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Post Infective Polyneuritis - Guillain Barre Syndrome (GBS): A Retrospective Study From 1988-1993

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SUMMARY

At Shaikh Zayed Hospital Lahore Pakistan, we reviewed 20 patients with Guillain Barre Syndrome (GBS) who were admitted over a period of five years between 1988 and 1993. The basic purpose of study was to assess the incidence, presenting features, time of stay in the hospital and role of plasmapheresis. Out of twenty patients 13 were males (65%) and 7 were females (35%). Almost all were preceded by non specific illness e.g sore throat or gastroenteritis followed always by weakness in the lower limbs. Average stay in hospital was 37.2 days (Shortest stay was 4 days and longest stay was 372 days). Five patients died therefore mortality was 25%. Out of remaining fifteen patients three (20%) received plasmapheresis (a total exchange of 10-12 litres of plasma) and all three (100%) showed quick and dramatic response with complete recovery. In comparison with the higher mortality rate over the years is due to early and correct diagnostic facility, ICU care and development in modern management techniques e.g immunoglobulins and plasmapheresis. However other neuromuscular disorders e.g poliomyelitis (especially in children) and motor neurone disease and electrolyte disturbances e.g severe hypokalaemia should carefully be excluded.

INTRODUCTION

Acute idiopathic polyradiculitis, Guillain Barre syndrome (GBS) is one of the most severe forms of paralysis[1]. It affects both sexes and becomes more common with advancing years and has a uniform world wide annual incidence of 1-2 per 100,000. It affects people of all races and ages. The etiology of GBS is believed to be autoimmune[2]. Although precise machanism is unknown. Plasmapheresis is presumed to be effective by removing circulating antibodies[3].

Many organisms e.g cytomegalovirus, campylobacter mycoplasma and Epstein Barr Virus have been implicated. There have been reports of GBS following surgery, influenza and hepatitis immunization[4]. The major presenting feature is progressive weakness usually affecting the lower extremities, trunk and even cranial nerves. Universal areflexia is the general rule, although in rare cases deep tendon reflexes are preserved but are very diminished. Respiratory muscle weakness is the most dangerous manifestation of this disorder and occurs approximately in one third of patients[5]. Bulbar and facial nerve palsy (unilateral or bilateral) occur in one third of patients.

Some paresthesia is frequently seen early in the course of the illness. Pain is a frequent complaint in GBS. Autonomic neuropathy both involving sympathetic and parasympathetic systems is common and potentially life threatening[6].

Other variants of GBS e.g Miller Fisher syndrome (ophthalmoplegia, ataxia, and areflexia) is one of the most drammatic[7] forms of GBS.

Diagnosis is made by examining cerebrospinal fluid (CSF) for raised protein (1-3 g/l) and electrophysiological studies e.g electromyography (EMG) and nerve conduction studies (NCS).

The major pathological change in GBS is discrete multifocal demyelination scattered throughout peripheral nervous system which are associated with mononuclear inflammatory cell infiltrates[8].

Thus cell mediated immune mechanisms are involved in the pathology of GBS. Koski and others[9,10] detected antiperipheral nerve myelin (anti-PNM) antibodies in the serum of patients with acute phase GBS. It is highest in the onset of disease and declines lateron. Treatment is essentially supportive. Steroid therapy is controversial although some studies[11,12,13] failed to show any beneficial effects.

Plasmapheresis is used to remove possible antibodies. Role of immunoglobulins in a recent study[14] is quite encouraging as compared to plasmapheresis but main disadvantage is its high cost.

RESULTS

Total number of patients included in this study were those who were admitted to the acute medical wards and intensive care unit through accident and emergency department from 1988 to 1993 (Five years).

A total of 20 patients were included. Table 1 shows male and female patients.

Table 1: Distribution of cases sex wise.

Sex	*No. of Patients*	*Percentage*
Male	13	65
Female	07	35
Total	**20**	**100**

The ages of patients also were quite variable. The youngest was eight year old while the oldest was of eighty years of age. Table 2 shows age distribution in our cases (Table 2).

