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ORIGINAL ARTICLE

Clinical and antibodies analysis of anti-GQ1b antibody syndrome: a case series of 15 patients

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Abstract

Objectives To investigate the clinical manifestations, immunity, laboratory test, treatment and prognosis of patients with anti-GQ1b antibody syndrome in Chongqing, China.

Methods We reviewed 15 patients with positive anti-ganglioside antibodies in the First Affiliated Hospital of Chongqing Medical University from 2016 to 2019.

Results Fifteen patients were included in the study (mean age, 54.4 years; age range, 27 to 80 years; 9 men (60%)). Ten patients presented with a history of preinfection, including flu-like syndrome ($n=6$, 60%), upper respiratory tract infection (URTI) ($n=3$, 30%), and digestive tract infection (GI) ($n=1$, 10%). The most common manifestation was ophthalmoplegia ($n=13$, 86.67%), followed by weakness ($n=12$, 80%), ataxia ($n=11$, 73.3%), paresthesia ($n=8$, 53.33%) and hypersomnolence ($n=5$, 33.33%). All 15 patients underwent antibody testing. Eight patients (53.33%, 7 men (87.5%)) of whom only have positive immunoglobulin G (IgG) against anti-GQ1b antibody while seven (46.67%, 2 men (28.57%)) were positive for multiple anti-ganglioside antibodies apart from anti-GQ1b antibodies. Nine patients (60%) received intravenous immunoglobulin (IVIG) therapy, four (26.67%) received plasma exchange (PE) and two (13.33%) received steroid therapy. Three patients were lost to follow-up at 6 months, 1 patient (6.67%) had persistent back numbness, and the other 11 patients (73.33%) had fully recovered.

Conclusion The clinical subtype of anti-GQ1b antibody syndrome correlates with the type of anti-ganglioside antibody. Patients who test positive for only anti-GQ1b antibody are more likely to be men. Most patients exhibit a unidirectional course with a good prognosis, but anti-GQ1b antibody syndrome is also associated with a risk of recurrence.

Keywords Anti-GQ1b antibody syndrome · Anti-ganglioside antibodies · Immunotherapy

Introduction

Gangliosides are commonly expressed in body tissues and fluids but are particularly abundant in the nervous system. They are involved in the maintenance and repair of neuronal cells, memory formation, and synaptic transmission [1]. On the other hand, certain viruses, bacteria, and parasites use gangliosides as attachment sites and cause diseases [1]. Anti-GQ1b antibody syndrome was first described in 2001 by Odaka and is characterized by common functions of the autoimmune mechanism [2]. The anti-GQ1b antibody syndrome has been reported to be associated with ophthalmoplegia, hypersomnolence, ataxia, bulbar palsy, and weakness [3]. The most common clinical feature of patients with anti-GQ1b antibody syndrome has been reported to be acute ophthalmoplegia (72.7%) [4]. According to clinical manifestations, the anti-GQ1b syndrome can be divided into the following six types of diagnosis: typical Miller Fisher syndrome (MFS), incomplete Miller Fisher syndrome, Guillain–Barré syndrome (GBS), Bickerstaff brain stem encephalitis (BBE), pharynx–neck–brachial muscle weakness, and different types of overlap [5]. The diagnosis of anti-GQ1b antibody syndrome depends on the presence of immunoglobulin G (IgG) antibodies against GQ1b gangliosides. Most patients with anti-GQ1b antibody syndrome have a history of preinfection. These infectious agents include Campylobacter jejuni, cytomegalovirus, Haemophilus influenzae, Epstein–Barr virus, and other microorganisms [6].

