GUILLAIN-BARRÉ SYNDROME (GBS) – AN ORPHAN DISEASE

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ABSTRACT

Guillain-Barré syndrome (GBS) is an unusual illness of the nervous system in which a person’s own immune system damages the nerve cells, causing muscle weakness, and sometimes, paralysis. This condition has an expected incidence of 1-2 cases per 100,000 individuals. The mortality rate due to misdiagnosis is very high. Though the expected number of cases to that are reported vary from underdeveloped and developing countries, and are very less. The actual reported cases of occurrence of GBS is nearly negligible from these countries. This may be attributed to the disease misdiagnosis. Misdiagnosis occurs due to lack of knowledge of GBS in many practitioners, where they misdiagnose GBS to be a case of paralysis. This becomes a serious issue as GBS may cause death when untreated within few hours to days. This review highlights the major symptoms including causes of misdiagnosis due to similar presenting signs and symptoms to other diseases and treatment of this rarely reported disease. This review aims to pass a safety message to all the healthcare practitioners regarding GBS and to aid them in recognizing the disease better. Hence, decreasing the misdiagnosis and mortality.

KEYWORDS: Guillain-Barré syndrome, GBS, increased mortality, Nervous system.

INTRODUCTION

Guillain-Barré syndrome (GBS) is an uncommon disorder in which a person’s self-immune system attacks part of the peripheral nervous system and causes damage to the nerve cells, thereby resulting in muscle weakness and paralysis. It can cause symptoms which usually last
for a few weeks.\cite{1, 2} It is often triggered by bacterial or viral infection and characterized by acute symmetric ascending flaccid paralysis with or without sensory changes in the body.\cite{3} GBS is a very rare but serious disorder. It can cause lethal complications if autonomic nervous system is involved or if the respiratory muscles are affected. The weakness reaches its peak in 2-4 weeks.\cite{4} It is named after the French physicians Georges Guillain and Jean Alexandre Barré, who described it in 1916. The best description of 'ascending paralysis' was made by a Frenchman named Jean Baptiste Octave Landry de Thézillat in 1859.\cite{5, 6}

SYNONYMS\cite{1, 3, 6}
Acute Idiopathic Polyradiculoneuritis / Acute Inflammatory Polyneuropathy / Demyelinating Polyradiculoneuropathy / Acute Idiopathic Polyneuritis / French Polio / Landry’s Ascending Paralysis and Landry Guillain-Barré Syndrome.

EPIDEMIOLOGY
The annual incidence of GBS is nearly 1-2/100,000. Men are affected approximately 1.5 times more than women.\cite{7} There are no incidence studies of GBS in Indian population, but some case based studies have been reported. It occurs evenly throughout the western hemisphere, without geographical clustering.\cite{8-10} It can occur in any individual irrespective of age. A mortality rate of 2% to 6% is seen in patients with GBS increasing to between 15% and 30% in patients requiring mechanical ventilation. Death due to acute cardiovascular collapse (in the setting of autonomic dysfunction) has been found to occur in up to 14% of patients.\cite{11}

PATHOPHYSIOLOGY
GBS is triggered by immunologic mechanisms, although exact pathogenesis remains incompletely defined. GBS is viewed as an autoimmune disease often triggered by an antecedent bacterial or viral infection, most commonly an upper respiratory tract infection or gastroenteritis.\cite{3, 4} Molecular mimicry is postulated to be responsible for inducing GBS. It is likely that immune responses directed toward the infecting organisms cross react with neural tissues, targeting epitopes in cranial and spinal nerves and roots. Types, symptoms and pathophysiology of the disease is depicted in the table 1.
Table 1: Types, symptoms and pathophysiology of Guillain-Barré syndrome\cite{1,4,5}

<table>
<thead>
<tr>
<th>TYPE</th>
<th>SYMPTOMS</th>
<th>PATHOPHYSIOLOGY</th>
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<tbody>
<tr>
<td>AIDP</td>
<td>Motor inflammatory demyelination, Axonal damage.</td>
<td>Macrophages invade intact myelin sheaths and denude the axons</td>
</tr>
<tr>
<td>AMAN</td>
<td>Motor respiratory involvement, primary axonal degeneration.</td>
<td>Macrophages invade the nodes of Ranvier where they insert between the axon and surrounding Schwann-cell axolemma, leaving the myelin sheath intact</td>
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<tr>
<td>AMSAN</td>
<td>Motor and sensory involvement with respiratory dysfunction, primary axonal degeneration with prognosis.</td>
<td>Similar to AMAN with the involvement of ventral and dorsal roots</td>
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<tr>
<td>MFS</td>
<td>Ophthalmoplegia, sensory ataxia, areflexia.</td>
<td>Abnormality in sensory conduction, although the underlying pathology is not clear</td>
</tr>
<tr>
<td>APN</td>
<td>Most rare form accompanied by encephalopathy.</td>
<td>Widespread sympathetic and parasympathetic failure occurs</td>
</tr>
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\textit{AIDP}- Acute inflammatory demyelinating polyradiculoneuropathy; \textit{AMAN}- Acute motor axonal neuropathy; \textit{AMSAN}- Acute motor and sensory axonal neuropathy; \textit{MFS}- Miller Fisher Syndrome; \textit{APN}- Acute Pandysautonomic Neuropathy.