Distribution of cases was almost same i.e around four cases per year but overall observation was that more patients were admitted and diagnosed as GBS during the later years of the study. The common presenting features are listed in Table 3.

Looking at these results it appears that significant number of patients developed preceeding symptoms of fever sore throat and even pneumonia. One patient had pulmonary tuber culosis and one developed GBS after being vaccinated for hepatitis. However weakness of lower limbs was experienced by almost every patient which was progressive and ascended upwards either gradually or more rapidly to involve the upper limbs and other vital organs.

Table 2: Age distribution.

Age (years)	*No. of Patients*	*Percentage*
0 - 10	2	10
11 - 20	6	30
21 - 30	4	20
31 - 40	3	15
41 - 60	3	15
61 - 80	2	10
Total	**20**	**100**

Table 3: Number of patients with main presenting features.

Symptoms	*No. of Patients*	*Percentage*
1. Fever due to upper respiratory tract infection.	8	40
2. Vague abdominal symptoms e.g vomiting and diarrhoea	4	20
3. Weakness of both lower limbs.	20	100
4. Difficulty in swallowing.	8	40
5. Difficulty in breathing.	10	50

The swallowing difficulty (dysphagia) was due to involvement of bulbar muscles. Respiratory difficulties were due to involvement of the diaphragmatic muscles and patient needed ventilatory support either through endotracheal intubation or tracheostomy. The stay of patients in the hospital varied from few days to more than a year (only one patient) (Table 4).

The young boy who stayed in the ICU for more that one year was advised a portable ventilator for use at home, as the recovery in this case was not as desired and he had permanent damage to respiratory muscles.

The complications which could be anticipated

during the course of illness were observed closely (Table 5).

Table 4: Stay in the hospital.

No. of days	*No. of Patients*	*Percentage*
0-10 Days	4	20
10-20 Days	8	40
21-30 Days	3	15
01-03 Months	2	10
04-06 Months	2	10
07-12 Months	1	5
Total	**20**	**100**

Table 5: List of complications.

Complications	*No. of Patients*	*Percentage*
1. Respiratory: Cough, difficulty in breathing.	7	35
2. Cardiovascular: Autonomic		
i) Postural Hypotension	4	18
ii) Dysrrhythmia (Bradycardia)	3	16
3. Deep vein thrombosis	0	0
4. Bed Sores	2	10
5. Bladder involvement: (catheterized)	16	80
6. Gestrointestinal:		
Ileus	3	15
Constipation	10	50
Diarrhoea	2	10
7. Nutrition:		
Oral	14	70
N/G (Nasogastric)	5	25
TPN (total parenteral nutrition)	1	5
8. Metabolic:		
Hypokalemia	3	15
Acidosis	3	15
9. Haematological:		
Anaemia	4	20

Other complications include psychological aspect e.g mood states including demoralisation, sadness, fear, anxiety,feeling of hopelessness and isolation.

Besides a typical history, the features required for diagnosis were follows:

a) Progressive motor weakness of more than one limb.
b) Areflexia or marked hyporeflexia
c) Rise in the CSF proteins and pleocytosis.

In this study interesting facts were observerd abort CSF proteins. Initially the CSF proteins were with in normal range but after few hours (48-72 hours) the CSF protein increased. Maximum rise was upto 300 mg (0.3 G) per dl in one of the cases. However rise upto 2 grams/dl is not unusual.

The management of these patients included following.

a) All received supportive therapy i.e skin, mouth, eye and bladder care. Making sure that extra care is taken for IV lines and CVP lines.
b) Drugs were given for pain relief and major psychosocial issues, e.g analgesics and anti-depressants.
c) No patient was given any steroids orally or parenterally in view of the fact that previous studies had failed to show any drammatic or significant improvement.
d) Plasmapheresis (total exchange of 10-12 litre) was tried in three patients and all showed a good and quick response with in four days with complete recovery (100%) of quadriplegia and facial weakness.
   i) One had quadriplegia and bilateral facial palsy.
   ii) Other had unilateral facial palsy and paraplegia.
e) Almost all patients had regular physiotherapy in the ICU which was continued on the wards too. Passive movements and stretching of the limbs were carried out by the trained personnels to maintain the range of movements. Help of splinting particularly of ankle and knees was taken to prevent contractures.