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Depending on the number of sialic acid residues attached (M for one, D for two, T for 3 and Q for 4) to the inner sugar moiety and according to their chromatographic mobility, gangliosides can be divided into GM1, GD1a, GT1a and GQ1b [7]. The distribution of different gangliosides in the nervous system has specific regions [2]. Anti-ganglioside antibodies reported to be associated with diseases include GM1, GM1b, GM2, GM3, GM4, GD1a, GD1b, GD3, GQ1b, GT1b9-OAc and GalNAc-GD1a. GQ1b, GM1, GM1b, GD1a, GT1b and GalNac-GD1a have been reported to be associated with Guillain–Barré syndrome and its subtypes [2, 3].

Currently, a large number of clinical studies have confirmed that intravenous gamma globulin (IVIG) and plasma exchange for the treatment of GBS can achieve a good prognosis, but treatment for MFS, BBE and other anti-GQ1b antibody syndromes still lack large-scale clinical samples. However, according to a previous study, only 85% of patients with MFS, 66% of patients with BBE and 24–26% of patients with GBS are positive for IgG anti-GQ1b antibodies [4–6, 8]. In China, because of the high cost of antibody detection and good prognosis of this disease, doctors and patients do not perform antibody detection as part of a routine examination. We have little understanding of the characteristics of these antibody-positive diseases. In this paper, we present a series of cases of anti-GQ1b syndrome from the First Affiliated Hospital of Chongqing Medical University. We also aimed to summarize the clinical characteristics and to discuss appropriate treatment options.

Patients and methods

Patients

The patients were recruited at the First Affiliated Hospital of Chongqing Medical University. A total of 54 patients diagnosed with MFS, GBS, BBE, or anti-GQ1b syndrome were enrolled in the study. Thirty-six of the patients were excluded because they had not been tested for anti-ganglioside antibodies, and three patients were excluded because they did not meet any of the diagnostic criteria for anti-GQ1b syndrome. Ultimately, 15 patients with positive IgG anti-GQ1b antibodies had samples submitted for analysis.

Methods

The main inclusion criteria were a clinical diagnosis of MFS, GBS, BBE or acute ophthalmoplegia and positive anti-ganglioside antibodies present in the cerebrospinal fluid or serum of the patient as previous studies [4, 7]. The following clinical data were collected from each patient: (1) the phenotypic data, including hypersomnolence, cranial nerve involvement, bulbar palsy, ataxia, muscle weakness, and paresthesia; (2) neurological examination data; (3) auxiliary examination data, including nerve conduction velocity (NCV), electromyography (EMG) and serum and cerebrospinal fluid (CSF) IgG antibodies of the ganglioside test; (4) treatment, course and prognosis. We designated the period when the patient was severity and no new clinical manifestations were present as nadir. One patient had been tested the positive GQ1b IgG antibodies and had a previous diagnosis of Miller Fisher syndrome 2 years ago. The other two patients had been carefully reviewed by clinical experts and a definitive diagnosis of Guillain–Barré syndrome was made after exclusion of other diseases 8 and 10 years ago, respectively. They all had complete recovery after treatment, which was consistent with anti-GQ1b antibody syndrome. However, because testing for anti-ganglioside antibodies was not common in China at that time, these two patients were not tested for anti-GQ1b antibodies.

Western blotting was used for detection the anti-ganglioside antibody (Chongqing Jinyu Medical Laboratory, Chongqing, China, using the EUROBlot Master II automatic Western blotting instrument for analysis). In addition to the detection of anti-GQlb antibody IgG and IgM bands on the test strip, all patients were also tested for the IgG and IgM bands of anti-GTlb, GDlb, GDla, GMl, GM2, and GM3 antibodies on the test strip.

Results

The general characteristics of the patients are as follows. Fifteen patients (9 (60%) male, 6 (40%) female) were included in this study. The patient ages ranged from 27 to 80 years (mean ± SD 54 ± 16 years). Twelve patients presented with the first episode and 3 patients with a second episode. During the 6-month follow-up, 3 patients were lost to follow-up, 11 patients recovered completely, and 1 patient partially recovered.

