasic course and time between onset-nadir within 12 h and 28 days	+	+	+	+/−
CSF cell count <50/mL	+	+/− (a)	−	+/−
CSF protein concentration > 60 mg/dL	+	+/− (a)	−	+/−
Nerve conduction study findings consistent with one of the GBS variants	+	+	−	+
No alternative diagnosis for weakness	+	+	+	+/−

+: present; −: absent; +/−: not conducted/obtained/resulted; (a) if CSF results are not available, then nerve conduction study findings must align with GBS variant.

Table 6
Findings suggestive of need for endotracheal intubation.

- Difficulty clearing secretions, weak cough
- Dyspnea
- Evidence of difficulty breathing
- Forced expiratory volume < 20 mL/kg or negative inspiratory force <30 cm H20
- Hypoxia
- Single breath count <20
- Vital sign instability (tachypnea, tachycardia)

point that can assist the decision to intubate a patient is forced vital capacity (FVC). FVC is the volume a patient can exhale after taking a large breath; this assesses the patient's inspiratory and expiratory abilities [79]. Generally, a FVC < 20 cc/kg or a progressive drop of >30% in repeat FVC indicates poor respiratory function that is highly associated with the need for mechanical ventilation [80]. The single breath count is a surrogate of spirometry tests if they are not possible or unavailable. To complete this test, the patient recites numbers starting at 1 in a normal voice after a full inhalation. The patient should recite two numbers per second, with a single breath count <20 suggesting the need for mechanical ventilation [81]. If the patient demonstrates respiratory compromise, noninvasive ventilation is typically not recommended, as it does not provide definitive airway protection and may increase the risk of aspiration [82,83]. Endotracheal intubation with mechanical ventilation is recommended if airway compromise or respiratory fatigue is present.

When proceeding with intubation, depolarizing agents such as succinylcholine are contraindicated in GBS [84-86]. Multiple case reports have shown that succinylcholine increases the risk of hyperkalemia [84-86]. In one case report, a GBS patient with initial potassium of 4.3 mmol/L became hyperkalemic with repeat potassium of 8.6 mmol/L after receiving succinylcholine. The patient ultimately developed ventricular tachycardia and died [84]. Another case report describes a pregnant patient with GBS who received succinylcholine during a cesarean section, developed a potassium of 9.2 mmol/L, and subsequently experienced cardiac arrest [86]. Succinylcholine is contraindicated in the acute phase of GBS, and it is also unclear whether it is safe to administer in the progressive, plateau, or recovery phases of the illness [84]. Despite not having a clear guideline for paralytics during intubation, nondepolarizing neuromuscular blocking agents such as rocuronium or vecuronium are favored to mitigate the risk of hyperkalemia, albeit the patient's sensitivity to the agent can vary, with some patients having prolonged paralysis [87,88]. The optimal dose of rocuronium in GBS patients is unknown; some authors have advocated using a decreased dose of rocuronium to decrease the risk of prolonged paralysis, while others have described using sugammadex to reverse the prolonged paralysis [89].

Management of dysautonomia may be necessary. Patients with dysautonomia can initially be hemodynamically stable and then rapidly decompensate, with studies demonstrating mortality rates approaching 7% [90]. Patients may experience several severe arrhythmias, including asystole, bradyarrhythmias, isolated atrial or ventricular arrhythmias, or most commonly sinus tachycardia (Table 7) [91]. Some patients who experience symptomatic or sustained bradycardia may require pacemaker placement [91]. In addition, patients can also experience sudden, severe oscillations in blood pressure. A devastating complication of severe hypertension is posterior reversible encephalopathy syndrome (PRES), which is a neurologic emergency characterized by visual disturbance, seizures, and altered mental status associated with radiographic evidence of parieto-posterior occipital white matter vasogenic edema. PRES is typically secondary to endothelial dysfunction from dysautoregulation of high blood pressure [92]. For example, one case report describes a patient who developed vision loss and had seizures from PRES, ultimately attributed to GBS [93].

Table 7
Cardiovascular complications of GBS.

Cardiovascular complications with GBS	Findings or symptoms
Arrhythmias	Bradyarrhythmias, tachyarrhythmias, sinus tachycardia, asystole
Blood pressure fluctuations	Hypertension or hypotension
Myocardial impact	Myocarditis, neurogenic stunned myocardium, heart failure, takotsubo cardiomyopathy
Coronary artery involvement	STEMI or coronary vasospasm
ECG Abnormalities	T wave changes, prolonged QT interval, AV blocks, bradycardia, tachycardia, ST-T changes

There are no clear guidelines for treating dysautonomia. A case report describes using epinephrine for cases of dysautonomia with bradycardia and hypotension. However, there is insufficient evidence and no clear recommendations for one specific vasopressor [94]. Despite the desire to manage extreme changes in blood pressure or heart rate variability, many experts caution against reflexively treating secondary to transient changes, which if treated, can lead to possible iatrogenic injury [95]. One case report describes managing tachycardia from dysautonomia with esmolol [96]. Additionally, there are case reports of using short-acting antihypertensives to treat severe hypertension with agents such as labetalol, esmolol, and nitroprusside [97]. Although most emergency clinicians will focus primarily on vital sign abnormalities, dysautonomia also affects other parts of the body, including the genitourinary and gastrointestinal systems; it can also cause vision changes with its impact on pupillary muscles and affect body temperature by its effects on the sudomotor system [95]. One retrospective study found adynamic ileus in 42% of patients [95].

