Clinical and Neurophysiological Pattern of Guillain-Barré Syndrome in Kuwait

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Key Words

Guillain-Barré syndrome · Acute inflammatory polyradiculoneuropathy · Acute idiopathic demyelinating polyradiculoneuropathy · Acute flaccid paralysis · Middle East · Mediterranean · Kuwait

Abstract

Objective: To study the clinical and neurophysiological pattern of Guillain-Barré syndrome (GBS) in Kuwait. **Materials and Methods:** The clinical records of consecutive GBS patients admitted to Ibn Sina Hospital, Kuwait, during a 7-year period between 1997 and 2003 were analyzed. **Results:** Of the 41 cases, 77% were male. The majority of the cases presented during the winter months and a preceding infection was reported in two thirds of them. Proximal lower limb (LL) weakness was the predominant clinical presentation. Nerve conduction studies (NCS) demonstrated a demyelinating pattern in 70%, an axonal pattern in 15%, mixed type in 5% and no abnormality in the remaining 5%. The majority of the patients (73%) improved with one course of intravenous immunoglobulin (IV IG). Mean recovery time (MRT) was 4.4 weeks. Delayed recovery (MRT $\geq$ 6 weeks) was noted in patients with predominant distal weakness in the LL (MRT 7.8 weeks; $p = 0.001$), proximal weakness in the upper limb (UL) (MRT 6 weeks; $p = 0.005$), autonomic disturbance (MRT 6.5 weeks; $p = 0.05$), and axonal type GBS (MRT 6 weeks; $p = 0.001$). **Conclusion:** The presence of predominant distal weakness in LL, proximal weak-

ness in UL, autonomic disturbance and axonal pattern in NCS predict a poor outcome. Hence we recommend early immunomodulatory therapy in patients presenting with these features.

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Introduction

Guillain-Barré syndrome (GBS) is an autoimmune polyradiculoneuropathy, the most common cause of acute flaccid paralysis in all age groups after the polio era. GBS is not a disease with variations but a group of syndromes with distinctive subtypes depending upon the site of the immune attack. The major subtypes are acute idiopathic demyelinating polyradiculoneuropathy if the primary target of attack is the myelin sheath, acute motor axonal neuropathy (AMAN) if it involves motor axons at the internodal area, and acute motor sensory axonal neuropathy (AMSAN) if both motor and sensory axons are affected [1]. The triad of ataxia, areflexia and ophthalmoplegia, known as Miller Fisher syndrome (MFS), is due to predominant (demyelinating) attack on extraocular motor nerves and proprioceptive sensory fibers. The incidence of these 4 major subtypes differs from region to region with acute idiopathic demyelinating polyradiculoneuropathy predominating in the West, AMAN in China, and MFS in Japan and Taiwan [1]. All of them are characterized by acute atonic areflexic motor weakness with albumino-cytological dissociation. With the ex-

ception of MFS the other subtypes cannot be easily distinguished by clinical features but can be differentiated by electrophysiological characteristics [1]. The natural course of the disease is the progression of motor weakness (up to 4 weeks) that reaches the maximum deficit (nadir) and remains at nadir for several weeks before improvement starts [2]. Early introduction (within 2 weeks of onset) of immunomodulatory therapy can arrest the progression and hasten the recovery. There are no proper clinical studies about adult GBS in the Gulf region. This study was carried out to analyze the clinical and neurophysiological pattern of GBS in Kuwait.

Materials and Methods

Ibn Sina Hospital is the only tertiary neurological care center in Kuwait that receives most of the GBS cases. The clinical records of all the GBS patients admitted to the hospital between January 1997 and December 2003 were analyzed. The patients who did not satisfy the Asbury and Cornblath [3] criteria were excluded from the study. The functional status of the patients was assessed using a modified objective scale of Miller published by Ammache et al. [4]. After clinical assessment, all the patients underwent lumbar puncture (LP) and nerve conduction studies (NCS) using standard techniques [5]. The Italian Guillain-Barré Study Group electrodiagnostic criteria were used to classify the NCS as demyelinating, axonal or mixed type [6]. Immediately after diagnosis, every patient was given intravenous immunoglobulin (IV IG) 0.4 g/kg body weight for 5 days if the functional grading was more than 2 on Miller's scale. If the weakness persisted over 10 days after the first course of IV IG, a second course of IV IG was given. If the functional grade deteriorated, the patient was subjected to plasma exchange (PE). The recovery time was calculated as the time the patients began to improve by one grade on Miller's scale from nadir. Since the deterioration or recovery may not be so dramatic over days, we used weeks as a scale of measure. From the mean recovery time (MRT), faster ($MRT - 1\text{ SD}$) and slower ($MRT + 1\text{ SD}$) recoveries were defined. The significance of MRT in any subset was taken into consideration if it involved more than 10% of the study population and was analyzed using Student's *t* test.