Clinical manifestations

More than half of the patients (10/15, or 66%) had a preceding infection, such as upper respiratory tract infection (URTI) ($n=3$), influenza-like syndrome ($n=6$), or gastrointestinal infection ($n=1$). All patients had a sudden onset and reached a nadir state after 2–8 days of onset (average 4 days). Ophthalmoplegia ($n=13$, 86.67%), followed by weakness ($n=12$, 80%), ataxia ($n=11$, 73.3%), paresthesia ($n=8$, 53.33%) and hypersomnolence ($n=5$, 33.33%) were the most common clinical manifestations. Areflexia or hyporeflexia were present in 13 patients (86.67%). The pattern of weakness including ocular muscle paralysis (13/15, 86.67%), facial palsy (8/15, 53.33%), limb weakness (6/15,

40%) and neck muscle weakness (1/15, 6.67%). 4 patients (4/15, 26.67%) had numbness, as well as the percentage of pain. These patients were diagnosed as MFS (2/15, 13.33%), MFS overlapped with classic GBS (2/15, 13.33%), Bickerstaff brain stem encephalitis (BBE) overlapped with classic GBS (2/15, 13.33%), classic GBS (1/15, 6.67%), Acute ophthalmoplegia (AO) ($n=1$), Acute ataxic hypersomnolence (AAH) ($n=1$), Bifacial weakness with distal paresthesia (BWDP) overlapped by AO ($n=1$), Bifacial weakness with distal paresthesia overlapped by MFS ($n=1$), MFS overlapped by pharyngeal–cervical–brachial weakness (PCBW), BWDP overlapped by BBE ($n=1$), PCBW overlapped by BBE ($n=1$) and classic GBS overlapped by AO ($n=1$), respectively (Table 1).

Cerebrospinal fluid features

All patients underwent lumbar puncture and cerebrospinal fluid examination. The timeframe of the lumbar puncture was from the 3rd to the 31st day (average 8 days) after the onset of the disease. The CSF analysis showed pleocytosis in one patient (1/15, 6.67%) and albuminocytological dissociation in six patients (6/15, 40%) (Table 2).

According to the difference in anti-ganglioside antibodies in serum or cerebrospinal fluid, we divided the 15 patients into 2 groups which was shown in Table 3. The immunological examination of eight patients (8/15, 53.33%) only showed positive IgG against anti-GQ1b antibody. Of the eight patients, seven patients were male (87.5%) (Table 2). These patients often had flu-like symptoms before the onset (5/8, 62.5%). The cranial nerves most commonly involved were pairs III and VI (6/8, 75%). The first symptoms at the time of onset were giddiness (6/8, 75%) and diplopia (4/8, 50%). After treatment, the time to fully recover was 32 ± 14 days for patients with a single positive antibody.

The immunological examination of seven patients (46.67%) showed positive IgG antibodies for multiple gangliosides, including anti-GD1b ($n=2$), anti-GD3 ($n=2$), anti-GT1a ($n=4$), anti-GT1b ($n=2$), anti-GM1 ($n=2$), anti-GM2 ($n=1$), anti-GM3 ($n=1$), and anti-GM4 ($n=1$) (Table 2). Among them, three patients (3/7, 42.8%) had upper respiratory tract infections, one patient had a flu-like syndrome, and one had a gastrointestinal infection. Compared to patients with only anti-GQ1b antibodies, patients with multiple anti-ganglioside antibodies were more commonly female (5/7, 71.42%). After treatment, patients with multiple positive anti-ganglioside antibodies reached recovery in 22 ± 9 days (Table 3).

