Guillain-Barre Syndrome in Thai Children: Retrospective Analysis of the Clinical and Outcome Prior to Intravenous Immune Globulin Era

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Abstract

The authors retrospectively reviewed Guillain-Barre syndrome (GBS) in 48 Thai children over a period of 20 years from 1970 to 1989. The clinical presentations of this syndrome were compared to those reported in previous studies of children in Western and Asian countries. Antecedent infection, including respiratory tract infection and nonspecific viral infection, in this group of patients is similar to previous studies in children. Cranial nerve involvement found in this study (45.8%) was higher than that in other studies. The outcome of GBS in Thai children in this study was not different from other reports even without IVIG administration. The authors emphasize that respiratory and supportive care are important in managing patients suffering from this syndrome.

Guillain-Barre syndrome (GBS) is an acquired and an acutely developed inflammatory demyelinating polyradiculopathy (AIDP). It consists of a monophasic rapidly progressive course and symmetrical flaccid weakness with areflexia[1,2]. The clinical presentation, in children of this disease has been extensively reviewed since it was first reported[3,4]. There are variants of the syndrome. Miller-Fisher syndrome, which is one of the variants is characterized by ataxia, and ophthalmoplegia on top of typical weakness and areflexia[5]. This syndrome was reported in children as young as 4 months[6]. The incidence of GBS as reported in many Western and South American studies ranged from 0.6 to 1.9 cases per 100,000 persons per year[7-10]. The incidence in children younger than 17 years old is about one-fourth that in adult patients[2,7]. In Asia, an annual incidence of 1.8 cases per 100,000 person-years has been reported in Korea[11] and China[12] which is close to that of the Western countries. The mortality rate of GBS was relatively low, however 10 per cent of the patients had permanent deficits[13]. In Thailand, there have been few reports of GBS in adult patients with clinical description and suggested causes[14,15]. There have been a few descriptive reports in children in Asian countries[16,17], but not from Thailand. The purpose of this study was to establish the basic data, clinical presentation and outcome of this syndrome in Thai children.

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PATIENTS AND METHOD

We retrospectively reviewed the medical records from June 1970 to December 1989 of all children aged under 15 years who were admitted to the Department of Pediatrics, Ramathibodi Hospital, Bangkok with a diagnosis of GBS according to established criteria[18] which included :

1. Progressive symmetrical motor weakness of extremities and reached maximum weakness within 4 weeks of the onset. This weakness might involve facial muscles, external ocular muscles or bulbar muscles.

2. Areflexia (loss of tendon jerks).

Any patient who had a history of hexacarbon abuse, recent infection by diphtheria, having abnormal porphyrin metabolism, had intoxication or any other toxic neuropathy was excluded from the study.

The following information was retrieved from the medical records; age, sex, month and season of the onset of the symptoms, predisposing factors or events, presenting symptoms, neurological signs upon admission, duration from the initial symptom to the maximum neurological deficits, cerebrospinal fluid findings and result of the treatment.

Improvement of the motor function was categorized as follows:

Good : motor power grade 4 to 5
Fair : motor power grade 3
Poor : motor power grade 0 to 2

Duration between the initial symptom and the first improvement of motor function of each patient was obtained and analyzed for correlation to other parameters using Kruskal-Willis test or Wilcoxan Rank Sum test which ever was applicable.

RESULTS

This study included 48 patients, 26 boys and 22 girls. The mean age was 6.5 years (range 8 months - 14 years and 5 months). The age distribution is shown in Fig. 1. There was no difference in disease occurrence during the year (Fig. 2) Nearly half of the patients (22/48) did not have any predisposing factor prior to the onset of GBS. In patients with prodromal symptoms, upper respiratory tract infection was the most common finding (20/48) (Table 1). The mean duration from the recovery of the predisposing illness to the onset of GBS was 11.7 days (range 5 to 18 days).

Thirty-one patients were admitted to the hospital within the first week, eleven within the second week and six beyond the second week after the onset of motor weakness. The motor weakness involved both upper and lower extremities in 42

