Journal of Pediatric Neurology 11 (2013) 159–163
DOI 10.3233/JPN-130622
IOS Press

Different subtypes of Guillane-Barré syndrome in children

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Received 31 July 2012
Revised 2 December 2012
Accepted 10 December 2012

Abstract. Guillan-Barré syndrome (GBS) is a debilitating illness with different subtypes depending on geographical area. In this study we review the GBS subtypes in Iranian children. One hundred and eight children below 15 yr entered the study during 7 yr (1998–2005), they were evaluated in 1st (95 cases) and 2nd wk (13 cases) diagnosed clinically, electrodiagnostically and their cerebrospinal fluid (CSF) were analyzed. Patients were divided into demyelinating and axonal forms. Data were analyzed by *t* test for continuous measures and the Fisher's exact test for categorical variables in SPSS 16. *P* less 0.05 was significant. The means age ± SD of affected patients are 4.8 ± 2.7 yr (minimum 1 yr, maximum 14.5 yr). CSF protein and pleocytosis were more common in 2nd wk group (77 mg/dL in first week versus 63 mg/dL in second week); 2% (first week) and 30% CSF pleocytosis occurred (second week). Demyelinating form happens in 47% of patients, axonal 40% and combined form of axonal and demyelinating form happened in 9%. Normal electrodiagnostic tests in spite of clinically confirmed GBS were observed in 4%. CSF protein was higher in demyelinating compared to axonal form (71 mg/dL and 54 mg/dL). There is no sex predilection for GBS affection (59 males, and 49 females). Peak incidence of GBS in children is below age of 5 yr (65%) ;axonal form of GBS (sensory and motor) make a considerable proportion of GBS in children (40%) with lower CSF protein compared to demyelinating type, but it is not statistically significant ($P > 0.05$).

Keywords: Guillan-Barré syndrome, children

1. Introduction

Guillan-Barré syndrome (GBS) is an acquired polyradiculopathy that leads to dysfunctional segmental demyelinating or axonal degeneration in all parts of peripheral nerves, in both sensory, motor spinal roots and rarely cranial nerves [1]. It happens usually following a febrile illness with incidence of 0.5–1.5/100,000 people under age 18 annually [2]. Division of subtypes of GBS were first described four decades ago, when the first guideline about GBS was described [3]. GBS firstly was delineated as demyelinating polyneuropathy but cell mediated immune response was suggested later for its pathogenesis [4,5]. Relation of GBS type and infectious causes was described in 1990s when the axonal form of GBS was divided to two subtypes as motor axonal and acute combined motor and sensory axonal mostly due infection by *Campylobacter jejuni* [6–11]. These types of GBS are difficult to distinguish by clinical aspects but electrodiagnostic tests play important role for diagnosis [12] GBS may also be associated with different electrodiagnostic findings. The most frequent abnormality observed in motor nerve conduction is prolonged or absent F-wave response followed by abnormal distal motor latency, reduction of compound motor action potential, conduction velocity and distal conduction block. Experience from Europe, North America and Australia has shown that acute inflammatory demyelinating polyneuropathy (AIDP) is the

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most common form of GBS while another pediatric review from Argentina showed that acute motor axonal neuropathy (AMAN) made up of 29% of cases, in other study from North China, axonal degeneration is the predominant category constituting up to two-thirds of patients with GBS [13].

The aim of this study was to find: a) the clinical and electrophysiological patterns of GBS, and b) describe the of GBS among children in Azerbyjan province with regard to how cerebrospinal fluid (CSF) and conduction nerve velocity can change during disease activity [1,14]. We tried to find epidemiology of different types of GBS relative to CSF protein changes in each subtype. We hoped that our findings can identify new concepts about GBS epidemiology in our area we also posed the question whether CSF changes identifies the subtype of GBS.

2. Materials and methods

During 7 yr from 1998 to 2005 we collected information of 108 patients diagnosed as GBS. They were diagnosed clinically and electrodiagnostic tests were performed. Exclusion criteria were age more than 15 yr and any previous neurological (central or peripheral disease); no cases had these criteria.