Nerve conduction studies

The results of nerve conduction studies of 15 patients were collected. Among them, 12 patients showed abnormalities (80%) (Table 4). Ten patients (83.33%) had damaged motor

Table 1 Clinical characters of 15 patients

Patient/sex/age	Preceding infection	Hypersomnolence	Neurologic signs during illness					Sub-type
			Decreased muscle power	Paresthesia	Ophthalmoplegia	Ataxia	Areflexia	
1/F/77	None	None	Four limbs	Numbness	None	None	Yes	CGBS
2/M/29	Flu-like syndrome	Yes	Facial, four limbs, bulbar palsy	Numbness	Yes	Yes	Yes	CGBS-BBE
3/M/58	Flu-like syndrome	Yes	Four limbs, bulbar palsy	None	Yes	Yes	Yes	CGBS-BBE
4/F/30	URTI	None	Facial, lower limbs, bulbar palsy	None	Yes	Yes	Yes	CGBS-MFS
5/F/61	Flu-like syndrome	None	Four limbs	Numbness	Yes	Yes	Yes	CGBS-MFS
6/M/60	Flu-like syndrome	None	Facial, four limbs	None	Yes	None	Yes	CGBS-AO
7/M/80	None	None	None	None	Yes	Yes	None	MFS
8/F/51	URTI	None	Bulbar palsy	None	Yes	Yes	Yes	MFS
9/M/50	Flu-like syndrome	None	Facial	Numbness/pain	Yes	Yes	Yes	MFS-BP
10/M/61	None	None	Facial, bulbar palsy	Pain	Yes	Yes	Yes	MFS-PCBw
11/M/45	None	None	None	Numbness	Yes	None	Yes	AO
12/F/67	GI	None	Facial	Numbness/pain	Yes	None	Yes	AO-BP
13/M/74	Flu-like syndrome	Yes	Facial, bulbar palsy	None	Yes	Yes	Yes	BBE-BP
14/F/27	URTI	Yes	Facial, cervical, bulbar palsy	Numbness/pain	Yes	Yes	Yes	BBE-PCBw
15/M/47	None	Yes	None	None	None	Yes	None	AAH

BBE Bickerstaff brainstem encephalitis; *CGBS* classic Guillain–Barré syndrome; *MFS* Miller Fisher syndrome; *PCBw* pharyngeal–cervical–brachial weakness; *BP* bifacial weakness with distal paraesthesias; *AO* acute ophthalmoplegia; *AAH* acute ataxic hypersomnolence

Table 2 Cerebrospinal fluid characteristics of 15 patients

Patient	Puncture time after onset (days)	CSF: protein (mg/dl)/ nucleated cells count (μl)	Positive anti-ganglioside antibodies
1	3	0.36/4	Anti-GQ1b, anti-GT1a
2	3	0.36/3	Anti-GQ1b, anti-GD1b, anti-GM2
3	8	0.31/1	Anti-GQ1b, anti-GT1a
4	15	1.09/2	Anti-GQ1b
5	3	0.26/0	Anti-GQ1b
6	7	1.26/2	Anti-GQ1b, anti-GD1b
7	8	0.87/2	Anti-GQ1b, anti-GT1a, anti-GT1a, anti-GD3
8	4	0.33/2	Anti-GQ1b, anti-GT1a, anti-GM3, anti-GM4, anti-GT1a, Anti-GD3
9	9	0.74/7	Anti-GQ1b
10	5	0.26/0	Anti-GQ1b
11	5	0.48/3	Anti-GQ1b
12	15	1.85/54	Anti-GQ1b, anti-GM1
13	31	2.13/3	Anti-GQ1b
14	6	0.39/2	Anti-GQ1b
15	8	Not know	Anti-GQ1b

nerves, nine patients showed impaired sensory nerves, and two patients (13.33%) had extended latency period. H-reflex and F-wave were reported abnormal in ten patients (83.33%), respectively, and seven patients showed abnormalities in both F-wave and H-reflexes.

