Guillain Barré Syndrome – Recent Advances

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Abstract. Guillain Barré Syndrome (GBS) is an acquired disease of the peripheral nerves that is characterized clinically by rapidly progressing paralysis, areflexia, and albumino-cytological dissociation. It affects both genders, involves people of all ages, is reported worldwide, and in the post-polio era, it is the most common cause of an acute generalized paralysis. The clinical features are distinct and a history and an examination generally lead to a high suspicion of the diagnosis that can then be confirmed by supportive laboratory tests and electrodiagnostic studies. This review discusses the recent advances in understanding of the different variants of GBS such as acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and the Fisher syndrome. The clinical, electrodiagnostic criteria, immunopathogenesis, and management of GBS and its variants are discussed. [Indian J Pediatr 2000; 67 (9) : 635-646]

Keywords : Guillain Barré syndrome; Acute inflammatory demyelinating polyneuropathy

Guillain Barré syndrome is an acquired disease of the peripheral nerves that is characterized by rapidly progressing paralysis, areflexia, and albumino-cytological dissociation. The syndrome was first described in 1859 by Jean-Baptiste Octave Landry, who unified the clinical features of this disease, separated it from other forms of chronic neuropathies, and termed it the "acute ascending paralysis". In 1916, Guillain, Barré, and Strohl published their observations of the albumino-cytological dissociation on cerebrospinal fluid examination of two soldiers who had presented with paralysis and areflexia. In 1949, Haymaker and Kernohan described the clinicopathological features of 50 fatal cases of GBS during World War II. They noted edema in the nerves, breakdown of myelin, and in some cases, axonal degeneration and lymphocytic infiltration. Two decades later (in 1959), Asbury et al described the presence of mononuclear infiltration and demyelination in the nerves and nerve roots of patients who died of GBS, including one patient who died within 30 hours of onset of symptoms. The 80s and 90s saw the development of plasma exchange, intravenous immunoglobulin, and improvements in critical care, all of which helped reduce the morbidity and mortality. The watershed development of this last decade, however, has been the characterization of variants of GBS and the recognition of pathological association of Campylobacter jejuni infection with the motor axonal form of GBS. In this paper the clinical features, electrodiagnostic findings, immunopathogenesis and treatment of GBS and its variants with special emphasis in children are studied.

Clinical types of GBS: The early reports on GBS from Guillain, Barré, and Strohl showed the variability in clinical severity of this condition. The variations in the severity and clinical course were felt to be the result of the severity of the inflammatory process. The clinical spectrum of the demyelinating form to axonal form was felt to represent the extent and severity of inflammatory process in the nerve and similar to the changes seen in AEN. Electrodiagnostic and pathologic studies have shown that the axonal form of GBS, referred as AMAN, is a distinct entity separate from the demyelinating form and not an expression of severe inflammation. Presently, based on clinical features, electrodiagnostic findings, and immunopathogenetic mechanisms, the following variants of GBS are recognized: (a) acute inflammatory demyelinating polyneuropathy (AIDP), (b) acute motor axonal neuropathy (AMAN), (c) acute motor sensory axonal neuropathy (AMSAN), (d) Miller-Fisher syndrome, and (d) Others (focal variants, acute sensory/autonomic neuropathy).
Epidemiology

Guillain Barré syndrome occurs in all age groups and has an annual incidence ranging from 0.4 to 1.7 cases per 100,000 population. The reported incidence for children under 15 years is similar to adults. Although there are documented cases of GBS in the newborn period, the syndrome is very rare in children less than one year of age. There is a slight male predominance with male to female ratio of 1.5 : 1. While most of the cases occur sporadically, occurrence of epidemic clusters of GBS has also been described. Cluster of cases of GBS were reported during the swine influenza immunization in 1976, but there is continuing debate whether those patients fulfilled the established criteria for GBS. The motor axonal form of GBS occurs in epidemics during summer in China, and predominantly affects children. Similar clusters of patients with GBS, especially associated with antecedent Campylobacter jejuni infection, have been reported from Mexico, Columbia, Japan and from Patiala, India.

Preceding infections, most commonly of the respiratory tract or the gastrointestinal tract, are frequent in patients with GBS. Less commonly, GBS follows other infections such as mycoplasma, cytomegalovirus, Epstein Barr virus, vaccinia, variola, hepatitis A and B, rubella, influenza A & B, Coxsackie, and Echo virus. More recently, the HIV virus has also been associated with GBS though there are no documented cases of this in children.

Pathogenesis and Pathology

Demyelinating form of GBS: Our understanding of the pathogenesis of GBS is based upon studies on biopsy/autopsy specimens, serum and from studies on an animal model of the experimental allergic neuritis (EAN). The model of EAN was first created by Waksman and Adams in 1955 when they injected peripheral nerve tissue and Freund's adjuvant in rabbits and the rabbits developed an acute paralytic illness associated with demyelination and mononuclear cell infiltration in the nerves. The EAN can be induced in all vertebrates but Lewis rats are the most commonly used animals. The changes in the nerve can be induced by injecting the nerve extract, P2 protein (component protein of myelin), polypeptides derived from the P2 protein polypeptides, P0 protein with galactocerebroside, or by the passive transfer of the sensitized T-cells in naive animals. The pathological changes in animal models of EAN are similar to those seen in what we now recognize as the AIDP variant of GBS which shows mononuclear infiltration (composed mainly of lymphocytes) and macrophage-mediated demyelination in a patchy, multifocal distribution involving a fascicle or a cluster of nerves. The axons stripped of their myelin sheaths are generally spared, except in severe forms in which Wallerian degeneration may occur. The inflammatory foci are around small venules in the nerves, though a few scattered mononuclear cells may be seen within the nerve fascicles. Plasma cells and lymphoblasts are seen in these foci roughly one week after the onset of illness. The lymphocytic infiltrates are composed of both CD 4+ and CD8+ cells with variable number of macrophages. The histological changes in human nerves are very similar to changes seen with EAN in Lewis rats.

The macrophages are the principal cells that produce demyelination in GBS. Ultrastructural studies have shown macrophages beneath the basement membranes of the nerves surrounding myelin lamellae and stripping of the myelin. The macrophages advance their processes along the minor dense lines of the myelin lamellae and through gaps in the sheaths. Another form of demyelination occurs through vesicular degeneration of the myelin sheath whereby whole segments of myelin sheath separates along the major dense lines. The vesicular form of demyelination is not seen frequently and is thought to be mediated by complement-mediated mechanisms.

These pathological changes and their similarity to EAN, the association with infectious agents, and the response to agents that modify immune response confirm that GBS is an immune-mediated disease. The evidence for autoimmune pathogenesis is even more compelling with some of the variants.

Axonal form of GBS: The existence of the "axonal " form of GBS was known for a long period. It was generally felt to represent the severe form of GBS, where the axonal degeneration occurred secondary to severe inflammatory response in the nerve. The axonal degeneration was felt to be similar to the axonal damage seen in the severe EAN produced by myelin antigens. Several years ago, Feasby and colleagues made the then heretical proposals that some cases of GBS were due to primary axonal degeneration without preceding demyelination, and that the target antigen might lie on the axon. The patients typically had fulminant paralysis and had slow and usually incomplete recovery. The electrodiagnostic findings were dominated by changes compatible with Wallerian-like degeneration of motor and sensory fibers. They suggested that the primary target might be the axon rather than the Schwann cell or myelin. Recent autopsy studies...