Results

Forty-one (41) patients satisfied the diagnostic criteria; 30 males and 11 females with a male to female ratio of 2.7:1. The mean age was 41 ± 15.9 years (range 16–72 years). The distributions of age, sex and nationality are given in table 1. Most of the admissions (59%) were during the winter months of November to March. Twenty-seven (66%) patients gave history of preceding illness of which respiratory illness (44%) was the commonest. Of 7 (17%) patients with gastro-intestinal problems, 6 had

Table 1. Age, sex and nationality distribution of patients with GBS and their MRT

Age	Kuwaiti n = 21		Non-Kuwaiti n = 20		Total n = 41		MRT n = 41 weeks
	M	F	M	F	n	%	
<20	2	–	1	–	3	7	3.3
20–29	1	3	3	–	7	17	4.6
30–39	3	–	5	2	10	25	4.5
40–49	1	2	6	1	10	25	3.9
50–59	–	1	2	0	3	7	6.0
60–69	3	2	–	–	5	12	5.4
>70	3	–	–	–	3	7	3.3
Total	13	8	17	3	41	100	4.4

diarrhea and 1 nonspecific abdominal pain. No prior illness was reported by 14 (34%) patients. The patients were admitted within 1 day to a maximum of 31 days after the onset of the illness with an average of 8.3 days.

Clinical Features

Of the 41 patients, three (7%) had MFS. With the exception of 1 MFS patient, all the others had motor weakness. In most of them, the weakness started in the lower limbs (LL), then ascended to involve the upper limbs (UL). Combined involvement of both proximal and distal muscle was predominant in the UL, whereas in the LL predominant proximal muscle weakness was noted. The deep tendon reflexes were absent in 38 (93%) patients, sluggish in 2 (5%) and present in 1 (2%) throughout the course of the illness. There were no sensory complaints in 18 (44%) patients at presentation. The patterns of sensory disturbance and motor weakness are given in table 2. The other clinical features like cranial nerve affection, autonomic disturbance and respiratory failure are summarized in table 3. Ophthalmoplegia occurred in all 3 MFS and in 1 GBS patient. Facial weakness was the commonest cranial nerve affection occurring in more than half of the patients. Bulbar weakness was noted in 6 patients (15%) and 5 of them developed autonomic disturbance and respiratory failure leading to prolonged ventilatory support and delayed recovery. In addition to these 5 patients, another 2 needed ventilatory support for a few hours and did not have either autonomic disturbance or bulbar palsy. Of the 7 patients requiring ventilatory support, 3 were Kuwaitis (2 male and 1 female) and 4 were of other nationalities (3 male and 1 female) and all of them of different ages. The commonest autonomic

Table 2. Patterns of motor weakness and sensory disturbances and the respective MRT in patients with GBS

Clinical features	Signs/pattern	Patients		MRT weeks
		n	%	
Evolution of motor weakness		40	98	4.5
	Ascending	37	91	4.5
	Descending	3	7	4.3
Weakness in UL		40	98	4.5
	Proximal > distal	7	17	6.0
	Distal > proximal	10	25	4.5
	Distal = proximal	23	56	4.0
Weakness in LL		40	98	4.5
	Proximal > distal	37	88	4.1
	Distal ≥ proximal	4	10	7.8
Sensory loss		23	56	4.7
	Paresthesia only	3	7	3.7
	Joint position sense only	5	12	4.2
	Glove and stocking only	4	10	5.8
	All 3 together	2	5	6.5
	Any combination of above	9	22	4.4

Table 3. Cranial nerve affection, autonomic disturbance and breathing pattern of GBS patients and the respective MRT

Clinical features	Signs/pattern	Patients		MRT weeks
		n	%	
Cranial nerve involvement	Ophthalmoplegia	4	10	3.8
	Unilateral facial involvement	1	2	5.0
	Bilateral facial involvement	20	49	4.3
	No facial involvement	20	49	4.6
	Bulbar palsy	6	15	5.5
Breathing pattern	Ventilatory support	7	17	6.1
	No ventilatory support	34	83	4.1
Autonomic disturbances		9	22	5.6
	Labile hypertension alone	3	8	4.6
	Retention of urine alone	1	2	5.0
	Both together	5	12	6.2

disturbance was a combination of labile hypertension and urinary retention. One patient had tachycardia and none developed gastric disturbance or pulmonary edema.

