REVIEW ARTICLE

The spectrum of anti-GQ1B antibody syndrome: beyond Miller Fisher syndrome and Bickerstaff brainstem encephalitis

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Abstract

Introduction Since the initial identification of Miller Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE),significant milestones have been achieved in understanding these diseases.Discoveries of common serum antibodies (IgG anti-GQ1b), antecedent infections, neurophysiological data, andneuroimaging suggested a shared autoimmune pathogenetic mechanism rather than distinct pathogenesis, leadingto the hypothesis that both diseases are part of a unified syndrome, termed *"Fisher-Bickerstaff syndrome"*. The subsequent identification of atypical anti-GQ1b-positive forms expanded the classification to a broader condition known as *"Anti-GQ1b-Antibody syndrome"*.

Methods An exhaustive literature review was conducted, analyzing a substantial body of research spanning from the initialdescriptions of the syndrome's components to recent developments in diagnostic classification and researchperspectives.

Results Anti-GQ1b syndrome encompasses a continuous spectrum of conditions defined by a common serological profilewith varying degrees of peripheral (PNS) and central nervous system (CNS) involvement. MFS and BBE represent theopposite ends of this spectrum, with MFS primarily affecting the PNS and BBE predominantly involving the CNS.Recently identified atypical forms, such as acute ophthalmoparesis, acute ataxic neuropathy withoutophthalmoparesis, Guillain-Barré syndrome (GBS) with ophthalmoparesis, MFS-GBS and BBE-GBS overlap syndromes,have broadened this spectrum.

Conclusion This work aims to provide an extensive, detailed, and updated overview of all aspects of the anti-GQ1b syndromewith the intention of serving as a stepping stone for further shaping thereof. Special attention was given to therecently identified atypical forms, underscoring their significance in redefining the boundaries of the syndrome.

Keywords "Miller Fisher syndrome" · "Bickerstaff brainstem encephalitis" · "Anti-GQ1b antibody syndrome" · "Anti-ganglioside antibody syndrome" · "Anti GQ1b" · "Ganglioside"

Introduction

Since the initial identification of Miller Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE), significant milestones have been achieved in the understanding of such diseases. Commonalities discovered in serum antibodies (IgG anti GQ1b), antecedent infection, neurophysiological data and neuroimaging suggested a shared autoimmune pathogenetic mechanism rather than distinct pathogenesis, thus allowing the hypothesis that both diseases are part of a unified syndrome, named *"Fisher-Bickerstaff syndrome"* [1].

The identification of anti-GQ1b-positive formes frustes has further led to the classification of a more inclusive condition known as *"Anti-GQ1b-Antibody syndrome"*. This syndrome encompasses a continuous spectrum of conditions defined by a common serological profile and varying degrees of peripheral nervous system (PNS) and central nervous system (CNS) involvement [2, 3].

Such a spectrum presents MFS and BBE at the opposite ends, with MFS primarily affecting the PNS and BBE

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predominantly involving the CNS, and includes various formes frustes such as acute ophthalmoparesis, acute ataxic neuropathy without ophthalmoparesis, Guillain-Barré syndrome (GBS) with ophthalmoparesis and MFS-GBS and BBE-GBS overlap syndromes [4].

The present work aims to provide an extensive, detailed and up-to-dated overview of all aspects of the anti-GQ1b syndrome through a review and analysis of a substantial body of literature, spanning from initial description of its components to recent developments in diagnostic classification and research perspectives.

Historical perspective

Original description

Cranial nerve involvement in GBS had already been postulated by Guillain himself, who, in the 1938 Belgian Symposium, described forms of the syndrome presenting isolated cranial nerve involvement and forms exhibiting polyneuropathy accompanied by impaired consciousness [5].

These early descriptions share similarities with MFS and BBE.

In the 1951 article "Mesencephalitis and rhomboencephalitis", Bickerstaff described three patients who displayed a gradual development of ataxia, external ophthalmoplegia and drowsiness following antecedent infection. The terms "mesencephalitis" and "rhomboencephalitis" were initially suggested to differentiate these conditions from classic forms of encephalitis [6].

Bickerstaff later expanded his case series in 1957, theorizing that the pathological process responsible for impaired cerebral function without damage to the organ itself was localized to the brainstem [7].

It was only in 1978 that Bickerstaff reviewed the syndrome for the Handbook of Clinical Neurology under the title "Brain stem encephalitis (Bickerstaff's encephalitis)" [8].

Meanwhile in 1956 Miller Fisher described three patients exhibiting ataxia, ophthalmoplegia and areflexia following an antecedent infection, one of which experienced mild drowsiness during the acute phase of the disease [9].

Evolving pathophysiology

The etiology of both conditions has long been debated. In his original description, Fisher considered ataxia to be the manifestation of an unusual peripheral neuron lesion, while also categorizing it as a cerebellar disturbance due to the disproportional clinical compared to sensory loss, even in the absence of pathological changes in the cerebellum and cerebellar dysarthria [9, 10].

In 1982 Al-Din and Bickerstaff reported 18 cases of brainstem encephalitis and MFS, suggesting a common central cause for both syndromes. All patients exhibited ophthalmoplegia and ataxia. Among them, a variable degree of impairment of consciousness was present in 12 patients and tendon reflexes were absent in 11 patients, normal in 3 and brisk in 4. Additionally, 4 patients showed long tract signs such as Babinski sign and 2 presented sensory disturbances. The initial trigger was presumed to be a hypersensitivity reaction following infection and the hypothesized pathogenesis included a cerebellar origin for ataxia and a supranuclear cause for ophthalmoplegia, while areflexia and impaired consciousness were thought to result from the involvement of the midbrain and the pontine reticular formation [11].

This hypothesis found support in several pieces of evidence: abnormal EEG findings present in 12 patients, brainstem lesions found in 3 MFS patients, and abnormal brainstem evoked potential in one. Moreover, the same hypothesis was also endorsed by Keane JR, but disputed by Ropper, who considered 6 of the 18 patients as having typical MFS and the remaining 12 as exhibiting obscure brainstem lesions without peripheral neuropathy [11–14].

Ropper himself, after conducting an in-depth electrophysiological study on MFS patient, suggested a purely peripheral etiology based on the observed alterations in joint position sense and muscle spindle proprioception [15].

The discovery of anti-GQ1b antibodies in MFS patients by Chiba in 1991 and later in BBE patients by Yuki made it evident that both conditions originate from the same immune-mediated process, triggered by an antecedent infective episode, thus leading to the establishment of a common spectrum referred to as "Fisher Bickerstaff syndrome" [1, 16, 17].

Subsequent findings of anti-GQ1b antibodies in atypical forms have then led to the development of a new nosological entity known as the "Anti-GQ1b antibody syndrome", comprising a continuous spectrum of phenotypes characterized by a common serological profile and variable degrees of CNS and PNS involvement [3, 18].

Evidence of lesions in MFS patients observed through neuroimaging, including glucose hypermetabolism in the cerebellar vermis and hemispheres using PET, and a reduced N-acetyl aspartate (NAA) to creatine (Cr) ratio (NAA/Cr) through Magnetic Resonance Spectroscopy (MRS) in these areas, suggests a cerebellar dysfunction, supporting the central involvement in the "peripheral" forms of the spectrum [19–26].

