An Overview on Guillain–Barré Syndrome Diagnostic and Management Approach

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ABSTRACT

Background: Guillain Barré Syndrome (GBS) is a rare but life-threatening condition that can lead to demyelination of the peripheral nervous system. It has many subtypes, with different etiologies. It needs immediate intervention since if the intervention is delayed, it might lead to the death of patients or permanent disability. Treatment of acute cases is plasmapheresis or intravenous immunoglobulin. **Objective**: The objective of this review is to discuss Guillain–Barré Syndrome, different presentation, and management plan with the outcome. **Method**: We searched the PubMed database looking for relevant articles to the topic using Mesh terms, "Guillain–Barré Syndrome". **Conclusion**: Early detection and intervention can prevent mortality and morbidity in a major portion of patients with Guillain–Barré Syndrome.

Key Words: *Guillain–Barré Syndrome, peripheral demyelination, Miller Fisher syndrome, intensive care unit, albuminocytological dissociation*

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INTRODUCTION

Now identified as the most frequent cause of acute post-infectious flaccid paralysis in the world, since 100 years by 2016 Guillain–Barré syndrome (GBS) was described for the first time [1, 2]. GBS continues to exist as an important neurological emergency, although rare with an incidence of 1–2 cases per 100 000. Holding within a heterogeneous group of clinical and pathological entities, GBS is an acute onset autoimmune disease that can affect the peripheral nervous system [3]. Most of the time preexisting infections are thought to stimulate an immune response, which subsequently cross-reacts with nerves causing them to demyelinate or cause degeneration of the axons [4]. Most GBS patients develop ascending paralysis, which initiates in the legs and typically spreads upwards to the arms [5]. Also, the involvement of cranial nerve is common, add to that, 25% of patients develop respiratory failure and require mechanical ventilator [6]. A rare subtype of GBS is Miller Fisher syndrome, in which ataxia and cranial nerve involvement are predominate [3]. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was considered to be synonymous with the term GBS, but with the increasing recognition of variants over the past decades, the number of disordered that fit under the title of GBS has grown to involve axonal variants and more narrowed variants, such as Miller Fisher syndrome (MFS) [7]. Came to notice through the clinical journey of

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GBS that it can follow a typical pattern that can be readily divided into two phases, constituent and elements, respectively [8]. Axonal and demyelination forms of GBS occur in diverse proportions across various geographical regions, and clinical variants, such as MFS, which are readily definable [9, 10]. Management wise, it has been evident that both intravenous immunoglobulin treatment and plasma exchange are of equal benefit [11]. Several factors help in defining the outcomes of GBS patients, as we will come to learn. Early diagnosis and treatment of GBS patients will prevent the compilations and the need for the intensive care unit and the need for the ventilator.

Pathogenesis:

GBS is neuropathy of a post-infection and recognized to be stimulated by certain infections, including *Haemophilus influenza, Campylobacter jejuni*, *cytomegalovirus, Mycoplasma pneumoniae*, *hepatitis E*, *Epstein–Barr virus,* and *influenza virus* [9, 12, 13]. One question that can be the concern of patients and have them ask their GP is: can the flu vaccine trigger GBS? Although this was thought to be an issue in the 1970s swine flu epidemic, the latest studies have revealed that the flu vaccine does not stimulate GBS, and in fact, patients who caught the influenza virus are at higher risk of developing GBS [12]. Great progress have been made to understand the mechanism of some GBS subtypes. The appearance of the histology of the AIDP subtype looks like experimental autoimmune neuritis, which is mainly caused by T cells directed against peptides from the myelin proteins, P2, P0, and PMP22 [14]. The T-cell-mediated immunity role in AIDP lasts uncertain yet there is evidence of antibody and complement system involvement [14]. There is now strong evidence that acute sensory and motor axonal neuropathy, acute motor axonal neuropathy, and GBS axonal subtypes are caused by autoantibodies against the gangliosides on the plasma membrane of the axon that enhances the macrophages to invade the axon at the node of Ranvier [15]. About 25 percent of the GBS patients had a recent *C. jejuni* infection, and axonal forms of the disease are more common and specific in these patients [5]. The lipooligosaccharide from the *C. jejuni* wall has ganglioside-like structures and when it is injected into rabbits, it can lead to neuropathy that mimics acute motor axonal neuropathy [5]. Antibodies to GD1a, GM1b, GM1, and Gal Nac GD1a are particularly involved in acute motor axonal disease, with the exception of Gal Nac GD1a, in acute sensory and motor axonal neuropathy [5].