Laboratory Features

Most of the patients had undergone LP. Three patients refused the test. In 11 of 12 patients, in whom the CSF protein was normal, the study was performed within 2 weeks of onset of the illness. The albumino-cytological dissociation was noted in 68%, with CSF protein elevation in 26 patients (table 4); mean value 1.215 and highest value 6.149 g/l; the mean CSF cell count was <1 cell/μl. Among MFS patients 1 had elevated CSF protein and

demyelinating type NCS and the other had normal CSF protein and NCS.

Forty of 41 patients had undergone NCS. The most commonly encountered neurophysiological abnormalities were absent or prolonged F wave: 90%, prolonged distal latency: 80%, absent H reflex: 76%, delayed nerve conduction velocity: 73%, partial or complete conduction block: 63%, abnormal blink reflex: 60%, reduced compound muscle action potentials (CMAP): 38% and abnormal sensory nerve action potentials (SNAP): 28%. Demyelination was the predominant type in the neurophysiological work-up followed by axonal type (table 4). Of the 6 patients with axonal forms, 3 had either absent or low

Table 4. Laboratory features of the disease with respective MRT

Investigation	Features	Patients		MRT weeks
		n	%	
CSF	No cells	29	70	4.5
	Less than 10 cells/ μ l	9	22	4.0
	Protein normal (<0.45 g)	12	29	4.4
	Protein 0.45–1 g	9	24	4.1
	1–2 g	10	26	4.1
	2–3 g	5	13	5.0
	>3 g	2	4	5.5
Nerve conduction	Demyelination type	28	68	4.4
	Axonal type	6	15	6.0
	Mixed type	2	5	3.5
	H reflex abnormality alone	2	5	3.5
	Normal	2	5	3.0

SNAP, which characterizes the AMSAN variant and the other 3 had normal SNAP, typical for the AMAN type.

Treatment and Outcome

Thirty-nine of 41 patients received IV IG. One patient was admitted and given IV IG on the day of illness onset; for two patients (5%), IV IG administration was delayed up to the 12th and 13th day of admission because of the atypical progression of their illness. Of the 6 patients with delayed admission, 3 received IV IG in the 3rd week and the other 3 in the 4th week after the onset of the neuritic symptoms. Recovery was accordingly delayed in these patients.

Of the 39 patients, 30 (77%) improved with one course of IV IG, 4 (10%) required a second course after an interval of 10 days and 5 (13%) deteriorated rapidly and required PE. Upon initiation of the treatment, disease progression was arrested, the duration of the plateau phase was shortened and the recovery started in most of the patients (table 5). In 9 patients, the progression continued up to 4 weeks, and 4 of them required ventilatory support and PE. Two (5%) patients, in whom the plateau phase was prolonged for more than 2 weeks, showed a delayed recovery. In 2 (5%) patients there was no plateau phase and they recovered early. No deterioration was noted, once the improvement started from nadir. No acute relapses (within 2–3 weeks of treatment) were noted in our patients.

The MRT was 4.4 ± 1.6 weeks and fast and slow recovery times were 2.8 and 6 weeks, respectively. The MRT was 4.3 weeks for males and 4.7 weeks for females.

Table 5. Treatment and outcome of the disease with respective MRT

Outcome	Features	Patients		MRT weeks
		n	%	
Arrest of progression	1st week	11	27	2.8
	2nd week	11	27	3.6
	3rd week	10	24	4.9
	4th week	9	22	6.9
Plateau duration	1 week	34	83	4.1
	2 weeks	3	7	6.8
	>2 weeks	2	5	8.0
Improvement	In 2nd week	2	5	2
	In 3rd week	15	37	3
	In 4th week	6	15	4
	In 5th week	10	24	5
	In 6th week	3	7	6
	In 7th week	1	2	7
	In 8th week	4	10	8
Treatment	No specific treatment	2	5	4.5
	One course of IV IG	30	77	3.8
	Two courses of IV IG	4	10	6.0
	Plasma exchange	5	13	7.0

Table 6. Evaluation of poor prognostic factors in our patients with GBS

Prognostic factors	Patients		MRT weeks	p value
	n	%		
Established factors				
Age > 70 years	3	7	3.3	NS
Ventilatory support	7	17	6.9	0.005
Grade 6 disability in <4 days	7	17	6.1	0.001
Plateau duration >14 days	6	15	7.0	0.001
CMAP of median nerve <1 mV	4	10	6.0	0.05
Proposed factors				
Proximal weakness in UL	7	17	6.0	0.005
Distal weakness in LL	4	10	7.8	0.001
Autonomic disturbance	5	12	6.2	0.025
Axonal NCS	6	15	6.0	0.001

There was no significant difference in the MRT with prior illness, whatever the pattern of DTR on admission and presence or absence of sensory loss. Similarly, the admission and initiation of treatment within the first 3 weeks of illness did not alter the recovery pattern. MFS and older patients had an early recovery (MRT 3.3 weeks).