At the neuronal level, stable creatine levels are used as a reference point against NAA levels, whit reductions

indicating neural dysfunction, localized to the cerebellum. The normalization of the NAA/Cr ratio at 2.5 months is associated with recovery [26, 27].

Autopsies of MFS patients have revealed evidence of the loss of Purkinje neurons in the cerebellum [28].

Epidemiology

The worldwide annual incidence of GBS is ~1–2/100,000 inhabitants. Of these, MFS represents a small fraction of the total, with the percentage varying according to the area considered. The literature shows a higher incidence in the East than the West: in Asian countries it accounts for ~15–25% of GBS cases (Taiwan 18%, Hong Kong 9%, Thailand 7.7%); it is lower in Europe: an Italian review estimated an incidence of 0.04–0.18 cases in 100,000 inhabitants (6%), while some reports reported an incidence of 7% in Spain [4, 10, 29–32].

Because of its rarity, there are no epidemiological studies on BBE in Europe, although clinical experience suggests a lower incidence. One epidemiological study on BBE in Japan reports an incidence of 0.078 in 100,000 [33].

Both MFS and BBE present a slight male prevalence, early age onset (average age 36) and autumn-winter peak [4, 34, 35].

Although atypical forms have a significantly lower incidence and no epidemiological studies have been conducted, the incidence of these forms appears to be higher in Asian countries [36, 37].

Clinical features

MFS is classically defined by the triad characterized by ophthalmoparesis, ataxia and osteotendinous areflexia, which appear in ~80% of patients [9, 10, 38]. Ophthalmoparesis, typically bilateral, progresses to complete external ophthalmoplegia within 1–2 weeks. Ataxia, often very severe, may result in an inability to walk without support despite normal strength. Areflexia, a less specific component of the triad (absent in 18%), may also be confined to an isolated body area [10, 39]. The triad is often accompanied by additional signs, including ptosis (60%), facial nerve palsy (30–50%), sensory deficits (20–50%), and hyposthenia (20–25%) [10, 18, 40–42]. MFS may present with atypical manifestations, such as an initial presentation with bilateral internal ophthalmoplegia, unilateral external ophthalmoplegia, bilateral abducent nerve palsy, or isolated bilateral ptosis [20, 43–46]. The literature documents numerous cases of MFS accompanied by optic neuritis, often bilateral, resulting in blurred vision without pain, color desaturation or field deficit [47]. MFS may also be accompanied by internuclear ophthalmoplegia (INO), mimicking posterior circulation stroke [48].

Bickerstaff originally described BBE as a clinical syndrome defined by progressive, relatively symmetric external ophthalmoplegia and ataxia within 4 weeks, accompanied by disturbances in consciousness or hyperreflexia [7, 11]. Although atypical cases of BBE not accompanied by ophthalmoplegia have been described, the predominant presence of this symptom in BBE cases makes its absence a marker suggesting a lower likelihood of anti-GQ1B antibody syndrome [49, 50]. Ataxia can manifest as both truncal and limb ataxia in 71% of cases, truncal only in 18%, and limb-only in 11% [34]. Other signs of CNS involvement include: varying degrees of impaired consciousness in 74% of patients, ranging from mild drowsiness (55%) to stupor (17%), semicoma (8%) and coma (20%); long tract signs, such as Babinski sign (43%), hemisensory loss and hyperreflexia (30%), found in all patients not exhibiting impaired consciousness [34, 51]. In addition, the literature describes decorticate posturing as a possible sign of CNS involvement [52, 53]. Central signs tend to be milder in children, and may manifest as irritability or hyperexcitability [54, 55]. Internal ophthalmoplegia (34%), blepharoptosis (29%) and nystagmus (27%) are relatively common [33, 34, 56]. Additional signs associated to these symptoms include limb weakness (60%) superficial sensory loss (31%), facial diplegia (45%), pupillary abnormalities and bulbar palsy (34%), oropharyngeal palsy, decreased or absent tendon reflex (67%).

Similar to MFS, cases of optic neuritis have been reported [57]. Deep sense impairment is rarer (2%) [51].

As evidenced in retrospective studies of both BBE and MFS, diplopia is the most common initial symptom, occurring in 63% of MFS cases and 52% of BBE cases, followed by ataxia, observed in 5% of MFS patients and 35% of BBE patients [34, 35]. In 23% of BBE cases, both conditions may develop on the same day (3,8,43–45) [35]. Other initial symptoms include dysesthesia (10% in MFS, 19% in BBE), limb weakness (15% in MFS, 11% in BBE), and dysarthria (15% in MFS, 11% in BBE) with similar percentages [34, 35].

The average time from infection to onset is shorter in BBE (5 days, ranging from 2 to 10). MFS exhibits higher variability and longer time to onset with ophthalmoparesis appearing on average at 7 days from infection (ranging from 1 to 30 days), followed by ataxia at 10 days (ranging from 1 to 30 days), and areflexia appearing with the highest variability at 14 days on average (ranging from 4 to 45 days) [35, 51].

BBE/MFS associated with GBS

Forms of BBE/MFS overlapping with GBS are described. Development of flaccid tetraparesis in BBE patients, observed in 60% of cases, may represent the epiphenomenon of a clinical profile otherwise indistinguishable from pure BBE [34, 58, 59]. Overlap syndromes can affect patient outcomes, with one-quarter of those scoring 3 on the MRC scale experiencing persistent limb weakness [34].

Atypical forms - Formes frustes

Atypical forms definited in literature like formes frustes are incomplete forms that, while sharing a common serological profile, may not fully meet the criteria for BBE/MFS. These encompass a broad clinical spectrum, including acute ataxic neuropathy (AAN), acute ophthalmoparesis (AO), pharyngeal-cervical-brachial (PCB) weakness, acute ptosis (AP), acute mydriasis (AM), acute oropharyngeal palsy (AOP), acute bulbar palsy (ABP), acute vestibular syndrome (AVS) [60].

AAN is characterized by profound ataxia without ophthalmoplegia and includes two conditions forming a continuous spectrum: ataxic GBS and acute sensory ataxic neuropathy (ASAN).

Ataxic GBS patients (69% of AAN) also exhibit negative Romberg sign, hypo/areflexia, distal paresthesias and cerebrospinal fluid (CSF) albuminocytological dissociation (ACD), placing this condition as a GBS variant [61, 62].

These features are absent in ASAN (31% of AAN), which more frequently exhibits a positive Romberg sign and is defined by the absence of sensory nerve action potentials (SNAP), normal CSF findings, loss of large myelinated fibers and axonal damage [63].

Possible initial symptoms of both conditions include distal dysesthesias (51% in ataxic GBS vs. 71% in ASAN), and gait disturbances (49% in ataxic GBS vs. 35% in ASAN). Over the course of the diseases, distal dysesthesias (70% in ataxic GBS vs. 88% in ASAN) and superficial sensory impairments (27% in ataxic GBS vs. 24% in ASAN) often develop. The average time to nadir is 4 days (ranging from 2 to 15 days) in ataxic GBS and 7 days (ranging from 3 to 13 days) in ASAN. The average length of hospital stay is 16 days (ranging from 3 to 68 days) in ataxic GBS and 22 days (ranging from 5 to 150 days) in ASAN [64].