Treatment and prognosis

Of the 15 patients, 9 (9/15, 60%) were treated with intravenous immunoglobulin, 2 (2/15, 13.33%) patients received plasma exchange, and 2 (2/15, 13.33%) patients were treated with intravenous immunoglobulin followed by plasma exchange. 2 (2/15, 13.33%) patients were treated with steroids, of which 1 patient who was treated with steroids also received intravenous immunoglobulin. The time to remission ranged from 5 to 40 days; most patients started remission within 2 weeks (12/15, 80%). The clinical symptoms of patients returned to the normal within 1 month (14/15, 93%, an average of 27 days). There were no pulmonary infections during the hospitalization of 13 patients (13/15, 86.6%). The length of hospitalization for most patients was less than 1 month (13/15, 86.6%). A telephone follow-up 6 months later showed that contact was lost with 3 patients, 11 patients had fully recovered, and 1 patient had back numbness. A second telephone follow-up 2 years later showed that none of the 12 patients had experienced recurrence (Table 5). Two patients were admitted to the hospital in relatively severe condition; both had combined Bickerstaff encephalitis and developed respiratory failure. One patient had only positive anti-GQ1b IgG antibodies in the cerebrospinal fluid, while the other had positive anti-GT1a antibodies in addition to positive anti-GQ1b IgG antibodies. One patient received plasma exchanges and intravenous immunoglobulin therapy, while the other received only intravenous immunoglobulin, but both patients made a full recovery.

Twelve patients were diagnosed with anti-GQ1b syndrome for the first time and had no history of autoimmune neurological disease. Three patients were the second episode. The characteristics of the three patients with recurrent anti-GQ1b syndrome are described in (Table 6). Patient 1 is a 27-year-old woman who tested positive for anti-GQ1b antibodies during her first episode 2 years ago, and she was also tested positive for GT1a antibodies during her second episode. For each of the two attacks, the patient received steroids and intravenous immunoglobulin respectively, but both recovered completely within 3 months. Patient 2 is an 80-year-old man who was treated with plasma exchange 10 years ago for diplopia and completely recovered. The second episode also presented as diplopia. Intravenous immunoglobulin and plasma exchange treatment were administered. Patient 3 is a 77-year-old woman whose initial onset was 8 years ago. Both episodes presented mainly with weakness and improved completely with the use of intravenous immunoglobulin (Table 6).

Discussion

Anti-GQ1b antibody syndrome is a group of autoimmune diseases that occur after the body is infected with pathogenic microorganisms [9]. The main results in our study are as follows: first, our study identified the clinical manifestation, cerebrospinal fluid biochemical examination, electromyography results, and treatment of patients with anti-GQ1b

Table 3 Clinical profiles of patients with anti-GQ1b antibody syndrome

	Anti-GQ1b IgG only ($n=8$)	Multiple anti-ganglioside antibodies ($n=7$)
Age, mean ± SD, year	56 ± 15	53 ± 20
Male, *n* (%)	7/8 (87.5)	2/7 (28.57)
Antecedent infection history, *n* (%)	5/8 (62.5)	5/7 (71.42)
URTI	0	3/7 (42.8)
Flu-like syndrome	5/8 (62.5)	1/7 (14.2)
GI	0	1/7 (14.2)
None	3/8 (37.5)	2/7 (28.5)
Initial symptoms		
Cranial nerve involvement		
None	1/8 (12.5)	1/7 (14.2)
II	1/8 (12.5)	2/7 (28.5)
III	6/8 (75)	7/7 (100)
IV	3/8 (37.5)	2/7 (28.5)
VI	6/8 (75)	4/7 (57.1)
VII	1/8 (12.5)	3/7 (42.8)
IX	1/8 (12.5)	4/7 (57.1)
XII	0	0
Numbness, *n* (%)	2/8 (25)	1/7 (14.28)
Giddy, *n* (%)	6/8 (75)	3/7 (42.85)
Weakness, *n* (%)	1/8 (12.5)	1/7 (14.2)
Treatment		
IVIG	5/8 (62.5)	7/7 (100)
PE	4/8 (50)	0
Steroid	1/8 (12.5)	1/7 (14.28)
Prognosis		
Recovery time, mean ± SD, day	32 ± 14	22 ± 9
Full recover	5/8 (62.5)	6/7(85.7)
Partial recover	0	1/7 (14.2)