GBS subtype was divided as follow: 1) Classic GBS or AIDP is rapidly progressive ascending paralysis with distal areflexia and a mild sensory deficit with weakness in proximal parts more than distal with albuminocytologic dissociation (no white blood cells but high protein) in CSF analysis. 2) AMAN with rapidly progressive ascending paralysis with normal reflexes and no sensory deficits. Respiratory failure is common but with good prognosis. 3) Acute motor sensory axonal neuropathy (AMSAN) was considered as rapidly progressive ascending paralysis with areflexia and moderate to severe sensory deficits, this is a fulminant form of GBS and is associated with widespread axonal injury with slow and incomplete recovery [1,15].

2.1. Electrodiagnostic tests

Motor nerve conduction studies were performed using standard techniques of supra maximal percutaneous stimulation and surface electrode recording. Proximal stimulation sites for median, ulnar, and peroneal conductions, which were traced below the elbow and fibular head respectively. The electrodiagnostic data examined included compound muscle action potential amplitude, conduction block or temporal dispersion, conduction velocity, distal latency, and F-wave latency to define the electrodiagnosis criteria for GBS [16]. These measurements were compared and age matched to normal reference values for each nerve [17].

2.2. Statistical analysis

All data were analyzed by SPSS 16 for quantitive continuous parametric values. *t* test and the Fisher's exact test were used for categorical variables. The McNemar test for correlated proportions was used to examine differences in sensitivity and specificity of the diagnostic criteria. $P < 0.05$ was considered statistically significant.

3. Results

One hundred and eight patients: 59 males and 49 females were diagnosed as GBS with average age of 4.8 ± 2.7 yr (minimum 1 yr, and maximum 14.5 yr). Seventy-nine cases (65%) were below 5 yr, 30 cases (31%) between 5–10 yr and four cases (4%) 10–15 yr. They were evaluated during acute phase in 1st and 2nd wk of illness. These two groups of patients were categorized on basis of their management-mostly in 1st wk 95 cases and 2nd wk other 13 cases.

CSF protein was higher in 2nd wk compared to 1st wk group but this difference was not statistically significant ($P > 0.05$). CSF pleocytosis, white blood cell count more than 10 cells/mm^3, was uncommon in first week (2% of cases) although it occurred mostly in 2nd week (30% of cases) (Table 1). The CSF protein level measured in different types of GBS, which shows high level of CSF protein occurs in classic (demyelinating) type of GBS compared to axonal form but this difference was not significant ($P > 0.05$). CSF protein concentration in all groups is showed in Fig. 1. Fifty-one cases (47.2%) were diagnosed as demyelinating

Table 1
Cerebrospinal fluid protein and white blood cells in first and second week after onset of Guillan-Barr ésyndrome

Features	First week	Second week
Cerebrospinal fluid protein (mg/dL)	63 ± 50	77 ± 38
Pleocytosis (> 10 cells/mm^3)	2/95 (2%)	4/13 (30%)

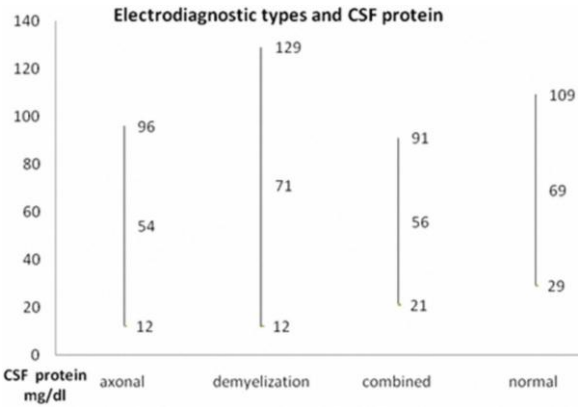

Fig. 1. Show cerebrospinal fluid protein in subtypes of Guillan-Barr ésyndrome.