AO is characterized by acute, symmetric, combined external and internal ophthalmoplegia without ataxia or areflexia, associated with anti-GQ1b seropositivity [51, 65, 66]. Unilateral involvement has been described in 27% of cases, making diagnosis more challenging [67].

PCB weakness is another extensive form, characterized by areflexia and weakness of the oropharyngeal, cervicobrachial and proximal muscles. The most common onset symptom is arm weakness (29% of cases), followed by dysphagia (17%) and diplopia (17%). Rarer initial symptoms include blepharoptosis, facial weakness, photophobia or dysgeusia. Patients frequently develop hypo/areflexia (91% in the arms, 86% in the legs), superficial sensory loss (59% in the arms and 38% in the legs), ophthalmoparesis (55%) and arm weakness, predominantly proximal in 47% of cases and distal in 28%. Ataxia (43%), autonomic dysfunction (20%) and consciousness disturbance (5%) are possible [36].

PCB weakness, initially classified among GBS variants, was included into the anti-GQ1b syndrome spectrum following a retrospective study on 100 "pure PCB" patients, 39 of whom tested positive for anti-GQ1b seropositivity. Possible overlap with MFS (26% of cases) and BBE (5% of cases), with subsequent development of ataxia, ophthalmoparesis or altered consciousness, provides additional evidence of PCB weakness's place within this spectrum [36, 68, 69].

AVS, recently incorporated into the spectrum, is characterized by an acute onset of dizziness, spontaneous or positional vertigo (80%), truncal (100%) or limb ataxia (86%), sensory abnormalities (43%) and various ocular motor findings, such as spontaneous (50%), gaze-evoked (50%), positional (30%) or head-shaking nystagmus (40%), all without ophthalmoplegia. Other possible symptoms include saccadic dysmetria (20%), ocular flutter or opsoclonus, downbeat nystagmus and central positional nystagmus [70].

ABP is a condition characterized by acute bulbar paralysis in conjunction with other cranial symptoms or ataxia, without the presence of limb or neck weakness. The onset of acute bulbar paralysis, a prominent symptom, commonly presents with dysarthria (50%), diplopia (35%), and dysphagia (35%). Less common manifestations include gait ataxia (14%), rhinolalia (11%), facial palsy (11%), and ptosis (3.6%). As the condition advances, external ophthalmoplegia (71%), hypo/areflexia (64%), facial palsy (61%), gait ataxia (50%), and sensory abnormality (50%) are frequently observed [37] Table 1.

Pathogenesis

The etiology of these conditions has been demonstrated to be immunological. Antecedent infections, as originally described, appears present in the majority of patients: in MFS preceding upper respiratory system infections are most common (56–76% of patients). Gastrointestinal infection (4%) and isolated fever (2%) are less frequent. MFS can also be associated with autoimmune disease, neoplasms, surgical procedures, use of medication such as TNF

Table 1 Atypical forms included in the spectrum with main clinical characteristics

Atypical forms	Clinical features
Acute ataxic neuropathy (AAN)	*Ataxia without ophthalmoplegia*
Acute ophthalmoparesis (AO)	*Ophthalmoparesis without ataxia or areflexia*
Pharyngeal-cervical-brachial (PCB) weakness	*Weakness of the oropharyngeal, cervicobrachial and proximal muscles with areflexia*
Acute oropharyngeal palsy (AOP)	*Weakness of the oropharyngeal muscles without areflexia*
Acute ptosis (AP)	*Isolated ptosis*
Acute mydriasis (AM)	*Isolated mydriasis*
Acute bulbar palsy (ABP),	*Acute bulbar paralysis with other cranial symptoms or ataxia, without the presence of limb or neck weakness*
Acute vestibular syndrome (AVS)	*Dizziness, vertigo and ataxia, without ophthalmoplegia*

α, heroine, anti-streptokinase, isotretinoin, bone marrow transplantation [42, 71–79].

In the case of BBE, a stronger correlation with antecedent infections has been identified, affecting approximately 92% of patients. Upper respiratory infections (66%), isolated fever (9%), fever and headache (6%), diarrhea only (5%), and a combination of respiratory infection symptoms and diarrhea (5%) have been observed [34]. Gastrointestinal infections are more commonly associated with classic GBS [80].

Specific pathogens are isolated in patients across this spectrum, with Campylobacter jejuni being the most frequently isolated (21% in MFS, 23% in BBE, and 31% in PCB), followed by Haemophilus influenzae (8% in MFS, 6% in BBE) [35, 36, 51].

Notably, no significant differences have been found in the relative frequencies of pathogens found in patients with pure forms of BBE and BBE-GBS overlap forms [34].

H. influenzae is isolated more frequently (18%) in formes frustes compared to C. jejuni (2%) [51].

Cytomegalovirus (CMV) has been isolated in PCB but not in other forms of this spectrum [36, 51].

In most forms of Anti-GQ1b antibody syndrome, no specific pathogens have been isolated [51].

The underlying mechanism appears to be related to "molecular mimicry". The activation of the immune system against lipo-oligosaccharides (LOS) present on the pathogens' membrane, which resemble the shape of human gangliosides (GQ1b, GM1, GD1a), triggers the production of autoantibodies. When the generated antibody is GM1 or GD1b, it results in the classic form of GBS, while the production of GQ1b antibodies leads to the development of anti-GQ1b antibody syndrome [10, 81]. Supporting this, the fact that the LOS of C. jejuni isolated from MFS or BBE patients, as well as H. influenzae isolated from an MFS patient, were demonstrated to mimic GQ1b [82–84].

It is interesting to note how the immune system's response towards the same pathogens leads to distinct clinical presentations, such as GBS and Anti-GQ1b antibody syndrome.

Essential to the production of gangliosides-like LOS are the presence of enzymes such as Campylobacter sialyltransferase (CstII), N-acetylgalactosaminyltransferase (CgtA) and galactosyltransferase (CgtB), encoded by bacterial genes found in C. jejuni isolated from anti-GQ1b seropositive patients [85, 86].

The specific antibody type produced is dictated by the 51st amino acid of CstII, which determines its enzyme activity: the presence of Threonine (Thr51) leads to the production of GM1- and GD1a-like LOS, while Asparagine (Asn51) leads to the production of GQ1b-like LOS [85, 87].

GQ1b is a ganglioside found predominantly in paranodal myelin, especially in oculomotor nerves (III-IV and VI cranial nerves), dorsal root ganglia (DRG), and fibers of neuromuscular spindles [10].

GQ1b would act by stabilizing the formation of the axoglial paranode, composed of Contactin-1 (CNTN1) and CASPR, expressed by neurons, which bind to the glial-derived NF-155 counterpart. This paranodal axo-glial structure is essential for the longitudinal conduction of nerve impulses, regulating ion channel clustering, propagating the action potential, and preventing the lateral diffusion of membrane proteins in myelinated nerve fibers. Antibody-mediated targeting of this epitope leads to an acute blockade of nerve impulse propagation, resulting in the sudden onset of symptoms [81, 88].

Given the presence of ganglioside GQ1b in the paranodal structure, the diagnostic process for suspected diseases in this spectrum requires the exclusion of paranodopathies, which present with similar clinical features but have different neurophysiological profiles [89].

As highlighted by Chiba, GQ1b accounts for 11–13% of ganglioside composition in oculomotor nerves, compared to 5–8% in all other cranial nerves, accounting for the symptomatologic triad of MFS patients: ophthalmoparesis, ataxia, and areflexia [4, 90].

