

Review Article.

Acute Inflammatory Demyelinating Polyradiculoneuropathy (Guillain-Barre' Syndrome).

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INTRODUCTION:

Poliomyelitis eradication, a dream few years earlier, now a truth with flesh and bones. Almost all countries round the world had achieved this goal, and the Sudan is not at all behind schedule. To accomplish this glorious victory against poliomyelitis, the team working in the Children Teaching Hospital at Wad Medani, Gezira State had reported during the last three and a half years, 42 cases of acute flaccid paralysis (AFP). All of these cases were negative for polio-virus in the two stool samples taken within 48 hours of presentation, and none of them showed any clinical evidence of poliomyelitis 60 days after their initial presentation. Most of these cases had clinical features and investigations suggestive of Guillain-Barre' syndrome. This is the reason why the recent literature addressing this illness was reviewed here.

Guillain-Barre' syndrome (GBS) is an immune-mediated, inflammatory, demyelinating disorder of generalized peripheral nerves, that may lead to severe weakness.¹ It was first described in 1916 by Guillain, Barre, and Strohl, who also stressed the benign nature of the condition and its tendency to recover spontaneously. This was in contrast to the ascending paralysis described by Landry in 1859, which was supposed to have a poor

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prognosis. The eponym Landry-Guillain-Barre syndrome is used by some, as there were many deaths of respiratory insufficiency, since the initial report of GBS.

Despite its name no specific infective agent has yet been isolated from patients with this disorder of which, the aetiology remains obscure. An antigen antibody reaction following a non-specific virus infection has, however, been postulated to activate cellular and humoral immune mechanisms, and also triggers inflammation and demyelination. The finding

of a decreased T- suppressor cell response may be the link between the syndrome and its varied triggering actions.^{2,3}

A preceding infectious disease is recognized in 65% of cases 3 days to 6 weeks before the onset of demyelinating symptoms. Cytomegalovirus, Epstein-Barr virus, Human immunodeficiency virus, vaccinia virus, antecedent leptospiral infection and *Compylobacter jejuni* bacterial diarrhoea are recognized causes of prodromal illness preceding acute inflammatory demyelinating polyradiculoneuropathy.⁴ Polyneuritis may follow some vaccines.⁵

Patients with GBS and a preceding *Campylobacter jejuni* infection manifest a significantly more severe form of the disease. Gastrointestinal symptoms not always present before the onset of GBS. A higher incidence of antibodies against glycoconjugates such as GM1 and GM1a was found among these patients. There is cross reactivity between antigens from *C. jejuni* and the P2 protein of the peripheral nerve myelin, which may explain the pathogenetic connection between infection and GBS.^{6,7}

GBS is a relatively rare condition with a crude incidence of 1- 2 per 100 000 population all over the world annually. The annual incidence is 0.8 per 100,000 in school-age children.⁸ The disease affects mainly this age group of children, but even young infants may be affected. The youngest reported patient was 4 month old and presented with advanced hypotonia.⁹ The illness is more common in boys with a male to female ratio of 1.5.¹⁰ Most studies showed only minor seasonal variations, except in northern China where there is yearly summer epidemics.^{11, 12}

CLINICAL PRESENTATION:

Symptoms often begin 1-3 weeks after a viral upper respiratory or gastrointestinal infection, immunization, abortion or surgery.¹³ Muscle pain may be the initial manifestation of the disease in children, involving the anterior and posterior thighs, buttocks and lower back.¹⁴ A typical patient with GBS reports a numb or tingling sensation in the arms and legs.

After a latent period of a few days or a few weeks there is sudden onset of weakness (*Landry's paralysis*). The muscle weakness is usually an ascending, symmetric and rapidly progressive. The pattern of weakness in extremities may be helpful in differential diagnosis, especially in early stages of the disease. Upper extremities weakness is mainly distal while it is mainly proximal in the lower extremities, with predilection for trunk muscle involvement, that is quite unusual in other types of polyneuropathy.¹⁵

Paralysis is maximal by one week in more than 50% of the patients, and by one month in more than 90%. Hyporeflexia or areflexia is invariably

present. Preservation of reflexes in a severely weakened patient should seriously challenge the diagnosis of GBS.⁶

A patient with a severe case of GBS may proceed rapidly within 24 hours of onset to complete flaccid quadriplegia including; bulbar paralysis and inability to breathe, swallow, and speak. Respiratory paralysis severe enough to necessitate mechanical ventilation is common. Ten to twenty per cent of patients require artificial respiration. Ventilatory support may be necessary even early in the course of the disease. Eighty percent of patients make an excellent recovery.¹

Meningeal irritation is rare in adults but occurs in almost one third of children.¹⁶ Facial palsy may be the only manifestation, in over 50% of patients and 10% have extra-ocular muscle paralysis. Other cranial nerves involvement is rare. Bladder dysfunction, mental alterations, headache and ataxia may be accompanying features. The patient may have mild impairment of distal sensation, but significant sensory loss is not seen.⁵

Many patients also have transient symptoms of autonomic dysfunction e.g. blurred vision, cramping abdominal pain, postural hypotension, labile hypertension, cardiac arrhythmia, disturbed sweating, impaired pulmonary function, bladder and bowel incontinence.⁸

DIAGNOSIS:

The cerebrospinal fluid (CSF) often shows a characteristic abnormality, with increased protein concentration and lack of inflammatory cellular response, usually less than 10 lymphocytes/mm³ (*cytoalbuminologic dissociation*). These parameters may, however be normal in the first week of the disease.¹ Glucose is normal, but gamma globulin may be elevated.