Out of 20 patients 5 died during their stay in the ICU and/or wards and the mode of death was mostly cardio-respiratory arrest. Overall mrtality was 25%.

Most of the patients were transferred to their respective wards either paediatric or medical wards for further rehabilitation after initial intensive

management in the ICU.

Patients who had regular follow-up were seen in the out patient departments. Only four out of 15 patients had some residual deficit in the form of grade-IV weakness and some wasting of the muscles of the extremities. Patients who had recieved plasmapheresis showed no residual neurological deficit.

DISCUSSION

Historical aspects of the GBS are traced from its first clear discription in 1916. Although a similar description in 1892 was by Osler[15]. Bradford, Bashford and Wilson[16] reported 30 patients with this disorder in 1918 in a report entitled "Acute infective polyneuritis".

It is important to lay down recommended diagnostic criteria (adopted from Asbury et al.[26] (Table 6).

It is also important to mention about GBS grading scale[27]

Table 6: Diagnostic criteria.

Required criteria
1. Progressive weakness of more than one limb.
2. Duration less than 4 weeks.
3. Absence of other cause of acute neuropathy.

Relative Criteria
1. Symmetrical weakness.
2. Mild sensory signs.
3. Cranial nerve involvement (7th nerve).
4. Autonomic dysfunction.
5. Vasomotor instability.
6. Absence of fever.
7. CSF showing elevated protein.

Neurophysiology
Slowing of nerve conduction suggestive of demyelination.

TABLE 7: GBS grading scale.

0. Healthy
1. Minor signs or symptoms.
2. Able to walk 5 meters without assistance.
3. Able to walk 5 meters with assistance.
4. Bed or wheel chair bound.
5. Requires assisted ventilation.
6. Dead.

Shaikh Zayed Hospital is a tertiary referral centre for most of the cases which can account for less number of patients admitted here during five year span. This may also be due to the fact that majority of patients are treated by quacks Hakims and local practitioners and lack of appropriate diagnosis increases the complications and when they are referred for ICU management most of the precious time period has already been lost. Although most patients with GBS recover spontaneously.

The three patients who had to be given plasma exchange immediately came to the hospital directly and assessed carefully for this mode of treatment. The use of this new medical treatment includes the use of venous catheters which are kept at inguinal or neck region, anticoagulation solutions to keep catheter open, BP, pulse and respiration monitoring as well as[17] electrolyte, fluid and acid base control.

A total of 200 to 250 ml of plasma per kg body weight is exchanged in 10-12 days. For this we need at least 40 to 50 donors of the same blood group and the kit is required. There are no significant difference in the nature of frquency of complications. These patients had more frequent episodes of hypotension.

The significant improvements started in ten days to 14 days and patient was able to breath spontaneously and move limbs. Plasmapheresis therefore significantly benefited patients acutely ill with GBS. However, plasmapheresis has less beneficial effect on patients with a longer interval between onset of disease and actual treatment.

Possible complications during plasmapheresis can be as follows:

1. Hypotension
2. Hypertension
3. Cardiac dysrrhythmias
4. Infection
5. Pulmonary embolus
6. Thrombophlebitis
7. Electrolyte imbalance.

Use of normal saline or albumin rather than FFP has decreased risk of infection and transfusion reactions[3].

Plasmapheresis for childhood GBS is a safe and effective treatment to shorten the time to recovery. Perhaps the most important benefit of plasmapheresis is to shorten the length of mechanical ventilation. Studies[19] have shown that

plasmapheresis is safe in children as young as 8 months.