Additionally, the presence of the GQ1b epitope in the optic nerve, glossopharyngeal nerve and vagus nerve accounts for possible optic and oropharyngeal involvement [1, 91].

Pupillary abnormalities are attributed to autoantibody-mediated ciliary nerves and ganglion involvement [92].

The varied symptomatology of AVS result from variable involvement of the peripheral and central vestibular system, both of which express the GQ1b epitope [70, 93–95].

How to explain the CNS involvement typical of BBE?

The mechanism underlying the typical central nervous system (CNS) involvement in BBE remains a subject of investigation. The most widely accepted hypothesis suggests a disruption of the blood-brain barrier (BBB), a protecting barrier against large circulating molecules, in BBE patients, which remains intact in MFS patients. An in vitro study demonstrated that the serum of BBE patients, but not MFS patients, could disrupt a BBB model by increasing production of matrix metalloproteinase-9 (MMP-9) secreted by human brain microvascular endothelial cells [96].

An alternative hypothesis involves the passage of antibodies at the area postrema, where the BBB is relatively permeable [97, 98].

These hypotheses are substantiated by post-mortem examinations in BBE patients, revealing inflammatory changes in the brainstem, including perivascular lymphocytic infiltration with oedema and glial nodules [7, 34].

An alternative explanation is provided by differences in antibody specificity among various forms of anti-GQ1b antibody syndrome: in contrast to ASAN, anti-GQ1b antibodies in MFS seldom exhibit cross-reactivity with anti-GD1b ganglioside [64].

The variable consciousness impairment typical of BBE suggests a variable degree of involvement of the reticular formation, rich in GQ1b.

A likely sequence of events in the pathogenesis of Anti-GQ1b antibody syndrome is as follows:

1. Antecedent infection by microorganisms carrying LOS mimicking GQ1b triggers the production of IgG anti-GQ1b;
2. Anti-GQ1b antibodies attach to the epitopes expressed on the oculomotor nerves, DRG, and fibers of neuromuscular spindles, inducing MFS;
3. Antibodies may potentially pass into the brainstem through areas where the BBB is deficient, where they attach to GQ1b in the reticular formation, leading to BBE.

The finding of anti-GQ1b seronegative MFS and ataxic GBS patients presenting anti-GM1, anti-GD1b, or anti-GalNAc-GD1a IgG antibodies may be explained by the presence of these relative gangliosides in their oculomotor nerves, primary sensory neurons and brainstems [99, 100].

Anti-GQ1b antibody syndrome and COVID

Neuromuscular manifestations have been frequent post-infective complications of Middle East respiratory syndrome (MERS) and COVID. In a retrospective analysis of 214 hospitalized patients, neurological complications were observed in 36% of the cases examined, with a higher incidence of central nervous system (CNS) involvement (24.8%) compared to peripheral nervous system (8.9%) [101]. These complications spanned a spectrum of severity, from mild symptoms like headache, dizziness, myalgia, and anosmia to more serious conditions, such as encephalopathy, encephalitis, necrotizing hemorrhagic encephalopathy, stroke, epileptic seizures, and Guillain-Barré syndrome [102].

In accordance with the ALBACOVID registry, patients with Guillain-Barré Syndrome (GBS) represented 0.5% of COVID-19-related hospitalizations. Among these, those with Miller Fisher Syndrome (MFS) constituted approximately 10%, while patients with pharyngeal-cervical-brachial weakness (PCB) accounted for around 2% [57, 103, 104]. While uncommon, there have been reports of multiple cases of MFS and BBE occurring after COVID-19 vaccination in various countries [105–109].

Diagnostic approach

The diagnostic process primarily relies on clinical assessment, although laboratory investigations can provide valuable support. Hyperproteinorrachia, a recognized marker of GBS, may not manifest in the early stages and might be absent in certain cases within the Anti-GQ1b antibody syndrome spectrum: the incidence of hyperproteinorrachia in this spectrum tends to progressively increase over the initial three weeks of onset. Notably, Albuminocytological dissociation (ACD) is detected in ~47% of MFS patients. Within this subgroup, the incidence rises from 66% within the first week to 82% by the third week [4].

Conversely, ACD is less common in BBE patients, with an occurrence rate of 25% during the initial week, escalating to 46% in the second week [34, 110]. Atypical forms exhibit an ACD incidence of approximately 30% [51, 64].

Cerebrospinal fluid (CSF) pleocytosis, characterized by an increased number of white blood cells in the CSF, is observed more frequently in BBE (32%) than in MFS (5%) and atypical forms (7%) [34, 51]. Consequently, CSF studies alone cannot clearly discriminate these forms.

In contrast, anti-GQ1b dosage demonstrates superior sensitivity and specificity during the initial week, with antibodies being detectable in 85% of MFS patients and 68% of BBE patients [3, 4]. Antibodies other than GQ1b may also be identified in different forms of the spectrum with varying incidence, as outlined in the following Tables [34, 36, 51, 64, 110–113] Table 2.

Anti-GT1a and anti-GM1 antibodies can function as anti-GQ1b equivalents in two ways:

1. As demonstrated in adult mouse brain models, these relative gangliosides, in addition to being found in the

Table 2 Antibodies other than GQ1b may also be identified in different forms of the spectrum, with varying incidence. We present in this table the relative incidences in percentages of ganglioside reported in the literature in the various forms of the spectrum. The dash indicates that there is no available literature data regarding the relative incidence of the corresponding element. It is interesting to note how Anti-GT1a and anti-GM1 antibodies can function as anti-GQ1b equivalents. Associative studies between anti-ganglioside antibodies and clinical phenotype have shown that GD1b and GT1b antibodies are linked to the worsening of ataxia, while anti-GT1a antibodies have been correlated with bulbar symptoms due to the high expression of GT1a gangliosides in the glossopharyngeal and vagus nerves. A correlation has been reported between GM1, GD1a, and GalNAc-GD1a antibodies and limb weakness. ACD= albuminocytological dissociation, MFS= Miller Fisher syndrome, BBE= Bickerstaff brainstem encephalitis, PCB= pharyngeal-cervical-brachial weakness, AVS= acute vestibular syndrome), AO= acute ophthalmoparesis without ataxia, ABP= acute bulbar palsy

	GQ1b	GD1a	GM1	GM1b	GT1a	GalNAc-GD1a	GD1b	ACD	CSF pleocytosis
MFS[51]	83	28	15	-	78	2	2	47	5
BBE[51]	68	13	13	-	60	2	2	46	32
PCB[36]	39	12	10	16	51	1	-	-	-
Ataxic GBS[64]	18	-	-	-	-	-	47	39	-
Acute sensory ataxic neuropathy[64]	65	-	-	-	-	-	46	30	-
AVS[70]	67	-	0	-	-	-	13	50	20
AO without ataxia[70]	80	-	8	-	-	-	23	73	6
GBS with ophthalmoparesis[2]	92	-	22	-	-	-	44	93	13
ABP[37]	59	-	-	-	78	-	-	-	48

peripheral nerve roots, thus explaining the limb weakness found in overlap forms, are also present in brainstem nuclei, thalamus and white matter tracts [114, 115];

1. Furthermore, these antibodies have the potential to cross-react with the ganglioside GQ1b [116, 117].

Associative studies between anti-ganglioside antibodies and clinical phenotype have suggested a correlation. Specifically, anti-GD1b and GT1b antibodies have been linked to the worsening of ataxia, while the presence of anti-GT1a antibodies has been correlated with a worsening of ophthalmoparesis [117]. In contrast, Kashihara et al. evidenced how anti-GT1a IgG antibodies in PCB weakness, ABP and AOP patients were associated with bulbar symptoms such as dysarthria, dysphagia and facial weakness. This association was attributed to the high expression of GT1a gangliosides in the glossopharyngeal and vagus nerves [37, 91, 118]. Additionally, Fukami et al. reported a correlation between GM1, GD1a, and GalNAc-GD1a antibodies and limb weakness [117].