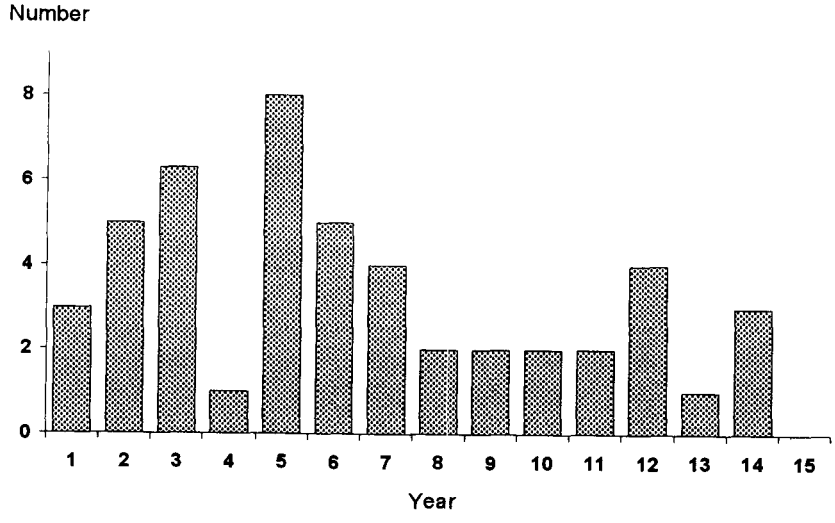

Fig. 1. Age distribution of 48 GBS patients (1970-1989).

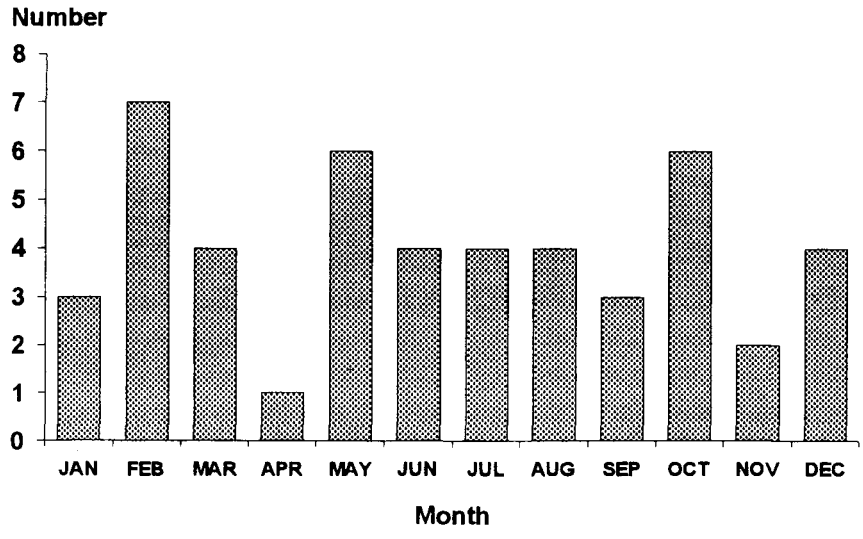

Fig. 2. Monthly distribution of 48 GBS patients (1970-1989).

Table 1. Predisposing infections prior to the onset of GBS in 48 patients (1970-1989).

Predisposing infections	No.
Rhino-pharyngitis	20
Unexplained fever	4
Measles	1
Chickenpox	1
No predisposing infection	22

Table 2. Cranial nerve impairment of 48 GBS patients (1970-1989).

Cranial nerve impairment	No.
IX + X	15
V II	12
V III	4
XI	3
VI	1
No involvement	26

patients, twenty two patients had no difference of weakness between upper and lower extremities and the other twenty patients had more severe weakness of the lower than the upper extremities. The remaining six patients had only weakness of the lower extremities. The severity of the motor weakness on admission revealed grade 3-4, grade 1-2 and grade 0 in 15, 25 and 8 patients respectively.

Cranial nerve involvement was found in 22 patients (46%) (Table 2). Some patients had multiple cranial nerve impairment. Papilledema associated with sixth cranial nerve palsy was found in one patient who had CSF protein level over 500 mg/dl. No typical Miller-Fisher syndrome was seen in this group of patients.

Substantial impairment to pain sensation was found in 25 per cent of patients, and 31.25 per cent of patients had only minimal impairment. The remainder (21/48) had no definite impairment.

Nineteen patients (39.58%) had transient autonomic dysfunctions during the acute stage of the disease. These included loss of anal sphincter tone (10 patients) bladder dysfunction (6 patients) and hypertension (3 patients).

Examination of the cerebrospinal fluid on admission revealed normal CSF pressure in 45 patients, the other 3 patients had a CSF pressure over 200 mm H_2O. The WBC count was less than 10 cells/mm^3 and most of the cells were mononuclear cell in all patients. The CSF protein level

was higher than 40 mg/dl in (31 patients) and the glucose concentration was normal.

Forty patients (83.33%) received treatment with prednisolone 2 mg/kg/day on admission and the medication was discontinued on day 7 of the treatment regardless of the clinical course of the patients.

Sixteen patients had respiratory failure which required supportive ventilation by using a respirator. The mean duration of respirator requirement was 19.7 days (range 2 to 135 days). Only one patient after having cardio respiratory arrest needed very long supportive ventilation for 135 days.

