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ORIGINAL ARTICLE

Guillain–Barré syndrome in children

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Abstract Guillain–Barré syndrome (GBS) is one of the reasons of acute polyneuropathy causing severe morbidity and mortality. Forty-six patients with GBS were included in our study. Clinical, laboratory, electrophysiological and prognostic features of the patients were evaluated retrospectively. Patients were divided into two groups. Group A consisted of children who attained a full recovery within 2 months from onset of the disease; group B consisted of children who experienced complete or partial recovery beyond 2 months from onset of the disease. Acute inflammatory demyelinating polyradiculoneuropathy was found in 56.5% of patients and axonal form in 43.5% patients. Antecedent events were found in 28 (60.9%) patients. Five patients (10.8%) needed mechanical ventilation and one patient (2.1%) died. Poor outcome was related with clinic stage and electrophysiological subtypes (axonal form). In our study, poor prognostic factors were related with clinic stage and electrophysiological subtypes (axonal form).

Keywords Guillain–Barré syndrome · Clinical features · Electrophysiological features · Prognosis

Introduction

Guillain–Barré syndrome (GBS) is an acute inflammatory polyneuropathy most commonly characterized by rapidly progressive, essentially symmetric weakness and areflexia [1]. Clinically, motor weakness and sensory loss begin in the lower extremities and progressively ascend to the upper extremities, with cranial neuropathy and autonomic symptoms often combined. Usually, prognosis is good in children than in adults. However, residual motor and sensory deficits may occur. Although rare, GBS may be fatal because of respiratory failure and cardiac arrhythmia.

Epidemiologic studies have reported an annual incidence of 0.6–4 per 100,000 population per year [2]. Although the pathogenesis of GBS remains unclear, there are increasing indications that it is an autoimmune disease, usually triggered by an infection, especially diarrhea due to infection and upper respiratory tract infections [1]. After acceptance of role of autoimmunity, plasmapheresis and intravenous immunoglobulin (IVIG) were used for the treatment. With both the treatments, the mortality and morbidity of the GBS decreased significantly. Based on the clinical features, etiology, pathological and electrophysiological studies, GBS may be subclassified into several forms, which were acute inflammatory demyelinating polyradiculoneuropathy (AIDP), and axonal forms of GBS, which include acute motor–sensory axonal neuropathy (AMSAN) and acute motor axonal neuropathy (AMAN) [3].

In this study, the aim is to detect clinical and electrophysiological findings and their effects on prognosis and to discuss with the literature.

Methods

A total of 46 children with GBS, seen at Cukurova University Hospital, between 1995 and 2006, were retrospectively studied. Their conditions fulfilled the clinical criteria for GBS [4].

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Data collected included age, gender, preceding events, presence of previous infection, seasonal distribution, neurological features, functional grade of motor deficit, need for intubations and laboratory findings (including CSF parameters and electrophysiological reports). The functional status at the time of maximum deficit was graded according to Hughes scale of disability as follows: 0: healthy, 1: minor signs and symptoms and is capable of running; 2: able to walk 5 m without assistance, but is unable to run. 3: able to walk with assistance, 4: confined to bed or chair bound, 5: requires assisted ventilation, and 6: died. The children were followed up for 1 year or more.

After the onset of disease in 7–20 days, needle electromyography (EMG) and nerve conduction studies were performed in all patients. Nerve conduction studies were performed depending on patients' age. The patients were classified into three groups according to electrophysiological studies as AIDP, AMAN and AMSAN. Autonomic symptoms were recorded (hypertension, hypotension, orthostatic hypotension, cardiac arrhythmias, bladder and gastrointestinal dysfunction).

A lumbar puncture was performed on 43 patients within 1 month of onset of illness, with a median of 9 days (range 6–24 days).

Patients classified into two groups according to prognosis. In group A, the patients have complete or partial recovery in 2 months and in B group beyond 2 months.

Statistical studies

Mann–Whitney *U* and Fisher's exact, Chi-square tests were both used to correlate clinical and electrophysiological findings.

Results

The age of the patients was ranged between 1 and 12 years (mean 71.07 ± 36.58 months). Forty-three (93.5%) patients were 10 years or younger. Of all 46 patients included in the study, 28 (60.9%) were male and 18 (39.1%) were female. Twenty-eight patients (60.9%) reported a history of infection in 4 weeks preceding the onset of symptoms: an upper respiratory infection was detected in 23 patients (82.1%) and a history of gastroenteritis in 3 patients (10.7%) and a varicella 2 patients (7.2%).

Disease distribution according to seasons was 17 patients (37.0%) in spring, 14 patients (30.4%) in winter, 10 patients (21.7%) in autumn and 5 patients (10.9%) in summer.