Instrumental investigations

In MFS patients, MRI remains normal in 99% of cases [51]. In the remaining 1%, MRI may reveal hyperintensity in T2-weighted images at the brainstem, cerebellum, middle cerebellar peduncle and cranial and spinal nerve root [10, 51, 119–121]. MRI abnormalities are more frequent in BBE (11% of cases), such as hyperintensity in the medulla oblongata, pons, thalamus, cerebellum, superior cerebellar peduncle or corpus callosum [51]. According to some authors, incidence of MRI abnormalities may reach 30% [34, 59, 122]. Hyperintensity and/or contrast enhancement

of the nerve roots, cauda equina-conus medullaris may be observed in MFS/BBE-GBS overlap forms, similar to several GBS patients [59, 123, 124].

EEG recordings show diffuse slowed activities in the θ or δ range at rest in 57% of BBE and 25% of MFS patients [51]. The higher incidence of neuroimaging and EEG abnormalities indicates greater CNS involvement in BBE, although found in varying degrees in MFS as well Table 3.

Neurophysiology

Neurophysiological findings in of Anti-GQ1b antibody syndrome are milder compared to those found in GBS. Unlike the latter, typical signs of acquired demyelinating polyneuropathy, such as reduced motor conduction velocity (MCV), marked temporal dispersion and conduction blocks, are absent in pure forms of the spectrum. In these forms motor and sensory conduction studies are normal. Reduced sensory nerve action potential (SNAP) amplitude disproportionate to the slowing of sensory conduction velocity or prolongation of the distal latencies, indicative of sensory neuropathy, may be found [125, 126].

The study of late responses, performed to assess the more proximal segment of nerves such as plexuses and roots, reveals the absence of soleus H-reflexes, the neurophysiological equivalent of the myotatic reflex [51, 126–128]. This neurophysiological abnormality, found in 75% of BBE and 94% of MFS patients, may be due to the selective involvement of the Ia muscle spindles expressing the GQ1b ganglioside [51, 127–129]. Reappearance of the H-reflex is associated with patient recovery [42].

Electrophysiological characteristics of atypical forms are less well documented: in AO and AVS, nerve conduction studies (NCSs) are usually normal; axonal damage similar

Table 3 Comparison between MFS and BBE: in both conditions, the etiology has been demonstrated to be immunological, secondary to 'molecular mimicry. Unlike MFS, BBE shows a stronger correlation with antecedent infections, with specific pathogens, particularly Campylobacter jejuni, frequently isolated. MFS is classically defined by the triad characterized by ophthalmoparesis, ataxia, and osteotendinous areflexia. On the other hand, BBE is defined as a clinical syndrome characterized by progressive, relatively symmetric external ophthalmoplegia and ataxia within 4 weeks, accompanied by disturbances in consciousness or hyperreflexia. The degree of consciousness disturbance varies from mild drowsiness to stupor, semicoma, and coma. Other signs of CNS involvement, such as Babinski sign, hemisensory loss, and hyperreflexia, can be found in all patients not exhibiting impaired consciousness. In both conditions, the triad of symptoms is frequently associated with additional signs. Unlike MFS, BBE may require assisted ventilation during the acute phase (1% vs. 34%) and presents a mortality rate of 4%, attributed to aspiration pneumonia and sudden cardiac arrest. Both conditions may recur, albeit in different percentages. Albuminocytological dissociation (ACD) is detected in similar percentages in both conditions, while cerebrospinal fluid (CSF) pleocytosis is observed more frequently in BBE than in MFS. For both, anti-GQ1b dosage demonstrates high sensitivity and specificity during the initial week. BBE presents a higher incidence of neuroimaging and EEG abnormalities, indicating greater CNS involvement, although such abnormalities are found in varying degrees in MFS as well. Percentages are derived from citations (3) (34) (51)

	MFS	BBE
Antecedent illness (%)	82%	92%
Upper respiratory infectious symptoms	56–76%	66%
Gastrointestinal infectious symptoms	4%	5%
Isolated fever	2%	9%
Pathogens isolated		
Campylobacter jejuni	21%	23%
Haemophilius influenzae	8%	6%
Clinical features		
Consciousness disturbance	0%	74%
Mild drowsiness	-	55%
Stupor	-	17%
Semicoma	-	8%
-Coma	-	20%
Blepharoptosis	60%	29%
External ophthalmoplegia	100%	100%
Internal ophthalmoplegia	35%	55%
Facial nerve palsy	30–50%	45%
Bulbar palsy	17%	34%
Mild limb weakness	20–25%	60%
Sensory deficits	20–50%	31%
Dysesthesia	45%	40%
Superficial sense impairment	7%	15%
Deep sense impairment	17%	2%
Ataxia	100%	100%
Babinski sign	2%	43%
Normal or brisk reflex	0	30%
Absent or decreased reflex	100%	67%
Outcome		
Assisted ventilation	1%	34%
Mortality rate	0%	4%
Recurrence rate	12%	25%
Paraclinical findings		
Albuminocytological dissociation (ACD)	47%	46%

Table 3 (continued)

	MFS	BBE
CSF pleocytosis	5%	32%
Serum IgG anti-GQ1b antibodies	85%	68%
MRI abnormal findings (%)	1%	11%
EEG abnormal findings (%)	25%	57%

to AMAN may be found in PCB, AAN [37, 64, 66, 70, 123, 130].

In ABP, a possible presence of facial nerve involvement with an abnormal blink reflex is observed in approximately 17% of patients [37].

In this form, despite clinical localization of hyposthenia restricted to motor cranial nerve territories, a subclinical limb neuropathy of varying severity can be detected in more than one-third of patients, thereby providing electrophysiological support for the current theory of ABP being part of a continuous spectrum [37, 131].

In both typical and atypical forms, the gradual improvement of SNAP amplitudes is linked to the recovery from pathology [132].

The overlapping of GBS with MFS and BBE may be expressed through electrophysiological findings of superimposed acute motor axonal neuropathy [123, 124].

Body sway analysis, a method used to study the proprioceptive afferent system, shows postural sway with a 1-Hz frequency in both MFS and BBE [51, 133]. Sway at this frequency, also found in tabes dorsalis and ataxic polyneuropathy patients, suggest concomitant and common proprioceptive afferent system dysfunction, supporting the hypothesis of continuity between these conditions [133, 134]. Auditory brainstem response (ABR), used to evaluate activation from the cochlea to the midbrain and detect damage, especially in the pons, may be helpful for the diagnosis and follow up in BBE: patients may exhibit low-evoked potentials without prolonged latency between I and V wave, caused by the loss of neural cells presenting anti-GQ1b [115, 135].