URTI upper respiratory tract infection; *GI* gastrointestinal illness; *IVIG* intravenous immunoglobulin; *PE* plasma exchange

antibody syndrome, and we investigated the connection between anti-GQ1b antibody syndrome and infection again [10]. Second, the type of antibody correlates with the clinical subtype of anti-GQ1b antibody syndrome as well as the patient's gender (patients with single positive anti-GQ1b antibodies are predominantly male). Finally, whereas anti-GQ1b antibody syndrome was previously considered to have a predominantly unidirectional course [11], we report three patients who presented with relapses and compare the characteristics of the two episodes.

After the body is infected, anti-ganglioside antibodies are produced through molecular simulation mechanisms [12]. These antibodies bind to gangliosides located on the oculomotor nerve [13], the trochlear nerve, the abducens nerve [14], the glossopharyngeal nerve, the vagus nerve, the limb muscle spindle [15], and the structure of the brainstem network and cause symptoms such as diplopia [16], dizziness, weakness, difficulty breathing, and drowsiness [17]. Consistent with what is reported in previous literatures [18–20], 10 patients in this group had a history of infection before onset (10/15, 66.67%), including respiratory tract infections ($n=9$, 90%) and gastrointestinal tract infections ($n=1$, 10%). 90% (9/10) patients in our group had post-respiratory infection and 10% (1/10) had pre-morbid acute gastroenteritis. Haemophilus influenzae (21%) is the most common pathogen that causes Miller Fisher syndrome, which often causes respiratory tract symptoms [20]. In our study, four patients with MFS had preinfection (4/6, 66.67%), and all showed upper respiratory tract infection (4/4); nine patients were not diagnosed with MFS or MFS overlapping phenotypes. In addition, six of these nine patients had a prodromal infection (6/9, 66.67%), including influenza-like syndrome ($n=4$, 66.67%), URTI ($n=1$, 16.67%) and GI ($n=1$, 16.67%).

Given that different gangliosides are enriched in different parts of the human body and that the mechanism of body damage mediated by different glycolipids is also diverse, these potential mechanisms can lead to types of diseases caused by different anti-ganglioside antibodies [2, 21]. The anti-ganglioside antibodies related to Guillain–Barré syndrome are mainly GT1b, GM1, GM1b, GD1a, and GQ1b, while GQ1b is mainly related to MFS, which is also closely related to BBE [3]. In our study, one patient with classic GBS was positive for anti-GQ1b/anti-GT1a/anti-GT1b/anti-GD3, four patients with classic GBS overlapped by MFS, incomplete MFS, or BBE were only positive for IgG of anti-GQ1b, which is in line with previous study that anti-GT1a and -GQ1b antibodies had significant associations with ophthalmoplegia [22].

In addition to simple paralysis of the ocular muscles, weakness of the oropharyngeal–cervical muscles (7, 46.67%) was also seen more frequently in our patients, in agreement with the 50% (3/6) reported in a previous study in the Indian region regarding GBS [23], and higher than that in childhood [24]. Eight patients had facial muscle weakness (8, 53.33%), while the five patients with COVID-19 reported by Toscano et al. in Guillain–Barré syndrome (GBS) had four cases of facial biparesis (80%) [25], and this percentage was similar to MFS (4/5, 80%) [26].

Among the cases with GQ1b single antibody positive, the proportion of men was significantly higher than that of women (7:1) and higher than that found in most foreign reports (1.5–2.2:1), while the proportion of men and women in cases with multiple anti-ganglioside antibody positives was (4:5), far below the Japanese report (1.7:1) [27, 28]. Eight of the 13 patients with acute ophthalmoplegia were male (8/13, 61.53%), which was consistent with previous reports that Chinese men are more likely to develop Fisher