Treatment for GBS should be initiated in the ED in consultation with the neurology specialist. The primary treatment for GBS includes IVIG or PLEX. Both have been associated with improved functional outcomes in GBS. The first large randomized controlled trial (RCT) published in 1992 including 150 patients demonstrated that IVIG and PLEX were similarly effective in improving functional outcomes at four weeks [98]. A follow-up international multicenter RCT published in 1997 involving 379 patients with severe GBS showed that IVIG and PLEX were equally efficacious in treating neurologic symptoms during the first 2 weeks of symptom onset [99]. The American Academy of Neurology recommends either treatment as equally efficacious, and the choice may depend on institutional protocols and resources [100].

The disposition of patients with GBS depends on their risk for decompensation, signs of respiratory compromise, and hemodynamic status. The Erasmus GBS Respiratory Insufficiency Score (EGRIS) is a prognostic tool developed from a Dutch cohort study to identify patients with GBS at high risk of respiratory deterioration who may require mechanical ventilation during their first week of admission [101]. The tool involves three components evaluated during admission: facial/bulbar weakness, an objective measurement of weakness (the Medical Research Council sum score), and the time between the onset of weakness and admission [101]. The score ranges from 0 to 7, with 7 points corresponding to a 90% likelihood of mechanical ventilation [101]. While EGRIS was found to be accurate in a validation study, the Medical Research Council Sum Score calculation may be unfamiliar to an emergency clinician, making EGRIS less useful in the ED setting [102]. Ultimately, the disposition should be based on the patient's clinical status, nursing and hospital capabilities, and clinical gestalt. However, even if a patient is clinically stable, ICU admission should be considered secondary to the risk of rapid decompensation.

Table 8 lists pearls and pitfalls in the evaluation and management of GBS.

Table 8
Pearls in the evaluation and management of GBS.

- GBS is a clinical diagnosis characterized by symmetrical ascending weakness that can progress over days to weeks and is associated with hyporeflexia or areflexia.
- GBS has variable presentations and can include sensory, bulbar, and autonomic symptoms in addition to muscle weakness.
- Antecedent infections, recent surgery, medications, and vaccines may be associated with GBS.
- Diagnosis in the ED setting is clinical, though laboratory assessment and CSF analysis may assist.
- Not all patients demonstrate albumino-cytological dissociation on CSF testing.
- Neurology consultation should be obtained to assist in the diagnosis and inpatient management of patients with GBS.
- Dysautonomia and respiratory involvement can result in hemodynamic and respiratory compromise.
- For management of heart rate or blood pressure fluctuations, a short-acting agent should be utilized (e.g., esmolol for severe tachycardia).
- The degree of respiratory muscle weakness will determine the need for intubation and the level of care.
- Succinylcholine is contraindicated in acute GBS due to the risk of hyperkalemia. The drug of choice should be a nondepolarizing muscular blockade drug (rocuronium or vecuronium) when performing rapid sequence intubation (RSI).
- PLEX or IVIG are equally efficacious first-line treatments for GBS and have been shown to improve functional outcomes.

4. Conclusion

GBS is a rare but potentially fatal disease that most commonly presents weeks after a bacterial or viral infection. The pathognomonic history and examination findings are a progressive ascending weakness associated with hyporeflexia, but GBS may impact the cranial nerves, respiratory system, and autonomic system. The presentation may be subtle or atypical, and the history of recent infection, vaccination, or surgery may be non-specific, making the diagnosis challenging. GBS is a clinical diagnosis in the ED setting. Assessment in the ED includes laboratory evaluation, CSF analysis, and potentially neuroimaging, which can increase the probability of the diagnosis. Several criteria exist to assist with diagnosis, including the NINDS and Brighton criteria. Treatment including stabilizing and resuscitating if necessary, with evaluation and potential management of autonomic and respiratory dysfunction. Neurology consultation is recommended, and definitive treatment includes PLEX or IVIG.

CRediT authorship contribution statement

Joshua Madden: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Conceptualization. **Anthony Spadaro:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources. **Alex Koyfman:** Visualization, Validation, Supervision, Resources. **Brit Long:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Conceptualization.

Declaration of Competing Interest

None.

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