Therapy

Due to the rarity of spectrum conditions, there are no randomized, double-blind, placebo-controlled trials on treatment of the Anti-GQ1b Antibody syndrome, and retrospective studies yield controversial results. An important retrospective study on 92 MFS patients, including 28 treated with intravenous immunoglobulin (IVIG) and 23 treated with plasma exchange (PLEX); while 41 remained untreated, evidenced a survival rate of 100%, regardless of therapeutic strategy employed. It is inferred that MFS is self-limiting and therapy is unlikely to affect the patients' outcome [136, 137].

For this condition time to remission of symptoms varies depending on those considered: ataxia subsides on average in 35 days (ranging from 10 to 121 days), ophthalmoplegia in 93 days (ranging from 18 to 244 days), and areflexia in 64 days, displaying the highest variability (ranging from 10 to 650 days). Complete remission occurs on average within 6 months with no sequelae [35].

On the other hand, BBE may require assisted ventilation during the acute phase (1% vs. 34%) and presents a mortality rate of 4%. Causes of death have been reported to be aspiration pneumonia and sudden cardiac arrest deat variable interval from onset [51]. Most patients achieve complete remission within 6 months, though some may continue to exhibit dysesthesia, diplopia or ataxia beyond this time frame [34].

IVIG and PLEX have been used in the treatment of both conditions. Considering the self-limiting course of MFS, the rate of mortality, and the requirement for assisted ventilation in BBE, the cost and potential side effects of treatment, the current recommendation would be not to treat patients unless signs of complications, such as a possible BBE diagnosis, manifest [137].

In the presence of PCB or forms overlapping with GBS, treatment with IVIG or PLEX is advisable, as is the case with pure GBS [123, 138, 139]. The overlap of Anti-GQ1b and GBS, along with the presence of bulbar and facial palsies, may represent a predictive factor of respiratory failure requiring mechanical ventilation [140]. Cases of severe BBE not responsive to IVIG or PLEX are described: these are effectively treated with Rituximab, anti-CD 20 monoclonal antibody [141]. Its effectiveness may be explained by the binding of anti-GQ1b antibodies to presynaptic motor nerve endings, leading to complement activation and membrane attack complex formation [142, 143].

Recurrent forms

Although typically monophasic, cases of recurrent MFS and BBE are described in literature: approximately 12% of MFS and about 25% of BBE cases can recur [144–150]. These forms are clinically, laboratoristically and electrophysiologically indistinguishable from non-recurrent forms and tend to present similar symptoms as in the first occurrence, albeit less severe, with an average interval of about six years between episodes [151]. Haplotype HLA-DR2 appears to be correlated with the recurrence of MFS [152].

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Yuki N (2009) Fisher syndrome and Bickerstaff brainstem encephalitis (Fisher-Bickerstaff syndrome). J Neuroimmunol 215:1–9. https://doi.org/10.1016/j.jneuroim.2009.05.020
2. Wakerley BR, Uncini A, Yuki N et al (2014) Guillain-Barré and Miller Fisher syndromes–new diagnostic classification. Nat Rev Neurol 10:537–544. https://doi.org/10.1038/nrneurol.2014.138
3. Shahrizaila N, Yuki N (2013) Bickerstaff brainstem encephalitis and Fisher syndrome: anti-GQ1b antibody syndrome. J Neurol Neurosurg Psychiatry 84:576–583. https://doi.org/10.1136/jnnp-2012-302824
4. Teener JW (2012) Miller Fisher's syndrome. Semin Neurol 32:512–516. https://doi.org/10.1055/s-0033-1334470
5. Guillain G (1938) Synthèse générale De La discussion. J Belge Neurol Psy 38:323–329
6. Bickerstaff ER, Cloake PCP (1951) Mesencephalitis and rhombencephalitis. Br Med J 2:77–81. https://doi.org/10.1136/bmj.2.4723.77
7. Bickerstaff ER (1957) Brain-stem encephalitis; further observations on a grave syndrome with benign prognosis. Br Med J 1:1384–1387. https://doi.org/10.1136/bmj.1.5032.1384
8. Bickerstaff E (1978) Brain stem encephalitis (Bickerstaff's encephalitis). Handbook of clinical neurolohy, infections of the nervous system. prat II 34:605
9. Fisher M (1956) An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 255:57–65. https://doi.org/10.1056/NEJM195607122550201
10. Noioso CM, Bevilacqua L, Acerra GM et al (2023) Miller Fisher syndrome: an updated narrative review. Front Neurol 14:1250774. https://doi.org/10.3389/fneur.2023.1250774
11. Al-Din AN, Anderson M, Bickerstaff ER, Harvey I (1982) Brainstem encephalitis and the syndrome of Miller Fisher: a clinical study. Brain 105(Pt 3):481–495. https://doi.org/10.1093/brain/105.3.481
12. Anderson M, Al-din AN, Bickerstaff ER, Harvey I (1984) The CNS in Guillain-Barré syndrome. Arch Neurol 41:705. https://doi.org/10.1001/archneur.1984.04050180027009
13. Keane JR, Finstead BA (1982) Upward gaze paralysis as the initial sign of Fisher's syndrome. Arch Neurol 39:781–782. https://doi.org/10.1001/archneur.1982.00510240043012
14. Ropper AH (1983) The CNS in Guillain-Barré syndrome. Arch Neurol 40:397–398. https://doi.org/10.1001/archneur.1983.04050070027003
15. Ropper AH (1988) Three patients with Fisher's syndrome and normal MRI. Neurology 38:1630–1631. https://doi.org/10.1212/wnl.38.10.1630
16. Chiba A, Kusunoki S, Shimizu T, Kanazawa I (1992) Serum IgG antibody to ganglioside GQ1b is a possible marker of Miller Fisher syndrome. Ann Neurol 31:677–679. https://doi.org/10.1002/ana.410310619
17. Yuki N, Sato S, Tsuji S et al (1993) An immunologic abnormality common to Bickerstaff's brain stem encephalitis and Fisher's syndrome. J Neurol Sci 118:83–87. https://doi.org/10.1016/0022-510x(93)90250-3
18. Mori M, Kuwabara S, Fukutake T et al (2001) Clinical features and prognosis of Miller Fisher syndrome. Neurology 56:1104–1106. https://doi.org/10.1212/wnl.56.8.1104
19. Lolekha P, Phanthumchinda K (2008) Optic neuritis in a patient with Miller-Fisher syndrome. J Med Assoc Thai 91:1909–1913
20. Bae JS, Kim JK, Kim SH, Kim OK (2009) Bilateral internal ophthalmoplegia as an initial sole manifestation of Miller Fisher syndrome. J Clin Neurosci 16:963–964. https://doi.org/10.1016/j.jocn.2008.09.009

21. Akinci G, Oztura I, Hiz-Kurul S (2010) Anti-GQ1b-negative Miller Fisher syndrome presented with one-sided horizontal gaze palsy. Turk J Pediatr 52:317–320

22. Yiş U, Bayram E, Topçu Y et al (2013) A case of atypical Miller Fisher syndrome with negative anti-GQ1b immunoglobulin G and importance of H reflex. Turk J Pediatr 55:235–236