Clinical Manifestations:

In the majority of GBS patients, the symptoms are almost always preceded by a preexisting condition. Within thirty days before the onset of the disease, about 40% reported that respiratory infections were the most familiar [16]. Also, about 20% had gastroenteritis as the preexisting cause [16]. The most familiar manifestation is limb weakness, which starts more proximal than distal [16]. In cranial nerve involvement, cranial nerve seven involvement which can lead to bell's palsy is the most common type (in 53%), after that, ophthalmoplegia, bulbar weakness, and weakness of the tongue [17]. In nearly half of the cases, the illness is proclaimed by sensory symptoms [16]. In total, about 80% had sensory symptoms, about 90% of patients had experienced pain, and it happens to be a very common symptom and often comes severe [18]. In about 65 percent of the cases autonomic dysfunction was observed, showing as either excessive or reduction in the activity of the sympathetic or parasympathetic nervous system. The most common indices of autonomic dysfunction are pulse and blood pressure fluctuating [19]. The start of symptoms can be manifest as acute or sub-acute. Following a plateau phase, a gradual recovery happens. The average time to reach nadir, improvement, and clinical recovery, based on a large multicenter study, were 12, 28, and 200 days, respectively. Beyond one month from the onset, it was found that 98%of patients reached the plateau phase. In another study, the mean duration of the plateau phase was found to be 12 days [20] (Table1)

Differential Diagnosis:

To diagnose GBS, Miller Fisher syndrome, and other subtypes can be difficult to distinguish in early disease, but with proper history and examination alone many differentials can be excluded [9] (Table 2). Other than GBS, a few cases can cause fast progressive quadriplegia and cranial neuropathy. The top deferential is acute cervical spinal cord injury when symptoms and signs are restricted to the upper and lower limbs [3]. If there is a recent history of falls in older people, spinal stenosis should be considered, whereas in younger patients transverse myelitis should be suspected [21]. Spinal injury is identified by brisk reflexes, a level of sensory loss, and often new-onset urination disturbance. This is rare but peripheral neuropathies may develop in acute phase [21]. Miller Fisher syndrome could be mistaken as brainstem stroke or myasthenia gravis, but if the patient has fatigability or very acute onset respectively these can be excluded [3].

Based on the examination and history of a patient alone a diagnosis of GBS can usually be made. Most patients (>60%) describe preexisting infectious symptoms. The most important triggers are infectious diarrhea caused by *C. jejuni* and upper respiratory tract infections [21]. Usually, neurological symptoms begin between 3 days and 6 weeks post-exposure [3]. Sensory symptoms very often appear prior to or at the start of weakness and many patients complain of a pricking or tingling paraesthesias in their feet and hands. GBS is generally progressive and

characteristically symmetrical [3]. When progressive bilateral ophthalmoplegia and ataxia happen, MFS is suggestive [21].

Diagnosis:

Patients, once in the hospital, will have a spinal cord and brain scan in order to exclude structural causes, followed by lumbar puncture, which particularly shows raised protein in the cerebrospinal fluid, however, absence of inflammatory cells [3]. Nerve conduction studies assist to prove the diagnosis, but, like cerebrospinal fluid, are non-diagnostic in up to 50% of cases within the first week of disease. Although should not be relied on, the presence of anti-ganglioside (IgG) antibodies may support the diagnosis [3].