Table 2

Types of Guillan-Barr ésyndrome subtypes and cerebrospinal fluid protein there is not any significant difference among Guillan-Barr é syndrome types and cerebrospinal fluid protein concentration

Guillan-Barre syndrome types	Frequency (%)	Cerebrospinal fluid protein (mg/dL)
Demyelization	47	71 ±58.9
Axonal	40	54.6 ±41.9
Combined	9	56.3 ±35.6
Normal tests	4	69.2 ±40.8

type with CSF protein 71 ± 58.9 mg/dL, 43 cases (40%) were diagnosed as axonal; their CSF protein was 54.6 ±41.9 mg/dL, 10 cases (9%) had characters similar to both axonal and demyelinating groups or combined type; their CSF protein were 56.3 ±35.6 mg/dL.

In spite of clinical characters of GBS, five (4%) cases had normal electrodiagnostic findings and their CSF protein was 69.2 ±40.8 mg/dL (Table 2). Electrodiagnostic findings show distal latency increased significantly in peroneal and ulnar nerves although it was more prominent in peroneal and ulnar but it was not delayed in median nerve significantly (Table 3). Nerve conduction velocity measured in peroneal, ulnar and median nerve show the nerve electrical pulse transfer was slow in all three nerves but it was more prominent in peroneal compared to ulnar and median nerve.

F-wave absence was observed in 83% of cases in peroneal nerve, 80% of ulnar nerve and 76% of median nerve. Wave amplitude also were measured in peroneal, ulnar and median nerves, wave amplitude decreased as much as 80% of wave length of peroneal nerve in 87% of cases while in ulnar nerve this decrement of wave length occurred in 75% of cases .In median nerve study 70% of cases showed wave length decrement more than 80% of wave length (Table 3).

4. Discussion

GBS is a post infectious immune mediated illness probably due to both humoral and cellular immune mechanisms [14]. GBS diagnosis is mainly based on clinical assessment although there are different subtypes of GBS, of which AIDP is considered as the most common form in western countries. GBS is mostly due to bacterial (40% seropositive for *Campylobacter jejuni*) [9,18,19] or viral infection with different recognized patterns of GBS like as AMAN and AMSAN [1,20–22]. The AMAN subtype is a purely motor disorder more prevalent in pediatrics, which, rapidly progress to respiratory failure [20]. AMAN may also affect rural population of pediatric and young adults especially in summer period [21]. The AMAN clinical features may be variable in different geographical area but recovery in many patients is favorable and this type may be hyperreflexic in one third of patients [1,22].

AMSAN is an acute severe form compared to AMAN that affects both sensory and motor nerves commonly of adults. It presents with rapid and severe motor and sensory dysfunction with marked muscle wasting with severe axonal degeneration and little demyelination [23,24]. Other uncommon recognized types of GBS are Miller Fisher variant with reduced or absent sensory nerve action potential, acute autonomic neuropathy and pure sensory neuropathy. It seems these types of denervation have different geographical variations where in North America, Western Europe and Australia most patients with GBS show demyelinating neuropathy but in Northern China axonal pathology is the cause for GBS in up to 65% of cases [21]. Epidemiologic studies show GBS also has a predilection for male (male to female ratio of 1.5:1) [25]. GBS may also affect all age groups between infancy and old age with a bimodal peak 15–35 years and 50–75 years. [26].

In this study we tried to define GBS epidemiology in pediatric group. We describe the electrodiagnostic patterns of GBS; we also tried to find the pattern of CSF protein changes especially among various GBS types. We defined the age and sex distribution of af-

Table 3
Electrodiagnostic patterns and abnormalities in patients

Characteristics	Peroneal nerve Mean ± SD (range)	Ulnar nerve Mean ± SD (range)	Median nerve Mean ± SD (range)
Distal latency (msec)	5.45 ±4.75 (2.29–3.25)	4 ±3.6 (1.1–2.2)	1.5 ±1 (1.7–3)
Nerve conduction velocity (m/s)	27.4 ±20.7 (51–57)	35 ±18 (55–60.5)	35 ±22 (54–66)
F wave absence	83%	80%	76%
Wave amplitude (mV)	0.59 ±0.78 (5.8–8.15)	2.2 ±2.32 (6–9.7)	2.7 ±2.3 (3.7–11.6)
Wave amplitude decrement occurrence more than 80%	87%	75%	70%