In all patients, the most common initial symptom was limb weakness, which was documented in 33 (71.8%) patients, followed by paresthesia or muscle pain in 14 (30.4%) patients. We detected cranial nerve involvement in 17 cases (36.9%) and autonomic involvement in 21 cases (45.7%). In 15 patients 9th and 10th cranial nerve involvement beside 2 patients with 7th nerve, 1 patient with 3rd cranial and 2 patients with unilateral 7th cranial nerve involvement were found.

In an electrodiagnostic study, 26 (56.5%) patients had primary demyelinating features while 20 (43.5%) had primary axonal disease. Of patients with the axonal variant, 18 (90% of axonal subgroup) had a pure motor syndrome (AMAN) and 2 (10% of subgroup) had AMSAN. The patients' data regarding clinical features are summarized in Table 1.

The evaluation of the patients prognosis resulted that 18 patients (39.1%) were placed in group A, and 28 patients (60.9%) in group B. The mean age of the patients in group A was 78.44 ± 32.64 months (12–132 months), and in group B was 67.54 ± 38.17 months (18–144 months). There was no statistically significant difference between two groups ($p > 0.05$).

In group A, the mean CSF protein level was 91.83 ± 43.24 mg/dl (24–180), in group B it was 103.29 ± 68.99 mg/dl (15–323). There was no statistically significant differences between two groups according to CSF protein levels ($p > 0.05$).

Table 1 Clinical features of patients

Clinical data	*n*	%
Sex (female/male)	18/28	39.1/60.9
Antecedent infection	28	60.9
Upper respiratory infection	23	82.1
Gastrointestinal infection	3	10.7
Varicella	2	7.2
Seasons		
Spring	17	37.0
Winter	14	30.4
Autumn	10	21.7
Summer	5	10.9
Signs and symptoms		
Weakness	33	71.8
Paresthesia	14	30.4
Cranial nerve involvement	17	36.9
Autonomic changes	21	45.7
Motor nerve studies		
AIDP	26	56.5
AMAN	18	39.1
AMSAN	2	4.4

AIDP Acute inflammatory demylinating polyradiculoneuropathy, *AMAN* acute motor axonal neuropathy, *AMSAN* acute motor–sensory axonal neuropathy

In group A, the ratio of patients having antecedent infection was 55.5% while in group B it was 67.8%. There was no significant difference between the groups ($p > 0.05$).

Cranial nerve involvement ratio was 27.7% in group A, and 46.4% in group B; autonomic findings ratios were 38.9 and 50%, respectively. Both factors have no effects on prognosis ($p > 0.05$).

Patients that needed intubations were two cases in group A, three cases in group B, and a patient in group B was died because of secondary reasons. There was no statistically significant difference between two groups ($p > 0.05$).

In group A, 55.5% of the patients were administered plasmapheresis and IVIG beside supportive measures, while in group B the ratio was 67.8% and it is found that the treatment has no effect on prognosis ($p > 0.05$).

Nerve conduction studies revealed 61.5% (16/26) of patients with demyelinating form in group A, 38.5% in group B. However, the ratios of axonal form in group A and B are 10 and 90%, respectively. The properties of the cases in GBS subgroups are shown in Table 1. Electrophysiological findings were detected to have significant effects on prognosis ($p = 0.001$).

Discussion

Guillain–Barré syndrome is a disease seen in all over the world and in all age groups including neonates. The median age of our study was 6 years and is consistent with reports of childhood GBS in other series [5, 6]. It is seen in boys 1.5- to 2.7-fold than in girls. Major differences in gender distribution were also noted in a Turkish study [5]. In our study this ratio was 1.55.

Limb weakness, especially in the distal part of the lower extremities, was the most prevalent symptom associated with hospitalization. Neuropathic pain was also a frequent initial presentation in as many as 50% of children [7]. Lee et al. [8] reported limb weakness in 53.6% patients and paresthesia or muscle pain in 28.5% patients. In all of our patients, we detected clinical features as limb weakness 71.8% and paresthesia or muscle pain 30.4%. Cranial nerve involvement is more common in children than in adults. Lee et al. [8] reported 15/56 (26.8%) patients observed with facial palsy. We found cranial nerve involvement in 17/46 (36.9%) patients and major cranial nerve (9th and 10th cranial nerve) was observed. Autonomic nervous system was reported to be involved in 25% of GBS patients, usually manifesting as blood pressure instability, sinus tachycardia, pupillary abnormality or sweating abnormality [9]. In our patients autonomic involvement was in 21 (45.7%) patients.

Although in the studies performed mostly, no relation was seen between GBS and season, while Larsen with Boucquey [10, 11] reported that in autumn and winter. Winer with Färkkilä detected that in spring season the disease seen more frequently [12, 13]. In most of the patients the disease appeared in spring and winter. The disease appeared least in summer.