CoSkum et al evaluated the value of serially obtained spinal magnetic resonance images (MRI) in the diagnosis and clinical follow-up of childhood GBS, and the time period for resolution of contrast enhancement during the course of illness. They suggested the use of MRI as a supplementary diagnostic modality in diagnosing GBS, especially when the clinical and electrophysiological findings are equivocal. Follow-up images may play a role in predicting the clinical course of the disease.¹⁷

PATHOLOGY:

The pathological features of GBS are distinctive and characteristic. Peripheral nerve biopsy may show multifocal areas of demyelination and mononuclear cell infiltration.³ Oedema of variable grades occurs, associated with endoneural lymphocytic and macrophages cells infiltration. Electron microscopy can show invasion of Schwann cells basement

membrane by microphage resulting in focal demyelination.^{18, 19} Secondary Wallerian degeneration with axonal loss eventually supervenes.²⁰ Complement fixing antibodies to peripheral nerve myelin may be demonstrated in some cases.^{3, 21}

ELECTROPHYSIOLOGICAL STUDIES:

Electrophysiological studies evaluation provides evidence for peripheral nerve demyelination. However, in the last few years it has become evident that a predominantly axonal pattern may also underlie GBS.²⁰

Electromyography (EMG) and nerve conduction velocities studies (NCS) may reveal marked disruption of saltatory conduction along the myelinated axons resulting in reduction and block of motor and sensory conduction velocity, this explains the flaccid weakness and impaired sensation in GBS. These electrophysiological changes do not correlate with the severity of motor disability during or after the acute phase of the illness.²²

Younger children less than 10 years of age have greater reduction of motor nerve conduction velocities than older children. Higher antibody levels against peripheral nerve myelin during the first week of the disease associated with more profound reduction.²³

*The following are the most common electrophysiological findings in children.*²⁴

- * Distal motor latency that prolonged to more than 150% of normal.
- * Nerve conduction velocities are reduced to 70% below normal.
- * Compound action motor potentials are significantly reduced with prolonged terminal dispersion.

DIFFERENTIAL DIAGNOSIS:

The condition must be differentiated from other causes of acute flaccid paralysis (AFP) evolving over hours or a few days. Acute anterior poliomyelitis in which the preceding meningitic illness is usually more severe and the paralysis is more patchy and less symmetrical.²⁵

Other (AFP) may follow paraviral or postviral immunologically mediated diseases like acute transverse myelitis,²⁶ or follows affection by toxins like diphtheria.²⁷ Neuromuscular junction may be blocked by tick toxin or botulinum toxin. Tick paralysis usually occurs seasonally (spring and summer), and usually found in the occipital hair, its removal is curative. Paralysis due to botulism occurs more commonly under age one, history and laboratory investigations are diagnostic.²⁸ Paralysis will rarely be due to metabolic (*periodic paralysis*) or inflammatory muscle disease (*myositis*).

Persistent asymmetry of weakness, persistent bowel or bladder dysfunction or CSF polymorphonuclear leucocytosis, are features that cast doubt on the diagnosis of GBS. The diagnosis of GBS is ruled out by history, clinical, or laboratory findings suggestive of; hexane abuse, acute intermittent porphria, diphtheritic infection, lead neuropathy; or other causes of acute flaccid paralysis.

MANAGEMENT:

The main stay of treatment is supportive, the aim being to prevent such complications as respiratory failure and vascular collapse. Patients who are severely affected and need mechanical ventilation are best managed in intensive care units, where facilities are available for monitoring and assisted respiration. Careful attention to nutritional, fluid and electrolyte balance is necessary. Psychological support from parents and doctors is very essential as the child is still mentally alert despite his paralysis and mechanical ventilation may be frightening.

Plasmapheresis (plasma exchange) is of proven benefit and may be very effective if started early within the first seven days of onset.^{29,30} It is however, expensive, time consuming, and not risk free; it should therefore only be offered to severely affected patients in the progressive phase of their illness, with inability to walk unaided, with significant reduction in respiratory capacity, or have bulbar insufficiency.¹⁴ Lamont et al; have demonstrated a shortened recovery time in five out of six children aged 5-15 years, treated with plasmapheresis.³¹ Epstein and Sladky in a controlled retrospective study showed faster recovery of independent ambulation in nine children who received plasmapheresis.³²

Intravenous immunoglobulins may shorten the course of the illness.³³ Plasma exchanges and intravenous immunoglobulin (IVIg) are the gold standard therapies for the demyelinating form and probably for the other variants. However, there is no documented benefit of using both plasma exchange and immunoglobulins therapies.³⁴

In the past, corticosteroids were often prescribed for patients with progressive downhill course, but recent studies have shown that these agents may affect the outcome adversely and even increase the time for recovery.²⁶

PROGNOSIS:

The prognosis is usually excellent for spontaneous recovery. However, the rate of progression, degree of impairment, and time for improvement vary greatly.²⁸ The mortality rate approaches 5%, with 10% to 15% remain permanently disabled.¹ The recovery does not continue after 2 years from onset.³⁵ At least 40% of children make a complete recovery 2 to 18 months after the disease onset. Whereas, one fourth of affected children have incomplete recovery.³⁶ In a few patients there may be relapses.³⁷ Both acute mortality and long term- disability in GBS seem to be related to an axonal involvement and a Hughes grade $>$ or $=2$ at nadir.³⁸

The predictors of severe disease and poor prognostic features are;

- * Old age $>$ or $=$ 50 years.
- * Rapid onset of symptoms
- * The need for artificial ventilation.
- * Severely decreased compound muscle action potentials ($<20\%$ of normal).
- * Acute axonal form of the disease.
- * Failure to improve after 3 weeks of reaching the peak deficit.
- * Preceding illness with C. jejuni.

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