Treatment:

Corticosteroids are useless in GBS, unlike various inflammatory conditions. Not all patients need treatment, but in nearly all centers the initial treatment starts with intravenous immunoglobulin (IVIG) or plasma exchange, if there is significant respiratory or bulbar muscle weaken, or weakness is quickly progressing [1]. 25% of patients still need admission to the ICU for mechanical ventilation [3]. There are some side effects, contraindications (absolute and relative) for the usage of intravenous immunoglobulin. (Table 3)

Complications & Prognosis:

Even with modern treatment, about 3% of patients with Guillain–Barré Syndrome up till now die and nearly 20% are left seriously disabled [6]. GBS patients' late complications, including postural hypotension, neuropathic pain, and fatigue can last for months beyond sensori-motor recovery, and these chronic symptoms may be managed by primary care practitioners as a practice of follow-up [3]. One-third of GBS patients proclaim ongoing pain one-year post-recovery, and opioids, gabapentin, and carbamazepine can be helpful in managing this [3]. However, some factors are found to be associated with a poor outcome. By means of etiology if the patient had a previous gastrointestinal infection, a *C jejuni* infection, or has encountered cytomegalovirus will most probably have a poor prognosis [22]. Also, some clinical features can make the outcome worse. For instance shorter latency to nadir, older age, the longer the time it takes for clinical improvement, the need for mechanical ventilation, if there was greater disease severity and disability [16].

CONCLUSION:

GBS is an immune-mediated monophasic neuropathy distinguished by acute onset of mainly motor weakness and is a common cause of respiratory depression. There are numerous variants of GBS with different manifestations and prognoses. The method of electrodiagnosis helps in the diagnosis. Definitely, immunotherapy is proven to make a huge difference in the recovery of GBS patients and both plasma exchange (PE) and intravenous immunoglobulin (IVIg) are effective equally. Because it has a fewer side effect profile and easier to be administered, IVIg may be preferred. Even so, a small volume PE can be used with the same efficacy due to cost restrictions. Watchful anticipatory supportive treatment is of equal importance in lowering the mortality and morbidity in GBS.

A severe axonal injury early prevention in the disease course is an important major focus, for the reason that it is an important limiting factor for achieving proper, long-term outcomes.

Tables:

Table 1: clinical signs of GBS

Clinical features of Guillain-Barré syndrome			
Autonomic dysfunction	**Motor dysfunction**	**Sensory dysfunction**	**Other**
Sinus bradycardia and tachycardia Other cardiac arrhythmias (both tachy and brady)	Symmetrical limb weakness: global, proximal, or distal	Pain	Papilloedema
Hypertension and postural hypotension	Neck muscle weakness	Loss of sense of joint position, distally touch and pain, vibration	
Wide fluctuations of blood pressure and pulse	Respiratory muscle weakness	Numbness, paresthesias	
Tonic pupils	Cranial nerve palsies: III–VII, IX–XII Areflexia	Ataxia	
Hypersalivation	Wasting of limb muscles		

Table 2: GBS VS Miller Fisher syndrome

Guillain–Barré syndrome	Clinical features of Both	Miller Fisher syndrome
All four limbs have weakness & areflexia	Symptoms of preceding infections	Ophthalmoplegia
Presence or absence of respiratory malfunction and cranial nerve involvement	Weakness is symmetrical	Ataxia

	Distal paresthesias existence before or at the start of weakness	Areflexia
	Mono-phasic disease course with an interval between onset and nadir of the weakness of 12h-28days, followed by the clinical plateau	

Table 3: Information about the use of intravenous immunoglobulin treatment

Information about the use of intravenous immunoglobulin treatment		
Adverse effects	**Contraindications**	**Relative contraindications**
Transient increase in liver enzymes	Selective IgA deficiency	Severe congestive cardiac failure
acute renal failure, Renal tubular necrosis	Anaphylaxis following previous intravenous infusion of immunoglobulin	Renal insufficiency
Nausea, vomiting		
Vasomotor symptoms, headache		

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