23. Waung MW, Singer MA (2012) An unusual case of Miller Fisher syndrome presenting with proptosis and chemosis. Muscle Nerve 45:764–766. https://doi.org/10.1002/mus.23285

24. Hara M, Morita A, Ichihara K et al (2012) Miller Fisher syndrome associated with influenza A infection. Intern Med 51:2621–2623. https://doi.org/10.2169/internalmedicine.51.7984

25. Kim YK, Kim JS, Jeong S-H et al (2009) Cerebral glucose metabolism in Fisher syndrome. J Neurol Neurosurg Psychiatry 80:512–517. https://doi.org/10.1136/jnnp.2008.154765

26. Sandler RD, Hoggard N, Hadjivassiliou M (2015) Miller-Fisher syndrome: is the ataxia central or peripheral? Cerebellum Ataxias 2:3. https://doi.org/10.1186/s40673-015-0021-3

27. Currie S, Hadjivassiliou M, Wilkinson ID et al (2013) Magnetic resonance spectroscopy of the normal cerebellum: what degree of variability can be expected? Cerebellum 12:205–211. https://doi.org/10.1007/s12311-012-0415-1

28. Berlit P, Rakicky J (1992) The Miller Fisher syndrome. Review of the literature. J Clin Neuroophthalmol 12:57–63

29. Ma Y-M, Liu TKT, Wong V (2010) Guillain-Barre syndrome in southern Chinese children: 32 year experience in Hong Kong. Pediatr Int 52:13–19. https://doi.org/10.1111/j.1442-200X.2009.02951.x

30. Lolekha P, Phanthumchinda K (2009) Miller-Fisher syndrome at King Chulalongkorn Memorial Hospital. J Med Assoc Thai 92:471–477

31. Clinical E, Neurology EP (1998) Guillain-Barré syndrome variants in Emilia-Romagna, Italy, 1992-3: incidence, clinical features, and prognosis. Emilia-Romagna Study Group on Clinical and Epidemiological Problems in Neurology. J Neurol Neurosurg Psychiatry 65:218–224. https://doi.org/10.1136/jnnp.65.2.218

32. Téllez-Zenteno JF, Jacinto-Tinajero JC, Avila-Funes A et al (2001) [Guillain-Barre syndrome. Experience in a third level hospital]. Rev Invest Clin 53:311–314

33. Koga M, Kusunoki S, Kaida K et al (2012) Nationwide survey of patients in Japan with Bickerstaff brainstem encephalitis: epidemiological and clinical characteristics. J Neurol Neurosurg Psychiatry 83:1210–1215. https://doi.org/10.1136/jnnp-2012-303060

34. Odaka M, Yuki N, Yamada M et al (2003) Bickerstaff's brainstem encephalitis: clinical features of 62 cases and a subgroup associated with Guillain-Barré syndrome. Brain 126:2279–2290. https://doi.org/10.1093/brain/awg233

35. San-Juan OD, Martínez-Herrera JF, García JM et al (2009) Miller Fisher syndrome: 10 years' experience in a third-level center. Eur Neurol 62:149–154. https://doi.org/10.1159/000226599

36. Nagashima T, Koga M, Odaka M et al (2007) Continuous spectrum of pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. Arch Neurol 64:1519–1523. https://doi.org/10.1001/archneur.64.10.1519

37. Cao Q, Chu H, Fu X et al (2020) Case Report: Acute Bulbar Palsy Plus Syndrome: a Guillain-Barré syndrome variant more prone to be a subtype than overlap of distinct subtypes. Front Neurol 11:566480. https://doi.org/10.3389/fneur.2020.566480

38. Collier J (1932) Peripheral neuritis. The Morrison Lectures, 1932, delivered before the Royal College of Physicians of Edinburgh, May 1932. Edinb Med J 39:601–618

39. Truong J, Conley J, Ashurst J (2020) Miller-Fisher syndrome: a Case Report and Review of the literature. Clin Pract Cases Emerg Med 4:653–655. https://doi.org/10.5811/cpcem.2020.7.48507

40. Lyu RK, Tang LM, Cheng SY et al (1997) Guillain-Barré syndrome in Taiwan: a clinical study of 167 patients. J Neurol Neurosurg Psychiatry 63:494–500. https://doi.org/10.1136/jnnp.63.4.494

41. Kollár K, Liptai Z, Rosdy B, Móser J (2009) [Guillain-Barré syndrome in childhood]. Ideggyogy Sz 62:399–404

42. Arányi Z, Kovács T, Sipos I, Bereczki D (2012) Miller Fisher syndrome: brief overview and update with a focus on electrophysiological findings. Eur J Neurol 19:15–20 e1-3. https://doi.org/10.1111/j.1468-1331.2011.03445.x

43. Smith J, Clarke L, Severn P, Boyce R (2007) Unilateral external ophthalmoplegia in Miller Fisher syndrome: case report. BMC Ophthalmol 7:7. https://doi.org/10.1186/1471-2415-7-7

44. Wertheim MS, Benzimra JD, Jadresic LP, Ferris JD (2008) Ocular presentation of pediatric Miller-Fisher syndrome. J Pediatr Ophthalmol Strabismus 45:245–246. https://doi.org/10.3928/01913913-20080701-16

45. Stalpers XL, Verhagen WIM, Meulstee J (2009) Isolated bilateral ptosis as the only ophthalmologic sign in the Fisher variant of Guillain-Barré syndrome. J Neuroophthalmol 29:354–355. https://doi.org/10.1097/WNO.0b013e3181b41445

46. Kinno R, Ichikawa H, Tanigawa H et al (2011) Unilateral abducens nerve Palsy as an early feature of multiple Mononeuropathy Associated with Anti-GQ1b antibody. Case Rep Neurol 3:82–85. https://doi.org/10.1159/000326340

47. Zhao T, Deng Y, Ding Y et al (2020) Anti-GQ1b antibody syndrome presenting with visual deterioration as the initial symptom: a case report. Med (Baltim) 99:e18805. https://doi.org/10.1097/MD.0000000000018805

48. Sim BNH, Joseph JP (2019) Forme fruste anti-GQ1b-negative Miller Fischer syndrome masquerading as posterior circulation stroke. J R Coll Physicians Edinb 49:304–306. https://doi.org/10.4997/JRCPE.2019.411

49. Koga M (2013) Another CNS phenotype of anti-GQ1b antibody syndrome. J Neurol Neurosurg Psychiatry 84:1185. https://doi.org/10.1136/jnnp-2013-305236

50. Wakerley BR, Soon D, Chan Y-C, Yuki N (2013) Atypical Bickerstaff brainstem encephalitis: ataxic hypersomnolence without ophthalmoplegia. J Neurol Neurosurg Psychiatry 84:1206–1207. https://doi.org/10.1136/jnnp-2013-304993

51. Ito M, Kuwabara S, Odaka M et al (2008) Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. J Neurol 255:674–682. https://doi.org/10.1007/s00415-008-0775-0

52. Kurihara M, Bannai T, Otsuka J et al (2018) Optic neuropathy and decorticate-like posture as presenting symptoms of Bickerstaff's brainstem encephalitis: a case report and literature review. Clin Neurol Neurosurg 173:159–162. https://doi.org/10.1016/j.clineuro.2018.08.019

