GUILLAIN-BARRÉ SYNDROME EXPLORED: FROM PATHOPHYSIOLOGY TO CLINICAL MANAGEMENT

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ABSTRACT

Guillain-Barré Syndrome (GBS) is an acute immune-mediated polyneuropathy characterized by rapidly progressive, symmetrical weakness and varying degrees of sensory disturbances. This review summarizes current understanding of GBS pathophysiology, clinical manifestations, diagnostic criteria, treatment strategies, and long-term outcomes. Recent advances in understanding the immunopathogenesis of GBS have led to improved diagnostic approaches and therapeutic interventions. Despite these advances, GBS continues to be associated with significant morbidity, highlighting the need for early diagnosis and prompt treatment. This review discusses the heterogeneity of GBS subtypes, the role of preceding infections, and emerging therapeutic strategies that may improve patient outcomes.

Keywords: Guillain-Barré Syndrome, Campylobacter jejuni, Sensory disturbances, Plasmapheresis

INTRODUCTION

Guillain-Barré Syndrome (GBS) is the most common cause of acute flaccid paralysis worldwide, with an annual incidence of 1-2 per 100,000 persons (1). First described by French neurologists Georges Guillain, Jean Alexandre Barré, and André Strohl in 1916, GBS is characterized by rapidly progressive, symmetrical weakness of the limbs, often accompanied by sensory symptoms and, in severe cases, respiratory failure requiring mechanical ventilation (2).

The clinical spectrum of GBS encompasses several variants, including acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome (MFS). These variants differ in their pathophysiology, clinical presentation, and prognosis, reflecting the heterogeneity of this disorder (3).

GBS is typically triggered by preceding infections, most commonly Campylobacter jejuni (C. jejuni), cytomegalovirus, Epstein-Barr virus, and Zika virus. The temporal association between infection and the onset of neurological symptoms supports an immune-mediated pathogenesis, involving both cellular and humoral immune responses directed against peripheral nerve components (4). This review aims to provide a comprehensive overview of the current understanding of GBS, including its pathophysiology, clinical features, diagnostic approaches, treatment strategies, and long-term outcomes, with a focus on recent advances that have improved

our understanding of this complex disorder. The figure 1 showed diagrammatic representation of GBS overview.

