Medical Journal of the
Islamic Republic of Iran

Volume 17
Number 2
Summer 1382
August 2003

EPIDEMIOLOGICAL, CLINICAL AND ELECTRODIAGNOSTIC FINDINGS IN CHILDHOOD GUILLAIN-BARRE SYNDROME

M. BARZEGAR,* M.D., Z. JALALI, M.D., AND V. TOPCHIZADEH, M.D.

From the Department of Pediatric Neurology, Tabriz Children's Medical Center, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, I.R Iran.

ABSTRACT

In order to identify the clinical and electrophysiological characteristics of childhood Guillain-Barre Syndrome (GBS) in East Azarbaijan province, clinical and electrophysiological data on 40 consecutive children with GBS, admitted to Tabriz Children's Medical Center from March 21st 1999 to March 20th 2002, were analyzed. All patients received intravenous immunoglobulin, 400 mg /kg/ day for five consecutive days.They were prospectively followed up for at least 3 months. Analysis of age distribution showed a high occurrence (55%) among children aged 1- 5 years old. Male patients outnumbered females with a sex ratio of 1.3: 1. The most frequent antecedent events were upper respiratory tract infections. The study subjects were subclassified according to electrophysiological data: 52.5% were found to have predominantly acute demyelinating neuropathy, 27.5% had acute motor axonal neuropathy and in 20% of patients the demyelinating type of GBS was observed with secondary axonal loss. The disease symptoms were relatively severe in our patients as only 15% of them were able (with and without aid) to walk at the peak of their illness. Electrodiagnostic criteria associated with poor outcome were severe reduction in compound muscle action potential (CMAP) amplitude and fibrillation potentials (p= 0.034).

MJIRI, Vol. 17, No. 2, 123-127, 2003.

Keywords: Childhood Guillain-Barre syndrome, Epidemiology, Clinical features, Electrodiagnosis, prognosis.

INTRODUCTION

The Guillain-Barre syndrome (GBS) is an immune mediated acute generalized peripheral neuropathy that may lead to severe weakness. Since the beginning of the program for control of poliomyelitis, GBS has emerged as the most important cause of acute flaccid paralysis in many countries including Iran,with an incidence of 1-2/ 100,000 per year in the general population.[1] The diagnosis of GBS is based on certain characteristic clinical criteria and mostly by exclusion of other causes of polyneuropathy. It is characterized by progressive symmetrical muscular weakness developing over a few days to 6 weeks, and universal areflexia or hyporeflexia.[2]

As demyelination is largely considered the mean pathological substrate, the syndrome has also been known as acute inflammatory demyelinating polyradiculoneuropathy (AIDP).[3] However, in the last few years, it had become evident that a predominantly axonal pattern may underlie GBS.[2] Epidemiologic studies of childhood GBS are relatively few and mostly from

*Corresponding author. Tel: 0411-3364672, Fax: 0411-3364659, E-mail address: mm_barzegar@yahoo.com

Europe and North America.

Up to now, no systematic study has been reported on childhood GBS from East Azarbaijan province. Thus we performed a prospective study to identify epidemiological, clinical and electrodiagnostic features of childhood GBS. Our hospital is the only referral center of childhood GBS patients because of the availability of intensive care facilities required in such cases. The study was conducted on all of these patients (from East Azarbaijan Province) admitted with systemic evidence of childhood GBS, from March 21st 1999 to March 20th, 2002. According to the national policy for the surveillance of controlling poliomyelitis, all cases of acute flaccid paralysis under 15 years old must be reported to health centers. There were only two extra cases reported by East Azerbaijan Health officials, indicating that Tabriz children's hospital is covering nearly the whole population of children with GBS; therefore our results can be considered a representative sample of childhood GBS in East Azerbaijan.