Thirty-seven patients with retrievable details had mean duration from the initial symptoms of GBS to the point of maximum motor weakness of 5 days. The average duration from the onset to the beginning of having recovery was 13 days, (range from 3 to 38 days). The hospital stay was $\geq$ 2, 2-4 and > 4 weeks in 27, 12, and 9 patients respectively.

There was no statistically significant correlation between recovery grade and duration of hospital admission, and duration from initial symptoms to the beginning of recovery. However, there was a significant correlation between age and recovery grade. The younger the patients, the poorer the recovery grade (between good recovery grade and poor recovery grade, $P = 0.002$)

The outcome of patients was divided into two periods, from 1970 to 1979 and 1980 to 1989. Between 1970 and 1979, there were 19 patients. Ten patients had complete recovery, and 3 patients recovered from motor weakness but had minimal brain damage due to asphyxia during the acute stage of motor weakness. The other 6 patients died. The cause of death and brain damage of these patients were related to improper ventilatory support and superimposed infections.

From 1980 to 1989, there were 29 patients. No death or brain damage was observed. Fifteen patients had improvement to grade 4 of motor function within two months. The follow-up examination at the 6th month revealed complete recovery in 20 patients and 4 patients had grade 4 of motor function. The other 5 patients who had severe motor weakness and required ventilatory support on admission still had grade 3 motor weakness of the dorsiflexor of the feet. However, at follow-up examination two years after the onset of GBS, all of these patients had nearly complete recovery of the motor function.

All patients had complete recovery of the cranial nerve dysfunction. Most of them recovered within 2 months. The improvement was observed more or less at the same time as that of the proximal muscle of the limbs, but prior to subtantial improvement of motor function of the distal part.

DISCUSSION

Guillain-Barre syndrome is an uncommonly acquired polyradiculo-neuropathy occurring in both adult and pediatric populations. In general, the clinical course of this syndrome in children is more favorable than in adults[19]. The incidence seems to be high in young patients[10,16,20,21].

This retrospective study includes only referral cases of a single hospital, therefore it was not possible to calculate the exact annual incidence of this syndrome in Thailand. During the 20 years, the mean annual number of patients was 2.4 (92/100,000 of the total cases admission of pediatric patients). As in other studies, boys seemed to have a higher chance of having this syndrome than girls (male and female ratio ranges from 1.07 to 1.66 to 1). No explanation has yet been given for the difference in the incidence between sexes.

The predisposing factors or antecedent infections which were found in 26 of the 48 patients is similar to those in previous studies in children. Combined respiratory tract and other infections were the most common finding.

A remarkable feature of the clinical presentation of the syndrome in this study is the high percentage of cranial nerve involvement. The findings in other studies ranged from 19-41 per cent (21-23). But in this study the cranial nerve involvement was found in 45.8 per cent. The most impaired cranial nerves in our study were glossopharyngeal and vagus nerves, as shown by a decreased gag reflex, difficulty in swallowing and drooling of saliva, which occurred in 31.25 per cent of all patients, which were observed in other series in less than 10 per cent of the cases. Bilateral facial nerve palsy was the second most common which was 25 per cent. This finding is similar to the other series which ranged from 8-33 per cent. However, Miller-Fisher syndrome, a variant of GBS with ophthalmoplegia, was not found in any of these patients.

Sensory deficit was not obvious in these patients. Usually, pain or disturbance of sensations ranged from 42-74 per cent of children in previous studies[10,21,22] and was 74 per cent in the Thai adult study[15]. However, sensory examination is a subjective test and may be less reliable in children younger than 5 years old, which comprised 43 per cent of our patients.

The time from the onset of first symptoms to the maximum motor weakness in this study ranged from 1 to 12 days with the mean duration of 5 days which is shorter than that in other studies[10,21,23]. During the clinical course, respiratory failure occurred in 33 per cent of the patients which is almost twice that found in the study from Finland[21]. These findings from this study may not represent Thai children in general owing to the fact that our institution is one of the large referral medical centers in Thailand, and received more severe cases than other centers such as provincial hospitals.

During the first period of this study (1970-1979) 6 patients died and 3 patients had brain damage, mainly associated with insufficient-respiratory care and superimposed respiratory tract infections. But in the second period (1980-1989) when better respiratory care and observation for respiratory complications were available, there was neither death nor patients with significant morbidity. In fact, all 25 patients had complete recovery of their motor function within two years after the onset of weakness and the remaining 4 patients had only minimal distal motor weakness. The majority of our patients was given corticosteroids, but this proved to have no beneficial effect in GBS [13,24]. During the study period none of our patients was given intravenous immunoglobulins or had plasmapheresis, which have been shown to shorten the duration of ventilatory support[25,26] and thus possibly help to improve motor function in GBS patients[2,26-28]. However, during the study period, IVIG was still in clinical trial and hence was not available in Thailand. At present IVIG is very expensive and there are some special requirements in performing plasmapheresis, thus, routine use of IVIG or plasmapheresis might not be recommended for all Thai children with GBS. Currently in our institution, IVIG will be given to all patients with rapidly progressive weakness with impending respiratory failure. We believe that the most important tools for treatment of any patients with GBS are still respiratory and supportive care. This study also confirms that GBS in general is a benign polyradiculo-neuropathy, which usually is a reversible disease with good outcome, clinical recovery can be expected in all children provided respiratory failure and autonomic involvement are appropriately managed.