Other environmental toxins related disease mimicking GBS symptoms: Toxins such as puffer fish toxin or shellfish poisoning, should be considered unlike GBS, toxic neuropathies generally are slowly progressive, with sensory loss far exceeding weakness and motor loss. However, the neuropathy seen with exposure to toxins such as organophosphates is more subacute and is predominately motor. The key to diagnosis of a toxic neuropathy is exposure history.\cite{12}

ETIOLOGY\cite{4,5}
RISKS ASSOCIATED WITH OCCURRENCE

Patients often complain of a preceding bacterial or viral infection. However, there are other acute neuropathies associated with infection such as diphtheria or botulism that must be considered.[13, 14] Appropriate diagnostic labs should be ordered based on the history. The medical history should also focus on factors that might point to a diagnosis other than GBS such as a previous toxin or heavy metal exposure (arsenic, organophosphates), or systemic symptoms of conditions that might produce acute weakness. Other important historical information includes a social history for risks such as HIV, a family history indicating a condition such as periodic paralysis, or a medical history of carcinoma. In the most severe cases, paralysis may involve the trunk and cranial nerves, leading to respiratory failure and death within several days. The system-wise risks are: Cardiovascular: Labile blood pressure, Hypertension, Hypotension, Tachyarrhythmia; Gastrointestinal: Dysphagia; Musculoskeletal: Myalgia, Skeletal muscle tenderness; Neurologic: Paralysis, Sensory deprivation isolation, Neurological muscle weakness, Cranial nerve disorder, Ataxia, Paraesthesia, Hyporeflexia; Ophthalmic: Optic disc oedema. Bacterial infectious disease such as infection with Campylobacter jejuni is the most frequent pathogenic antecedent to be associated with GBS. Infection with Mycoplasma pneumoniae has also been implicated. Numerous viruses have been implicated in GBS, but convincing data are available only for cytomegalovirus, Epstein Barr virus, and varicella zoster virus. CMV infections (upper respiratory tract infection, pneumonia, nonspecific flu-like illness) comprise the most common viral triggers of GBS (10% to 20%).

DIAGNOSIS[4, 15]

I. Lumbar Puncture (LP): Cerebrospinal fluid with elevated protein level. A lumbar puncture is an important diagnostic aid in the diagnosis of GBS. The cerebrospinal fluid typically demonstrates a normal WBC count and an elevated protein level, though the protein level may initially be normal, then rise to a peak in 4 to 6 weeks.

II. Nerve Conduction Velocity (NCV) & Electromyogram (EMG): Performed with EMG, and together, they are often referred to as EMG/NCV studies. NCV analyses the speed at which signals pass along the nerves. Electromyogram (EMG) records muscle activity which can display the loss of reflexes is disease characteristic lagging of nerve responses. Electro-diagnostic studies usually reveal reduced motor nerve conduction velocities or block, prolonged distal latencies, and an abnormal F response.
III. Other tests

**Electrolytes measurement:** serum Arterial blood gas analysis.

**White blood cell count with differential:** A moderate leucocytosis is present and the lymphocyte count is decreased, although B cells are increased.

**Pulmonary function test:** Forced vital capacity <20 mL/kg, maximal inspiratory pressure <30 cm H2O, or maximal expiratory pressure <40 cm H2O may predict respiratory failure.

**MANAGEMENT**

There is no specific treatment for Guillain-Barré syndrome. However, there are therapies that lessen the severity of the illness and accelerate the recovery in most patients. There are also a number of ways to treat the complications of the disease.

I. **Plasma exchange (Plasmapheresis):** Plasma exchange has proven to be helpful in the management of GBS. It is still unknown exactly how Plasmapheresis is helpful in GBS, but it seems to reduce the severity of the disease episode. This may be due to the fact that plasma exchange can clear away antibodies and other immune cell-derived factors that could contribute to nerve damage.

II. **Immunoglobulin therapy:** In high-dose immunoglobulin therapy, intravenous injections of the proteins are administered in small quantities which the immune system uses naturally to fight against invading organisms. Studies suggest that high doses of these immunoglobulins, derived from a pool of thousands of normal donors, to GBS patients can diminish the immune attacks on the nervous system.

III. **Use of steroid hormones:** It has also been tested as a way to decrease the severity of Guillain-Barré, but controlled clinical trials have demonstrated that this treatment not only is not effective but may even have a deleterious effect on the disease. Usually dosing is 0.4 g/kg/day IV for 5 doses.

**DISCUSSION**

An orphan disease is defined as a condition that affects fewer people worldwide. This includes diseases as familiar as Melioidosis, Tired All The Time Syndrome (Chronic Fatigue Syndrome), Beauty Parlour Syndrome, Fat Wallet Syndrome, Male Breast Cancer, Selfie syndrome and many more are of increased concern and clinicians must be made aware of these Orphan diseases for better diagnosis and management.
There is a deficit of medical and scientific knowledge related to these diseases. Doctors, researchers and policy makers were unaware of most of the rare diseases and until very recently there was no real research concerning issues related to the field. There is no cure for most rare diseases, but the appropriate treatment and medical care can improve the quality of life of those affected.

**CONCLUSION**

Guillain-Barré Syndrome can be a devastating disorder because of its sudden and unexpected onset. In addition, recovery is not necessarily quick. As discussed above, patients usually reach the point of considerable weakness or paralysis within few days or weeks after the first symptoms occur. Patients face not only physical difficulties, but emotionally painful periods as well. It is often awfully difficult for patients to accustom to sudden paralysis and depend on others for help with routine daily activities. Hence, if there is awareness among patients and clinicians related to this disease will definitely help improve the current status of care.

**REFERENCES**