PATIENTS AND METHODS

All patients who met the clinical diagnostic criteria of GBS[2] were admitted to the hospital and entered into the study. Daily medical records were entered on the preset data collection forms which included neurological examinations performed by a pediatric neurologist and ruling out poliovirus infection (two stool samples were taken apart within two weeks of muscular weakness onset). Cerebrospinal fluid (CSF) examination for cell count, protein and glucose was accomplished in all patients, along with routine blood tests (complete blood count, urea and electrolytes). All children underwent at least one electrodiagnostic evaluation performed by a physiatrist at the time of admission. The median interval between onset of neuropathy and performance of the first electrodiagnostic study was 6.3 days (range 3 to 27 days). According to the neurophysiological findings the subjects were classified into three groups: 1) demyelinating type: patients with reduced nerve conduction velocity (NCV), prolonged distal motor latency, abnormal temporal dispersion and prolonged F-wave latency, 2) demyelinating type with axonal loss: patients with reduced NCV and prolonged distal latency, with low amplitude compound muscle action potentials (CMAP), and 3) axonal type: patients with nearly normal NCV and low amplitudeCMAP (<10% of the lower limit of normal).[4] Patient's maximal deficits was calculated, according to Haughes and colleagues'[5] graded scale with slight modification as follows: Grade 0-Normal functional state, Grade 1- Minor signs and symptoms not interfering with normal social life, Grade 2- Able to walk without assistance, Grade 3- Ambulation only with support, Grade 4-Confined to bed or chairbound and, Grade 5-Assisted ventilation required. All children were treated with intravenous immunoglobulin (IVIG) at a dose of 400 mg /kg /day for 5 consecutive days. Improvement by at least one grade in the functional score at 4 weeks after IVIG administration was considered as an efficacy criterion for IVIG treatment. After discharge, all children were followed monthly for at least 3 months. Statistical analysis was performed on a personal computer using EPI INFO 6 program.

RESULTS

A consecutives series of 40 hospitalized cases of GBS were observed from March 21st 1999 to March 20th 2002. Age and sex distribution of these patients are shown in Table I.

Twenty-nine patients (72.5%) had a history of an acute infectious illness preceding the onset of neurologic symptoms, including upper respiratory illness (flu-like) in 24 patients (60%) and gastroenteritis in 5 cases (12.5%).

Analysis of seasonal incidence has shown that 67.5% of the cases occurred in cold seasons (37.5% in the winter and 30% in autumn). The clinical features of patients are shown in Table II.

Fisher syndrome (FS) which is characterized by a triad of ataxia, areflexia and ophthalmoplegia has been recognized as a clinical variant of GBS[2] and was seen in one patient (2.5%). Cerebrospinal fluid (CSF) was ob-

Table I. Age and sex distribution of 40 children with GBS.

Age (years)	Number of patients		Total
	Males	Females	
1-5	13 (32.5%)	9 (22.5%)	22 (55%)
6-10	7 (17.5%)	6 (15%)	13 (32.5%)
11-15	3 (7.5%)	2 (5%)	5 (12.5%)
Total	23 (57.5%)	17 (42.5%)	40 (100%)

Table II. Clinical manifestations of 40 children with GBS.

Signs or Symptoms	Number of patients (percent)
Objective weakness	40 (100%)
Areflexia or hyporeflexia	40 (100%)
Sensory symptoms, pain (limbs)	22 (55%)
Cranial nerve dysfunction	21 (52.5%)
VII	12 (30%)
IX, X	4 (10%)
VII,IX,X	5 (12.5%)
Sphincter disturbances	3(7.5%)
Autonomic changes	8 (20%)
Respiratory failure requiring assisted ventilation	5 (12.5%)
Morbidity	1 (2.5%)

Table III. Functional grading at peak and 3 months after treatment with IVIG.

Grade		Number of patients	
		At peak	3 months later
0	Healthy	0	0
1	Minor symptoms	0	5 (12.5%)
2	Able to walk 5 meters	1 (2.5%)	17 (42.5%)
3	Able to walk 5 meters with aid	5 (12.5%)	13 (32.5%)
4	Bedridden or chairbound	29 (72.5%)	5 (12.5%)
5	Requires assisted ventilation	5 (12.5%)	0

tained from all patients. All samples showed fewer than 15 cells per milliliter, and an increased protein level (>50 mg/dL) was encountered in 34 (85%) patients, protein levels were normal (<50 mg/dL) in 6 (15%) patients in whom CSF was obtained only in the first week of illness.

Neurophysiological examinations were performed by a physiatrist on days 3 to 27 (mean 6.3 days) after onset of weakness and usually near the peak of the illness three patterns emerged: 1) in twenty one (52. 5%) patients the demyelinating type of GBS, 2) eight (20%) patients had the demyelinating type of GBS with secondary axonal loss, and 3) eleven (27.5%) patients had axonal type GBS .

The functional grading at the peak of neurological deficit, and 3 months after treatment with IVIG is shown in Table III. Improvement by one functional grade 4 weeks after IVIG administration was achieved in 80% of the patients.

With respect to outcome, only 1 of 40 patients was able to walk independently at the peak of illness (Grade 0- 2), whereas by 3 months, 22 children (55%) had regained independent locomotion.