The MRT for each subgroup of patients are shown in tables 2–6.

Patients with predominant distal weakness in the LL, proximal weakness in the UL, autonomic disturbance and axonal type of GBS had a poor outcome (table 6).

Discussion

GBS is a disease with a worldwide distribution affecting all ages, gender and ethnic groups. Usually, the incidence of GBS increases with age and is more common in persons 60 years or older with a male to female ratio of 1.6:1 compared to 2.7:1 in this study. The higher male to female ratio and the predominance of GBS cases in the middle-aged population of this study are probably a reflection of the fact that of the 41 cases, 20 were non-Kuwaitis (table 1). Generally, the non-Kuwaiti population predominantly consists of young males. For Kuwaitis, the male to female ratio was 1.8:1 and higher incidence in elderly as in other studies [4–10]. In an earlier study of childhood GBS in Kuwait, girls were reported to be affected more than boys [11].

GBS is a nonseasonal disease [9, 12] but seasonal clustering has been reported during summer in Northern China [13], spring in Taiwan [14] and winter and spring (September to March) in the Arabian Gulf region [8, 11] and in the present study during the winter months of November to March.

The incidence of MFS in this study was similar to that observed in the Western hemisphere [15] whereas in Taiwan [14] and Japan [16] the incidence was 19 and 25%, respectively. The incidence of AMAN in our population is the same as that in Western countries in contrast to an incidence of 15–20% in Japan, 40% in Latin America and 60–70% in Northern China [1]. Western studies indicate a poor recovery for AMSAN and a faster recovery for AMAN [1,17]. Kuwabara et al. [18] reported a variable pattern of recovery (both fast and slow recovery) for AMAN. Both AMSAN and the axonal type showed a delayed recovery pattern in our study. Our patients with predominant distal weakness in LL and proximal weakness in UL had delayed recovery. This type of muscle weakness and recovery pattern were not reported in most of the other studies.

Bulbar weakness and dysautonomia were considered poor prognostic signs in a Spanish study [10] whereas they were not relevant in a Taiwanese study [14]. We observed that the development of bulbar weakness was a bad prognostic sign as these patients went on to develop autonomic

disturbance and respiratory failure needing prolonged ventilatory support. The 7 patients who required ventilatory support and the 5 patients who had a combination of urinary retention and labile hypertension had a prolonged course of their illness.

Most of the studies report autonomic disturbance in 66% and ventilatory support in 30% of GBS patients [5, 9, 10, 19]. The incidence of autonomic disturbance (22%) and requirement for ventilatory support (17%) was much lower in our patients. Though GBS is a monophasic illness, there are reports of acute and long-term relapses in several studies [6, 9, 19, 20] but we did not observe any acute relapse. Mortality in GBS has decreased from 33 to 5% after the introduction of positive pressure ventilatory support and advanced intensive care management [5, 9, 21]. No deaths were recorded in our study most probably due to the early initiation of treatment. Over the years, treatment of GBS moved from symptomatic to specific immunomodulatory therapy. PE and IV IG are of equal benefit and cost effectiveness [22]. We chose IV IG as initial therapy because of its ease of administration. Several controlled clinical trials have shown that both PE and IV IG shorten the time to recovery when used in the early stages of the neuropathy [7]. In our study, IV IG was effective up to 3 weeks after the onset of illness.

There are numerous studies about long-term prognostic pointers in GBS [2, 5, 8–10, 18, 22–24]. Although we concur with most of the commonly mentioned poor prognostic factors, they do not help in the early evaluation (within 2 weeks) of those patients who are not qualified for treatment at the outset. Hence a need exists for having clinical and electrophysiological pointers to institute early immunomodulatory therapy for the patients with less than grade 2 disability even when the weakness is still in the progressive phase. In some patients there may be late progression after 2 weeks and a favorable outcome will be denied to them if the treatment is delayed. The patients with predominant distal weakness in the LL, proximal weakness in the UL, autonomic disturbance (both hypertension and urinary incontinence together) and those with an axonal type tend to have a delayed recovery. We recommend that patients with any of these factors be given immunomodulatory therapy irrespective of other clinical factors. Since our study population was small, studies with a larger number of patients are needed before making these factors a universal guide to early initiation of treatment.

Conclusion

Our data show that recovery is delayed in GBS patients with predominant distal weakness in the LL, proximal weakness in the UL, autonomic disturbance (both

hypertension and urinary incontinence together) and those with an axonal type in the NCS. Hence, patients with any of these features should be given immunotherapy early in the course of the disease.

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