Table 4 Nerve conduction study in 15 patients

Patient	Motor nerves		Sensory nerves		Latent	F-Wave	H-reflex
	CMAP	Velocity	CMAP	Velocity			
1	Normal	Abn	Normal	Normal	Normal	Abn	Abn
2	Abn	Normal	Abn	Normal	Normal	Abn	None
3	Abn	Abn	Abn	Abn	Abn	Abn	Abn
4	Normal	Abn	Normal	Abn	Normal	Abn	Normal
5	Normal	Abn	Normal	Abn	Normal	Abn	Abn
6	Normal	Abn	Normal	Abn	Normal	Abn	Abn
7	Normal	Abn	Normal	Abn	Normal	Normal	Abn
8	Normal	Normal	Normal	Normal	Normal	Normal	Abn
9	Abn	Abn	Abn	Normal	Abn	Abn	Abn
10	Normal	Abn	None	None	Normal	Abn	Abn
11	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	Normal	Abn	Normal	Abn	Normal	Abn	Abn
13	Normal	Normal	Normal	Abn	Normal	Normal	Abn
14	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	Normal	Normal	Normal	Normal	Normal	Abn	Normal

CMAP Abn reduced compound muscle action potential; *Velocity Abn* decreased conduction velocity; *Latent Abn* prolonged latency; *F-Wave Abn* reduced or disappeared F-wave; *H-reflex Abn* absent H-reflexes

Table 5 Treatment and prognosis of 15 patients

Patient	Time to nadir (days)	Treatment/days after onset			Initial recovery time (days)	Complications	Complete recovery time (days)	Prognosis
		IVIG	PE	Steroids				
1	5	IVIG/21			8	Diabetes	27	Back numbness
2	3	IVIG/6			7	No	14	Recover
3	6	IVIG/17			12	Diabetes	17	Recover
4	2	IVIG/28	PE/15		31	No	33	Unclear
5	5			Steroids/10	20	No	23	Unclear
6	2		PE/10		11	No	29	Unclear
7	Unclear	IVIG/39			40	No	43	Recover
8	2	IVIG/16			11	No	21	Recover
9	3	IVIG/8		Steroids/3	11	No	18	Recover
10	3	IVIG/7			10	No	38	Recover
11	3	IVIG/9			9	No	21	Recover
12	7	IVIG/10			12	Diabetes, pneumonia	31	Recover
13	8		PE/13		14	Bronchial asthma	25	Recover
14	3	IVIG/16	PE/3		12	Pneumonia, epilepsy, gastrointestinal dysfunction	62	Recover
15	3	IVIG/5			5	No	13	Recover

IVIG intravenous immunoglobulin; *PE* plasma exchange

syndrome than females (1.6:1.0); however, the specific reasons need to be further studied [27]. Consistent with the results of foreign studies [29], there was no significant difference between males and females in terms of age of onset, clinical manifestations, and course of disease, which may prompt the thought that gender is not a factor that affects the clinical characteristics of the disease.

Most patients presented with an acute single course of the disease, and 3 of 15 patients (20%) had recurrence. This outcome is higher than that reported in the literature where the recurrence rate of GBS is 1–7% and 12% (4/34) with MFS [30, 31]. Compared with the first episode, two relapsed patients in this case had similar symptoms, which is consistent with the report of Orr, C F, and C E Storey [32].

Table 6 Characters of patients with recurrent anti-GQ1b syndrome

	Patient 1		Patient 2		Patient 3	
	Female/27 years		Male/80 years		Female/77 years	
	First episode	Second episode	First episode	Second episode	First episode	Second episode
Antecedent infection	URTI	URTI	Unclear	None	Unclear	None
Manifestation	Diplopia, giddy	Diplopia, weakness, bulbar palsy	Diplopia	Diplopia	Weakness	Weakness, numbness
Diagnose	MFS	BBE-PCBw	GBS	MFS	GBS	CGBS
Anti-ganglioside antibodies	Anti-GQ1b	Anti-GQ1b, anti-GT1a	Unclear	Anti-GQ1b	Unclear	Anti-GQ1b, anti-GT1a, anti-GT1a, anti-GD3
Treatment	Steroid	IVIG	PE	PE + IVIG	IVIG	IVIG
Recovery time	2 months	1 month	Unclear	Unclear	1 month	1 month
Prognosis	Full recover	Full recover	Full recover	Unclear	Full recover	Full recover
Interval time	2 years		10 years		8 years	