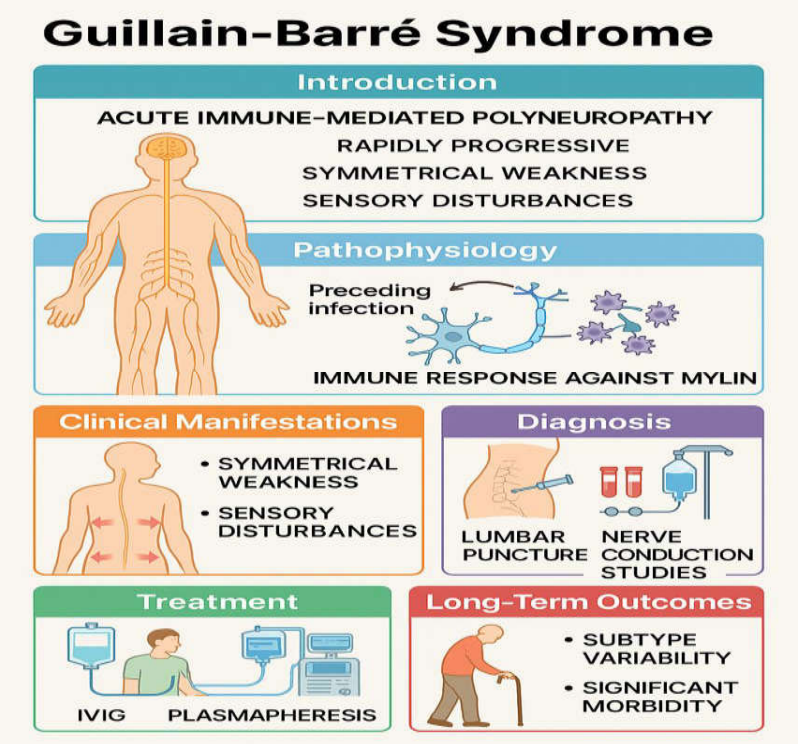

Figure1: Diagrammatic representation GBS overview

PATHOPHYSIOLOGY

Molecular Mimicry and Autoimmunity

The pathogenesis of GBS involves an aberrant immune response triggered by a preceding infection. Molecular mimicry, in which microbial antigens share structural similarities with gangliocytes or myelin components of peripheral nerves, is considered the primary mechanism underlying GBS (5).

The best-characterized example is C. jejuni infection preceding AMAN. The lipo-oligosaccharides on the bacterial wall of C. jejuni share structural homology with gangliosides present on axolemma, particularly GM1 and GD1a. This molecular mimicry leads to the production of cross-reactive antibodies that target peripheral nerve components, resulting in nerve damage (6).

Different GBS subtypes are associated with distinct antibody specificities: anti-GM1 and anti-GD1a antibodies in AMAN, anti-GQ1b antibodies in MFS, and antibodies against myelin proteins such as P0, P2, and PMP22 in AIDP (7).

Immune-Mediated Nerve Damage

In AIDP, the predominant form in Western countries, the immune response targets myelin components, leading to demyelination and secondary axonal damage. This involves both humoral and cell-mediated mechanisms, with infiltration of macrophages, T cells, and complement deposition in peripheral nerves (8).

In contrast, AMAN and AMSAN are characterized by primary axonal damage without significant demyelination. Anti-ganglioside antibodies bind to axolemma at the nodes of Ranvier, activating complement and disrupting sodium channel clusters, leading to conduction failure and axonal degeneration (9).

Complement activation plays a crucial role in both demyelinating and axonal forms of GBS. The membrane attack complex (C5b-9) causes transmembrane pore formation, leading to calcium influx, which triggers various degradative processes resulting in demyelination or axonal degeneration (10).

CLINICAL MANIFESTATIONS

Typical Presentation

The classic presentation of GBS is characterized by rapidly progressive, symmetrical weakness, typically beginning in the lower limbs and ascending to involve the upper limbs and, in severe cases, bulbar and respiratory muscles (11). Sensory symptoms, including paraesthesia and numbness, often precede or accompany motor deficits.

Deep tendon reflexes are typically reduced or absent early in the disease course. Autonomic dysfunction, manifesting as cardiac arrhythmias, blood pressure fluctuations, ileus, or urinary retention, occurs in approximately 70% of patients and can be life-threatening (12).

The disease typically progresses over days to weeks, with maximal deficits reached within four weeks of symptom onset. The nadir is followed by a plateau phase of variable duration, after which recovery begins (13).

GBS Variants

AIDP, the most common variant in North America and Europe, presents with both motor and sensory deficits, with electrophysiological evidence of demyelination. AMAN, more common in Asia, presents predominantly with motor deficits and electrophysiological evidence of axonal damage.

MFS, characterized by the triad of ophthalmoplegia, ataxia, and areflexia, accounts for approximately 5-10% of GBS cases worldwide. It is strongly associated with anti-GQ1b antibodies and typically has a favourable prognosis.

Other regional variants include pharyngeal-cervical-brachial weakness, paraparetic GBS, and bilateral facial palsy with paraesthesia, each with distinct clinical and electrophysiological features (14).

DIAGNOSIS

Clinical Criteria

The diagnosis of GBS is primarily clinical, based on the characteristic pattern of rapidly progressive, symmetrical weakness with reduced or absent reflexes. The Brighton Collaboration criteria provide a standardized approach to diagnosis, classifying cases into levels of diagnostic certainty based on clinical, laboratory, and electrophysiological findings.

