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A retrospective analysis of possible triggers of Guillain–Barre syndrome

Bing Yang [a], Ying Lian [b], Ying Liu [c], Bing-Yun Wu [c], Rui-Sheng Duan [a,*]

[a] Department of Neurology, Shandong Provincial Qianfoshan Hospital, Shandong University, Jinan 250014, PR China
[b] Department of Case Administration, Shandong Provincial Qianfoshan Hospital, Shandong University, Jinan 250014, PR China
[c] Department of Electromyography, Shandong Provincial Qianfoshan Hospital, Shandong University, Jinan 250014, PR China

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ABSTRACT

Antecedent infections have been found to be the most common trigger for Guillain–Barre syndrome (GBS). In the present study, we retrospectively analyzed 36 adult patients with GBS and found that surgery, trauma and treatment with ganglioside were also common before the onset of GBS. The proportion of the axonal subtype of GBS in post-surgical/traumatic patients was higher than that in non-surgical/traumatic patients ($P = 0.013$) in the present study. In conclusion, this study has shown that prior infection, surgery, trauma and ganglioside may be clinical contributors to the onset of GBS and raised the possibility that they may act synergistically as triggers for the development of GBS.

1. Introduction

Guillain–Barre syndrome (GBS) is an autoimmune polyneuropathy presenting with acute neuromuscular paralysis and albuminocytological dissociation in the cerebrospinal fluid (CSF) (Yuki and Hartung, 2012). The worldwide incidence of GBS is reported to be 1.2 to 2.3 100,000 persons per year (Van Doorn et al., 2008). About two-thirds of patients have antecedent infections 6 weeks before the onset of GBS. The most common pathogens reported to be associated with these prior infections are *Campylobacter jejuni*, *Haemophilus influenzae*, *Epstein–Barr virus*, cytomegalovirus, *Mycoplasma pneumoniae* and influenza virus (Jacobs et al., 1998; Yuki and Hartung, 2012).

The severity of the disease can range from mild to severe. For the majority of patients, treatment includes plasma exchange or intravenous immunoglobulin; at the same time supportive treatment is also important. However, the mortality of GBS can be 5%, even with modern treatment (Yuki and Hartung, 2012). The underlying etiology and pathogenesis of GBS are not fully understood, but the disease is believed to have a humoral and cell-mediated immune basis (Pithadia and Kakadia, 2010).

A prior history of infection has been identified as a risk factor; respiratory tract infection (RTI) or gastrointestinal infection (GII) are the most common infections reported (Guillain–Barre Syndrome Study, 2000). In addition, many cases of post-surgical and post-vaccination GBS have been described in literature (Campbell et al., 2009; Olivier et al., 2010; Renlund et al., 1987; Shuert and Gamble, 1972). Gensicke et al. reported that 6 of 63 (9.5%) GBS patients had a surgery within a six-week period prior to symptomatic presentation (Gensicke et al., 2012).

In a study by Sipilä, the proportion of post-surgical GBS in adults was reported to be 5.8% (4/69) (Sipila and Soilu-Hanninen, 2015). Other studies have reported the onset of GBS following the administration of ganglioside (Figueras et al., 1992; Latov et al., 1991). We have noticed cases of GBS following surgery, trauma or administration of ganglioside in our clinical work. In the present study, we performed a retrospective study of the possible risk factors of GBS in adults over the last four years in Shandong Provincial Qianfoshan Hospital. Clinical features of GBS following different triggers were studied.

2. Patients and methods

2.1. Patients

All patients who were admitted to Shandong Provincial Qianfoshan Hospital from June 2011 to May 2015 were studied. Clinical diagnoses were classified according to the standards of the International Classification of Disease Tenth Revision (ICD-10). Patients diagnosed with an ICD-10 diagnosis of GBS (ICD-10 category G61.0) and the Chinese diagnostic criteria of GBS published in 2010 were selected and reviewed.

Abbreviations: AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; CSF, cerebrospinal fluid; GBS, Guillain–Barre syndrome; ICD-10, International Classification of Disease Tenth Revision; GII, gastrointestinal infection; MFS, Miller–Fisher syndrome; NCS, nerve conduction studies; RTI, respiratory tract infection; tSAH, traumatic subarachnoid hemorrhage.

* Corresponding author at: Department of Neurology, Shandong Provincial Qianfoshan Hospital, Shandong University, Jinan 250014, PR China.
E-mail address: ruisheng_duan@yahoo.com (R.-S. Duan).

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Details of the patients' information were collected, including age, gender, previous infections, surgeries, trauma, treatment with ganglioside, days to onset of symptoms, nerve conduction studies (NCS), CSF, respiratory failure and duration of hospital stay.

Dantec Keypoint 4 electromyograph was used during the study period for electrophysiological examination, and results were reviewed by two electrophysiologists.

2.2. Ethical considerations

This retrospective clinical study was done with all clinical and patient data collected in a confidential way. This study received local ethical approval from the medical ethics committee of Shandong Provincial Qianfoshan Hospital with the following reference number: 2015(006).

2.3. Statistical analysis

Proportions of GBS subtype, intubation and mean duration of hospitalization of non-surgical/traumatic patients were calculated, and they were compared with the data of post-surgical/traumatic patients respectively. Proportions of possible triggers for GBS were calculated, and they were compared with the data of Sipilä's study respectively (Sipila and Soilu-Hanninen, 2015). Pearson's Chi-square test was used to compare the proportion of potential triggers in study population and those reported previously in literature. For quantitative data, comparison between two groups was undertaken using the Student's t-test. Statistical analyses were performed using the SPSS software, version 19.0. A significant level was set at $P < 0.05$.