In the literature, two-thirds of GBS patients have history of antecedent disease. The most common disease of them is respiratory infections followed by gastroenteritis caused by *C. jejuni* that is isolated in most of the cases [14]. Antecedent infection and respiratory infection rates are reported as follows: in China 78 and 68%, in Sweden 70 and 47% while in Italy 60 and 46% [15–17]. Some other factors such as immunization, surgical operation and immune deficiency states may also predispose to GBS. In our study, 23 (82,1%) of the 28 patients having predisposing factor have respiratory infections, 3 of them (10.7%) have gastroenteritis and 2 (7.2%) have varicella. Eighteen (39.1%) patients have no detected leading states in their history.

In GBS, cranial nerve involvements may also take place. In younger children 9th and 10th cranial nerves are involved more common while in older ones facial nerve involved generally [18]. Although there is no clear relation between cranial nerve involvement and prognosis, some studies reported that in child with cranial nerve involvement, respiratory muscle involvement and intubation need were seen more than the others while the prognosis also worse [18]. Our case in group A that is intubated has also cranial nerve involvement. In group B, three patients were intubated while two of them have this involvement. In group A 27.7%, and group B 42.8% cranial nerve involvement was determined. But no significant relationship detected between prognosis and CNS involvement.

Guillain–Barré syndrome is evaluated in three groups as demyelinating, motor axonal and motor-sensorial axonal degenerative according to the clinical and electrophysiological findings. AIDP had changes consistent with demyelination in two or more motor nerves. AMAN is a term that has been applied to an electrodiagnostic pattern consistent with selective degeneration of motor axons without suggestive of demyelination. However, AMSAN is a severe, axon-destructive disorder that exhibits both motor and sensory nerve involvement. Since AMAN and AMSAN are not clinical entities readily distinguishable from AIDP, electrodiagnostic studies are extensively used for the definition of both subtypes of GBS. In first week in 5–14% cases electrophysiological abnormalities may be detected [4]. Typical findings are prolonged wave latency, conduction block and prolonged distal latency. The most common sign is conduction block when the paralysis is most significant. In numerous epidemiological studies, the distribution of GBS types was observed to be distinct in

different ethnic or geographical places. AIDP is the most common GBS form that is shown in studies in America and Europe [3]. In Japan study, Nagasawa et al. [6] informed that 48% of the GBS patients are in axonal, 35% in AIDP form and in Chinese studies axonal form was found as 65–86% of the patients [19]. In our study it is found that AIDP occupies 56.5% and axonal form (AMAN and AMSAN) was 43.5%. In our study distribution of GBS types was similar to European countries. It is revealed that generally axonal group prognosis is worse than others. We found similar to the literature that, axonal group patients have prognosis worse.

Guillain–Barré syndrome seen at childhood has a better prognosis than adults. The factors affecting prognosis still are not known completely. In different studies, both clinical and electrophysiological causes are studied. In our study, we investigated age, gender, season, antecedent infection, cranial and autonomic involvement, BOS protein, intubation need, treatment, electrophysiological findings and clinical grade for this purpose. We detected a relation between clinical grade and electrophysiological findings with prognosis. In a study, Cheng et al. [20] detected that, like our results, the most important factors are electrodiagnostic features on prognosis. Lyu et al. [21] reported that intubation need as negative prognostic factor. This result may be related with the high number of intubated cases.

In the community-based studies, the reported mortality rate related to GBS was reported as 10% and intubation need was 20–45% [12, 22]. Italian GBS study revealed mortality rate as 11% [17]. Intubation rate was found as 27% in the study made in Taiwan by Cheng et al. [23]. In our study, five patients needed intubation. Two of them were in AIDP while remaining three were in axonal GBS group. Durand et al. [24] reported that demyelinating type of GBS patients needs intubation more than the other forms. Our mortality rate was 2.1% while intubation-needed patients ratio was 10.8%.

Today, the most commonly used procedures for the treatment of GBS include IVIG and plasma exchange. There are studies about effects of these treatment on prognosis in GBS. In a multi-centered study, Korinthenberg and Monting [25] showed that IVIG-administered patients have better prognosis than others. In the previous study by Jansen et al. [26], plasma exchange done in first 7 days shorten the disease duration. In other two studies reported, IVIG and plasma exchange are equally efficacious by Hughes et al. [27] and Tsai et al. [28]. In our cases, group A 55.5% and group B 67.8% patients had IVIG and plasma exchange. But, we have not detected a significant difference affecting prognosis.

In conclusion, we found that clinical grade and electrophysiological findings (axonal form) are related with prognosis. But it is clear that more crowded and multi-centered studies are needed.

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