Laboratory and Electrophysiological Studies

Cerebrospinal fluid (CSF) analysis typically reveals albuminocytologic dissociation—elevated protein with normal cell count. However, this finding may be absent in the early stages of the disease.

Electrophysiological studies are crucial for confirming the diagnosis and determining the GBS subtype. In AIDP, nerve conduction studies show features of demyelination, including prolonged distal latencies, reduced conduction velocities, conduction block, and temporal dispersion. In AMAN and AMSAN, studies show reduced compound muscle action potential amplitudes with relatively preserved conduction velocities, indicating axonal damage.

Serum anti-ganglioside antibodies, particularly anti-GM1, anti-GD1a, and anti-GQ1b, can help confirm the diagnosis and predict the clinical phenotype, though their absence does not exclude GBS.

TREATMENT

Supportive Care

Supportive care is the cornerstone of GBS management. Patients with rapid progression, bulbar involvement, or respiratory compromise should be monitored in an intensive care unit. Approximately 20-30% of patients require mechanical ventilation due to respiratory failure (15).

Regular monitoring of vital capacity, negative inspiratory force, and arterial blood gases guides the need for intubation and mechanical ventilation. Autonomic dysfunction should be monitored and managed appropriately (16).

Deep vein thrombosis prophylaxis, pressure ulcer prevention, pain management, and early rehabilitation are essential components of supportive care.

Immunotherapy

Intravenous immunoglobulin (IVIg) and plasma exchange (PE) are the mainstay of immunotherapy for GBS, with comparable efficacy when initiated within two weeks of symptom onset. IVIg (0.4 g/kg/day for 5 days) is often preferred due to its convenience and favourable side effect profile.

The exact mechanism of IVIg remains unclear but likely involves neutralization of pathogenic antibodies, inhibition of complement activation, and modulation of Fc receptor function. PE removes pathogenic antibodies, complement components, and cytokines from the circulation.

Corticosteroids have not shown benefit in GBS and are not recommended as monotherapy. The combination of IVIg and methylprednisolone has not demonstrated superior efficacy compared to IVIg alone in most studies (16).

Emerging Therapies

Complement inhibitors, such as eculizumab, have shown promise in experimental models and small clinical trials. Eculizumab, a humanized monoclonal antibody against C5, prevents the formation of the membrane attack complex and may limit nerve damage in GBS.

Other potential therapies under investigation include selective immunoadsorption, which removes specific pathogenic antibodies while preserving other plasma components, and immunomodulatory agents targeting specific aspects of the immune response.

PROGNOSIS AND LONG-TERM OUTCOMES

Despite advances in supportive care and immunotherapy, GBS is associated with significant morbidity and mortality. Approximately 20% of patients remain severely disabled at one year, and 3-7% die despite optimal treatment, typically from complications such as respiratory failure, autonomic dysfunction, or thromboembolic events.

Factors associated with poor prognosis include older age, severe disability at nadir, need for mechanical ventilation, preceding diarrhoea, and axonal involvement on electrophysiological studies (17-20).

Recovery follows a predictable pattern, with proximal muscles recovering before distal ones. Motor recovery precedes sensory recovery, and recovery of fine motor skills may take months to years. Persistent fatigue affects up to 70% of patients and can significantly impact quality of life.

CONCLUSION

GBS represents a heterogeneous group of immune-mediated neuropathies with diverse clinical presentations, pathophysiological mechanisms, and outcomes. Advances in understanding the immunopathogenesis of GBS have led to improved diagnostic approaches and therapeutic interventions. Early diagnosis and prompt initiation of immunotherapy, along with meticulous supportive care, remain the cornerstones of management. Emerging therapies targeting specific pathophysiological mechanisms offer hope for improved outcomes in the future. Despite these advances, GBS continues to be associated with significant morbidity and mortality, highlighting the need for ongoing research to further elucidate its pathophysiology and develop more effective therapeutic strategies.

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