Plasmapheresis is also performed for treatment of certain intoxications, metabolic diseases and disease presumed to be immunologically mediated and not responding to other conventional therapies[20]. Half of the 20,000 to 30,000 plasmapheresis performed annually in the United States are on patients with neurological disorders[20].

Early completion of plasmapheresis may be followed by relapse which may respond to additional exchanges[21]. In the North American study[22] there was a better outcome associated with the use of the continuous flow plasmapheresis when compared with the intermittent flow mode [3]. This proceedure is quite costly, risky and causes patient's discomfort therrefore it is not justified in mildly affected patients[23]. However in a newly diagnosed patient the clinical course may not be clear. Delay in early plasmapheresis may be harmful as these patients may develop serious problems. Therefore these patients should be observed closely. If weakness develeops rapidly or patient is unable to walk plasmapheresis should be instituted. Patients with stable disease for more than one week or patients with mild course are not offered plasmapheresis.

There is a risk that plasmapheresis may worsen the disease by inducing a rebound antibody production[21]. This consideration gave reason to combine steroid therapy in the past but it was of no use and had to be abandoned[25].

Other important modality of treatment is intravenous imunoglobulins IVIg. This treatment is given if plasmapheresis is contraindicated e.g in severe sepsis or cardiac instability. A large Dutch multicentre trial[11] has been completed comparing IVIG and plasmapheresis. In this trial 0.4 g/kg/day of pooled gamma globulins were given for at least 2 weeks. Actual mechanism is not known. Both specific and non-specific mechanisms have been suggested including competitive blockade of macrophages by preferential binding of IgG-coated RBCs, and antiidiotypic binding of autoantibodies presumed to be involved in the pathogenesis of disease[28]. At present, the synergistic effect of IVIg with other immune modalities is being studied which might be superior.

Other modalities like methotrexate and cyclophosphamide are of no use. There has been long discussions on the use of high dose steroids but its use in the GBS currently lacks justification as supported by quite a few multicentre large controlled studies[11,12,13].

GBS can occur in pregnancy and mortality rate is double in pregnant patients[29]. Hurley and others[30] reported three cases in 1991 in which aggressive plasmapheresis in pregnancy prevented the need for ventilatory support as there is increased susceptibility of the pregnant patient to respiratory compromise. Diaphragmatic pacing might be helpful[31].

It is also important to keep in mind other conditions which can mimic GBS e.g severe hypokalaemia resulting in muscular weakness. It is very difficult to differentiate in children with GBS and poliomyelitis. However there is a long list of differential diagnosis.

The mortality in the UK and France is slightly more than 10% where as in the USA it is only 3%. Full recovery is expected in 70-75% of patients, 20% are left with residual disability and 5-7% relapse.

Forty percent of patients with GBS reach a nadir within one week, 70% within 2 weeks, 86% with in 3 weeks and 100% within 4 weeks. One third begin to improve with in 2 weeks of attaining the nadir, one third with in 4 weeks and most of those remaining with in 8 weeks. Median time to walk unaided is nearly 3 months without the benefit of plasma exchange and slightly less than 2 months with plasma exchange. Poor prognosis is associated with rapid onset (becoming bedbound with in one week) need for ventilation, prolonged plateau phase, old age and small muscle action potentials evoked by stimulation of distal nerves.

CONCLUSION

GBS in quite common but is misdiagnosed and therefore referral to specialised centres is delayed. Incidence is more in males as compared to females and usual outcome is good but few cases may not recover at all. History taking and clinical examination is the most important. One should if possible with a cell separator machine if available try for plasmapheresis as it results in remarkable recovery. Immunoglobulins are very expensive. Steroids have no role in management of GBS.

GBS should be carefully differentiated from hysteria locked in syndrome, brain stem lesions, spinal cord lesions and neuromuscular transmission defects (myasthenia and botulism). Other include

drugs, toxins, alcohol, vitamin deficiencies, lyme disease, SLE, sarcoidosis and polyarteritis nodosa.

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