fected patients in electrodiagnostic test and compared neuroelectrical characters in three different nerves in affected group. Our study shows the peak age for affecting to GBS in our area is between 3 to 6.5 yr. Our study shows infants have the lowest risk of GBS: same as other studies in other developing regions [26]. The lowest recorded age of patient with GBS was 1 yr and the mean age in our study was 4.8 ± 2 yr. In another review the age of 1 to 5 yr constituted 70 patients or 65% of all cases. This fact confirms the claim that most of GBS cases that are seen worldwide are below age four. This may be due to exposure to several infections, toxins and increased susceptibility of immature myelin to demyelination [27–29].

In spite of predilection of male to female in other studies performed in adult group [26] our study showed equal sex distribution in children with GBS (54% males and 46% females). Although GBS diagnosis is based on clinical ground, nerve conduction abnormalities consistent with demyelination are sensitive and specific for classic GBS [30]. On nerve conduction study demyelination is characterized by nerve conduction slowing, prolongation of the distal latencies, prolongation of the F-wave, conduction block, and/or temporal dispersion. These results should be present in at least two nerves in anatomically distinct areas. In the axonal variant of the disease, absent, or markedly reduced distal compound muscle action potential are observed in nerve conduction study, profuse and early denervation are supportive for axonal injury. Neurophysiologic tests may be normal rarely due to site of demyelinating lesions [31].

Electrodiagnostic tests demonstrates features of demyelinating such as slow conduction velocities and prolonged distal and F-wave latencies [32] in other studies absence of F-wave in electrodiagnostic studies was introduced as the most frequent abnormality in motor nerve conduction, which occurred in 59% of cases, followed by abnormal distal motor latency (35%). Absent or reduced median and ulnar sensory nerve action potential were seen in 51%. Three patients out of 20 (15%) with GBS had normal nerve conduction study at initial presentation [32].

As our study peroneal, ulnar and median nerve were evaluated, with peroneal nerve showing most conduction abnormalities during disease activity In peroneal nerve F-wave absence was observed in 83% and decrease wave length occurred in 87% of cases, these measures in ulnar nerve were 80% (F-wave absence) and 75% (cases with decreased wave length) while in median nerve F-wave absence and wave length decrement were 76% and 70% respectively.

CSF changes during the acute phase GBS include elevation of CSF protein without an elevation in white blood cell [32]. In our report we tried to correlate sub types in GBS (demyelinating, axonal, and combined) with changes that may occur in CSF especially in protein concentration relative to frequency of these types of GBS in our area.

In North America and Europe, classic form of GBS (AIDP) happens in 90%, the frequency of AIDP decrease to 63% in Israel and 46% in Pakistan [12]. Our study shows classic form or of GBS (AIDP) frequency in our area among children is not different from other studies, in Middle East and Pakistan. The frequency of AIDP in our group was (47%) and the frequency of ASMAN was 9% in our study. This was higher than European studies but incidence of ASMAN was not so different than a study performed in Bangladesh (11%) and Israel (15%) [12]. We show also that although AIDP is associated with higher CSF protein compared to axonal type, (which happens in 40%) and AMSAN, these differences were not significant. In fact CSF protein in ASMAN form (that occur in 9% of patients) and to axonal form were similar. There was also a smaller group as much as 4% with clinical criteria of GBS with normal measures of electrodiagnostic tests at the time of presentation and relatively high CSF protein in our study although this was considered a rare presentation in other study [31].

GBS mainly affects children between age 1–5 yr; there is no sex predilection in children as shown in our study. The frequency of distribution of different subtypes of GBS in children is different from studies reported in Europe and North Western countries but more close to some countries like as Israel and Pakistan, although these studies were performed in adults group. Peroneal nerve is most useful nerve to detect GBS cases and F-wave absence and decrease wave amplitude were detected most commonly in our electrodiagnostic studies. CSF protein cannot help to discriminate different subtypes of GBS as demonstrated in our study.

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