Complications

Pulmonary complications such as aspiration pneumonia and collapse occurred in 9 patients (22.5%), transient arrhythmia was observed in 5 patients (12.5%) and in 2 patients (5%) transient hypertension was detected. In 4(10%) patients both aspiration pneumonia and arrhythmia occurred. Unfortunately in one of the patients (2.5%), bradyarrhythmia and respiratory arrest lead to hypoxic-ischemic insult and after discharge the child suffered from cerebral palsy(quadriplegia).

Prognostic considerations

Age, sex, presence of antecedent events, autonomic involvement, cranial nerve impairment, maximum grade scored, together with CSF and electrodiagnostic parameters were plotted against the outcome at the end point

of follow up. Time to reach Grade 2 or 3 and disability scores at month 3 were used as an estimation for the outcome. None of the clinical parameters showed a positive predictive value, however evidence of severe reduction of the mean amplitude of the CMAPs (<10% of lower limit of normal) showed predominant axonal damage, (subgroup of axonal type of GBS) produced more severe weakness and delayed recovery (p= 0.034).

DISCUSSION

Several observations emerged from this prospective study of 40 children with GBS admitted to Tabriz Children's Hospital.

The syndrome occurred at all ages, but the distribution per age groups demonstrated that it predominantly affects children aged 1-5 years (55%), which is consistent with the findings of other studies.[6,7,8] However in one study GBS was most frequent between ages 4 and 9 years.[3]

The male-to-female ratio of 1.3:1 found in this study is in accordance with other series.[6,7,8,9]

GBS is the prototypic postinfectious disease with about two-thirds of the patients reporting antecedent illnesses, in most cases the precise infection was not clear from medical history and has often resolved by the time neuropathic symptoms develop. Respiratory infections were the most frequently reported preceding diseases, followed by gastrointestinal (GI) infections.[9]

In our study 72.5% of patients gave a history of an acute infectious illness preceding the onset of neurologic symptoms, including upper respiratory tract infection (URI) in 60% and GI infection in 12.5% of cases. Our findings are similar to the results from other studies.[6,7,8,9,10]

Most studies have failed to identify a relationship between the incidence of GBS and a season. Our study showed that 67. 5% of cases appeared over autumn- winter, mostly because of the higher frequency of URI during these cold seasons in East Azarbaijan province. Nevertheless our sample size was too small to show a reliable correlation with seasonality.

No remarkable difference in clinical presentation was found between our findings and those of previously published reports.[3,6,7,8,9,10,11] However, our case material is slanted toward severe cases (85% were in Grade 4 or 5), mostly because of referral bias due to the availability of a pediatric ICU at our hospital. These observations were in parallel to an accomplished study in Mofid Children's Hospital, Tehran[12] and some other studies.[8,11,13] In general there are mild cases of GBS that never come to the attention of a neurologist. In a study on 254 patients during 8 years, only 4. 7% were able to walk throughout their entire course of GBS.[13] Respiratory support was necessary in 12.5% of our patients which was in agreement with some other studies, in which it ranged from 5% to 26%.[8,11, 12, 14] This difference could be explained by the difference in indication for intubation between different studies.

In recent years it has been shown that GBS includes at least two distinct conditions: acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and the other acute motor or motor-sensory axonal neuropathy (AMAN). In western populations the clinical picture of GBS is usually produced by AIDP, and a small percentage of cases are due to acute motor or motor-sensory axonal neuropathy.[9] Although most of our knowledge of axonal type GBS arises from Chinese patients,[15,16] recently this type of GBS has been reported from other countries. Typical AMAN occurs in only 5% of GBS cases in western countries, 15% to 20% of cases in Japan, perhaps up to 40% of cases in Latin America, and nearly two-thirds of cases in northern China.[1] In a recent study from Argentina about 30% of patients were in this subgroub.[7] Our results are similar to Mofid Children's Hospital in Tehran, in which about 30% of cases were of the AMAN subtype of GBS.[17] However it is necessary to carry out further investigations in Iran.

Moreover it became evident that AMAN is usually preceded by *Campylobacter jejuni* infection.[1,9,18] Unfortunately it was not possible for us to investigate this organism in our patients.

The results of this study showed that IVIG is effective and safe in the treatment of GBS, which is in agreement with other studies.[19,20,21] Some authors suggest IVIG as initial therapy for pediatric GBS.[19] Our study is in agreement with others[7,11,22,23,24] in showing that an early severe reduction in CMAP amplitude and/or denervation potentials both reflecting pre-exisiting axonal degeneration were associated with a poor outcome (p= 0.034).

In conclusion axonal type GBS is a relatively common form of childhood GBS in East Azarbaijan, and has more disability compared to AIDP.

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