3. Results

3.1. Patient characteristics

The clinical data of 36 patients who fulfilled the diagnostic criteria of GBS were analyzed. The mean age of onset was 50.7 years (SD: 16.7, range: 16–74); the ratio between man and women was 3.5 (77.8% for men and 22.2% for women). Lumbar puncture was performed on 26 patients (72.2%). A raised CSF protein with a normal mononuclear cell count or <50 cells/mm^3 was found in 21 patients (80.8%) (Table 1).

Thirty-two of 36 patients (88.9%) had electrophysiological examination. According to electrophysiological findings and clinical features, 17 patients had acute inflammatory demyelinating polyneuropathy (AIDP); 4 had acute motor axonal neuropathy (AMAN); 5 had acute motor and sensory axonal neuropathy (AMSAN); 2 had Miller–Fisher syndrome and 4 patients could not be classified.

Among 27 non-surgical/traumatic patients, 4 patients did not have electrophysiological examination; 4 could not be classified; 14 (73.7%) had a demyelinating subtype; 3 (15.8%) had an axonal subtype (including AMAN and AMSAN) and 2 (10.5%) had a MFS. Among 9 post-surgical/traumatic patients, 3 (33.3%) had a demyelinating subtype of GBS and 6 (66.7%) axonal subtype (Table 2).

The proportion of axonal subtype GBS in post-surgical/traumatic patients was higher than that in non-surgical/traumatic patients ($P = 0.013$). The proportion of patients requiring intubation in the non-surgical/traumatic patient group was 11.1% (3/27) and 33.3% (3/9) in the post-surgical/traumatic patients. There was no significant difference between the two groups ($P > 0.05$) (Table 2).

The mean inpatient days of all patients was 19.8, non-surgical/traumatic patients 15.1 and post-surgical/traumatic patients 33.7. Post-surgical/traumatic GBS patients had longer hospital stays than non-surgical/traumatic patients ($P < 0.05$) (Table 2).

3.2. Potential triggers of GBS

In the 36 patients with GBS studied, the possible clinical triggers were identified in 22 patients (61.1%) within 6 weeks preceding GBS. Seventeen patients (47.2%) had symptoms of infection before the onset of GBS and 4 of them also underwent surgery/trauma and administration of ganglioside.

Of the infections preceding the onset of GBS symptoms, RTI was found in 19.4% (7/36) patients, followed by gastrointestinal tract infection in 16.7% (6/36) patients. Surgery was performed on 7 patients (19.4%) within 6 weeks before the onset of GBS. Two (5.6%) had symptoms following trauma. One patient suffered from a road traffic accident which led to traumatic subarachnoid hemorrhage (tSAH) and rib fracture, the other had head and facial trauma, diffuse axonal injury, cerebral contusions and pulmonary infection following a car accident. Eight post-surgical/traumatic GBS patients were given ganglioside before the onset of symptoms, 4 of whom simultaneously had infections (Table 3). Fourteen (38.9%) patients had no prior risk factors that we could find from retrospective examination of their clinical notes. No cases of post-vaccination GBS were found in our study.

When we compared the findings from our study with those previously published by Sipilä et al., the proportion of infections before GBS in the present study was 47.2%; this was lower than that in the report of Sipilä ($P < 0.05$) (Sipila and Soilu-Hanninen, 2015). However, the proportion of cases of post-surgical GBS in the present study was 19.4%, which was greater than that in the study led by Sipilä and colleagues ($P < 0.05$) (Table 4). Although the proportion of prior vaccination between the two studies showed no statistical differences, no cases of GBS were found following vaccination in the present research.

4. Discussion

Thirty-six patients were included in this retrospective study of the possible association for the onset of GBS. In the patients studied, the

Table 1
Demographics, clinical and diagnostic characteristics in patients with Guillain–Barre syndrome (GBS), sorted by potential trigger factors.

Possible triggers	No. (%)	M/F	Mean age (years)	Mean days to onset	Pathological NCS[a]			CSF[b]		
					Present no. (%)	Not done	Absent no.	Present no. (%)	Not done	Absent no.
Infection (all)	17/47.2	14/3	43.7	8.7	14/93.3	2	1	8/66.7	5	4
GII	6/16.7	5/1	53.3	12.5	4/80	1	1	3/75	2	1
RTI	7/19.4	5/2	32.3	5.6	6/100	1	0	4/66.7	1	2
Surgery	7/19.4	6/1	60.0	10.9	7/100	0	0	4/100	3	0
Trauma[c]	2/5.6	2/0	45.0	9.0	2/100	0	0	1/100	1	0
Surgery + ganglioside	6/16.7	5/1	59.0	–	6/100	0	0	3/100	3	0
Administration of ganglioside	8/22.2	7/1	55.5	9.1	8/100	0	0	4/100	4	0
No trigger factor	14/38.9	10/4	55.1	–	9/75	2	3	9/81.8	3	2
All patients	36/100	28/8	50.7	–	28/87.5	4	4	21/80.8	10	5

GBS, Guillain–Barre syndrome; GII, gastrointestinal infection; RTI, respiratory tract infection; NCS, nerve conduction studies; CSF, cerebrospinal fluid.

[a] Electrophysiological abnormalities conformed to demyelinating or axonal lesion of peripheral nerves (prolonged distal latencies, decreased nerve conduction velocities, temporal dispersion of motor action potentials, slowed or absent F-wave responses, lowed distal compound muscle action potential amplitude more than 20%).

[b] Albumino-cytological dissociation in cerebrospinal fluid (CSF) (elevated protein, 50 or fewer mononuclear leucocytes/mm^3).

[c] Both post-traumatic GBS patients were treated with ganglioside.