There is a regional variant of GBS found in India and China, the so-called acute motor axonal neuropathy or AMAN. This syndrome, which is associated with campylobacter infection[29], has different pathology, electrophysiologic findings and a more severe outcome than typical GBS[29,30]. Owing to the lack of electrophysiologic study and serologic tests which were not available during the period of our study, it was not possible to document this entity in our patients. However, more extensive investigations including electrophysiologic study and more serologic tests might be helpful in establishing the existence of this variant in new cases of Guillain-Barre syndrome in Thai children.

(Received for publication on April 24, 1998)

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การศึกษากลุ่มอาการกีลัง-บาเรในผู้ป่วยเด็กไทย ก่อนยุคการใช้การรักษาด้วยอิมมูโนโกลบูลินฉีดเข้าหลอดเลือดดำ ที่โรงพยาบาลรามาธิบดี

อนันต์นิตย์ วิสุทธิพันธ์, พ.บ., พงษ์ศักดิ์ วิสุทธิพันธ์, พ.บ.*, สุรางค์ เจียมจรรยา, พ.บ.*, มนตรี เวียงเพิ่ม, พ.บ.**

คณะผู้รายงานได้ทำการศึกษากลุ่มอาการ Guillain-Barre ในผู้ป่วยเด็กไทย อายุต่ำกว่า 15 ปี ซึ่งได้มารับการรักษาที่ภาควิชากุมารเวชศาสตร์ โรงพยาบาลรามาธิบดี จำนวน 48 คน ในระหว่าง พ.ศ.2513 และ พ.ศ.2532 เป็นเวลารวม 20 ปี พบว่าอาการ อาการแสดง ตลอดจนสาเหตุของกลุ่มอาการนี้ในผู้ป่วยเด็กไทยไม่มีความแตกต่างจากรายงานในต่างประเทศ ยกเว้นอาการแสดงความผิดปกติของเส้นประสาทสมอง ซึ่งพบสูงถึงร้อยละ 45.8 ถึงแม้ว่าในช่วงระยะเวลาดังกล่าวไม่มีผู้ป่วยคนใดได้รับการรักษาด้วยอิมมูนโกลบูลิน หรือการเปลี่ยนพลาสม่าพบว่าผู้ป่วยส่วนใหญ่ (ร้อยละ 77) มีการฟื้นตัวจากอาการอ่อนแรงจนเป็นปกติเมื่อได้ติดตามการรักษาในระยะยาว ซึ่งใกล้เคียงกับรายงานจากต่างประเทศ ในการศึกษานี้พบว่ามีผู้ป่วย 9 คน เสียชีวิต หรือมีภาวะสมองพิการซึ่งเกิดจากปัญหาการหายใจล้มเหลว ทำให้เกิดภาวะสมองขาดออกซิเจน ซึ่งเป็นผู้ป่วยระหว่างช่วง 10 ปีแรกของการศึกษา (พ.ศ.2513-2522) ภายหลังจากที่มีการปรับปรุงการดูแลปัญหาระบบทางเดินหายใจ พบว่าในช่วง 10 ปีหลังของการศึกษาไม่มีผู้ป่วยคนใดเสียชีวิตหรือมีปัญหาแทรกซ้อนร้ายแรง คณะผู้รายงานมีความเห็นว่าถึงแม้ว่ากลุ่มอาการ Guillain-Barre นี้อาจจะมีอาการและอาการแสดงรุนแรงในผู้ป่วยบางคน และในปัจจุบันนี้มีการแนะนำให้ใช้อิมมูนโกลบูลินในการรักษาในผู้ป่วยที่มีอาการรุนแรงดังกล่าว แต่ในผู้ป่วยส่วนใหญ่แล้ว การให้ความสำคัญต่อการรักษาแบบประคับประคอง ตลอดจนการที่แพทย์ผู้ดูแลรักษาผู้ป่วยให้ความสำคัญต่อการดูแลปัญหาแทรกซ้อนโดยเฉพาะระบบทางเดินหายใจ จะเป็นสิ่งสำคัญในการช่วยให้ผู้ป่วยสามารถฟื้นตัวจากความผิดปกติ โดยที่ไม่มีความพิการเหลืออยู่เลย

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