BBE Bickerstaff brainstem encephalitis; *CGBS* classic Guillain–Barré syndrome; *MFS* Miller Fisher syndrome; *PCBw* Pharyngeal–cervical–brachial weakness; *URTl* upper respiratory tract infection; *IVIG* intravenous immunoglobulin; *PE* plasma exchange

Previous trials and Cochrane reviews have shown that the use of PE or IVIG within 2 weeks after onset can speed recovery, but that the administration of IVIg after PE will not bring about significant additional benefits [33]. Randomized controlled trials have shown that five drug trials (interferon β-1a, brain-derived neurotrophic factor, tripterygium polyglycoside, corticosteroids, and eculizumab) other than intravenous immunoglobulin or plasma exchange have not been tested to have important clinical significance for patients with Guillain–Barré syndrome (GBS) [33]. However, the treatment regimen and therapeutic effect of other types of anti-GQ1b syndrome, such as MFS, BBE, and pharyngeal–cervical–brachial muscle weakness, are still unclear. Since IVIG is more convenient to implement clinically, ten patients in this study were treated with intravenous immunoglobulin, two patients with plasma exchange, and two patients with IVIG after plasma exchange. All patients without serious adverse reactions. In terms of the start time of treatment, four patients started treatment 2 weeks after the onset of symptoms (16–39 days), and the average time to reach the lowest point of symptoms was 27 days (17–43 days). Eleven patients started treatment within 2 weeks of onset, and the average time to reach the lowest point of symptoms was 9.85 days (5–14 days). The time to reach the lowest point of symptoms for patients with the PE + IVIG treatment regimen was 33 days and 62 days, respectively. The length of the illness was the same as previously reported (an average of 2.5 months) [28].

Most patients with anti-GQ1b antibody syndrome have a good prognosis; a poor prognosis is mostly related to patients with complicated lung infection, respiratory failure, cerebral edema, epilepsy, and brain stem injury [8, 34]. In the literature, a young patient has been reported in the literature that a young female patient died of sepsis [35]. In our study, two patients were serious and all had pulmonary infection and respiratory failure. These patients had elevated immunoglobulin G targeting GQ1b. However, in previous reports, patients with positive anti-GD1a antibodies have required mechanical ventilation and had a poor prognosis. GQ1b is significantly higher in the oculomotor nerve, trochlear nerve, and abducens nerve myelin, while other cranial and peripheral nerves lack such gangliosides [36, 37].

We acknowledge that this study is retrospective, that there were biases in the selection of patients, and that patients were used to measure serum anti-ganglioside antibodies. This selection bias should have affected the demographic characteristics of a single anti-GQ1b antibody-related neurological syndrome and multiple anti-GQ1b antibody-related neurological syndromes. Therefore, a comparative analysis of patients with different anti-ganglioside antibodies should be carried out by expanding the sample size and prospective design.

Conclusion

A history of antecedent infection of the respiratory or gastrointestinal system is a prevalent hallmark of anti-GQ1b antibody syndrome, with ophthalmoplegia, weakness ataxia, and areflexia, being the most typical clinical presentation. Patients with single positive anti-GQ1b antibodies are predominantly male. Immunotherapy is the most common treatment for this illness. Regardless of gender, population and antibody type, most patients exhibit a unidirectional course with a good prognosis, but anti-GQ1b antibody syndrome is also associated with a risk of recurrence.

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Declarations

Conflict of interest All the authors declared that they have no potential conflict of interest.

Ethical approval Patients and public were not involved in the study as this was a retrospective cohort study.

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