53. Shimozono K, Shimono K, Kusunoki S (2012) [Case of Bickerstaff brainstem encephalitis associated with spindle coma and decorticate posture]. Rinsho Shinkeigaku 52:656–659. https://doi.org/10.5692/clinicalneurol.52.656

54. Santoro JD, Lazzareschi DV, Campen CJ, Van Haren KP (2018) Pediatric Bickerstaff brainstem encephalitis: a systematic review of literature and case series. J Neurol 265:141–150. https://doi.org/10.1007/s00415-017-8684-8

55. Cai L, Hu Z, Liao J et al (2021) Clinical characterization of Anti-GQ1b antibody syndrome in Childhood. Front Pediatr 9:649053. https://doi.org/10.3389/fped.2021.649053

56. Jebaraj AP, Swiston CJ, Vegunta S, Warner JEA (2022) Isolated bilateral Internal Ophthalmoplegia as an atypical initial presentation of anti-GQ1b antibody syndrome. J Neuroophthalmol 42:e389–e390. https://doi.org/10.1097/WNO.0000000000001314

57. Kim JE, Heo JH, Kim HO et al (2017) Neurological complications during treatment of Middle East Respiratory Syndrome. J Clin Neurol 13:227–233. https://doi.org/10.3988/jcn.2017.13.3.227

58. Rho YI (2014) Overlapping Guillain-Barré syndrome and Bickerstaff's brainstem encephalitis associated with Epstein Barr virus. Korean J Pediatr 57:457–460. https://doi.org/10.3345/kjp.2014.57.10.457

59. Michev A, Musso P, Foiadelli T et al (2019) Bickerstaff Brainstem Encephalitis and overlapping Guillain-Barré syndrome in children: report of two cases and review of the literature. Eur J Paediatr Neurol 23:43–52. https://doi.org/10.1016/j.ejpn.2018.11.008

60. de Bruyn A, Poesen K, Bossuyt X et al (2019) Clinical spectrum of the anti-GQ1b antibody syndrome: a case series of eight patients. Acta Neurol Belg 119:29–36. https://doi.org/10.1007/s13760-019-01093-8

61. Richter RB (1962) The ataxic form of polyradiculoneuritis (Landry-Guillain-Barre syndrome). Clinical and pathologic observations. J Neuropathol Exp Neurol 21:171–184

62. Mihori A, Nakayama M, Ono S, Shimizu N (1998) [Ataxic form of Guillain-Barré syndrome associated with acute hepatitis A–a case report]. Rinsho Shinkeigaku 38:242–245

63. Windebank AJ, Blexrud MD, Dyck PJ et al (1990) The syndrome of acute sensory neuropathy: clinical features and electrophysiologic and pathologic changes. Neurology 40:584–591. https://doi.org/10.1212/wnl.40.4.584

64. Ito M, Matsuno K, Sakumoto Y et al (2011) Ataxic Guillain-Barré syndrome and acute sensory ataxic neuropathy form a continuous spectrum. J Neurol Neurosurg Psychiatry 82:294–299. https://doi.org/10.1136/jnnp.2010.222836

65. Du FH, Yerevanian A, Shtrahman M (2020) Acute ophthalmoplegia in a patient with anti-GQ1b antibody and chronic facial diplegia. BMJ Case Rep 13:e234319. https://doi.org/10.1136/bcr-2020-234319

66. Lee S-H, Lim G-H, Kim JS et al (2008) Acute ophthalmoplegia (without ataxia) associated with anti-GQ1b antibody. Neurology 71:426–429. https://doi.org/10.1212/01.wnl.0000324266.95814.74

67. Susuki K, Yuki N, Muramatsu M, Hirata K (2000) Unilateral ophthalmoparesis and limb ataxia associated with anti-GQ1b IgG antibody. J Neurol 247:652–653. https://doi.org/10.1007/s004150070139

68. Wakerley BR, Yuki N (2014) Pharyngeal-cervical-brachial variant of Guillain-Barre syndrome. J Neurol Neurosurg Psychiatry 85:339–344. https://doi.org/10.1136/jnnp-2013-305397

69. Ropper AH (1994) Further regional variants of acute immune polyneuropathy. Bifacial weakness or sixth nerve paresis with paresthesias, lumbar polyradiculopathy, and ataxia with pharyngeal-cervical-brachial weakness. Arch Neurol 51:671–675. https://doi.org/10.1001/archneur.1994.00540190051014

70. Lee S-U, Kim H-J, Choi J-Y et al (2019) Acute vestibular syndrome associated with anti-GQ1b antibody. Neurology 93:e1085–e1092. https://doi.org/10.1212/WNL.0000000000008107

71. Gentile S, Messina M, Rainero I et al (2006) Miller Fisher syndrome associated with Burkitt's lymphoma. Eur J Neurol 13:430. https://doi.org/10.1111/j.1468-1331.2006.01254.x

72. Lo YL (2007) Clinical and immunological spectrum of the Miller Fisher syndrome. Muscle Nerve 36:615–627. https://doi.org/10.1002/mus.20835

73. Roquer J, Pou Serradell A (1992) [Paraneoplastic Miller-Fisher syndrome?]. Neurologia 7:40

74. Csépány T, Boczán J, Magyar MT et al (2004) Miller Fisher syndrome–a presenting clinical manifestation of lung cancer in a previously apparently healthy individual. J Neurol 251:898–900. https://doi.org/10.1007/s00415-004-0465-5

75. Shin I-SJ, Baer AN, Kwon HJ et al (2006) Guillain-Barré and Miller Fisher syndromes occurring with tumor necrosis factor alpha antagonist therapy. Arthritis Rheum 54:1429–1434. https://doi.org/10.1002/art.21814

76. Pritchard J, Appleton R, Howard R, Hughes R, a. C (2004) Guillain-Barré syndrome seen in users of isotretinoin. BMJ 328:1537. https://doi.org/10.1136/bmj.328.7455.1537

77. Yu EH, Geraldi-Samara D (2020) Pharyngeal-Cervico-Brachial/Miller Fisher Overlap Syndrome with Infliximab exposure. J Clin Neuromuscul Dis 21:157–158. https://doi.org/10.1097/CND.0000000000000274

78. Desai SS, Allen E, Deodhar A (2002) Miller Fisher syndrome in adult onset still's disease: case report and review of the literature of other neurological manifestations. Rheumatology (Oxford) 41:216–222. https://doi.org/10.1093/rheumatology/41.2.216

79. Rubio-Nazabal E, Marey-Lopez J, Torres-Carrete JP et al (2002) Miller-Fisher syndrome and Hodgkin's disease. J Neurol Neurosurg Psychiatry 73:344. https://doi.org/10.1136/jnnp.73.3.344

80. Yuki N (2001) Infectious origins of, and molecular mimicry in, Guillain-Barré and Fisher syndromes. Lancet Infect Dis 1:29–37. https://doi.org/10.1016/S1473-3099(01)00019-6

81. Martín-Aguilar L, Pascual-Goñi E, Querol L (2019) Autoantibodies in immune-mediated inflammatory neuropathies. Med Clin (Barc) 153:360–367. https://doi.org/10.1016/j.medcli.2019.06.007

82. Kimoto K, Koga M, Odaka M et al (2006) Relationship of bacterial strains to clinical syndromes of Campylobacter-associated neuropathies. Neurology 67:1837–1843. https://doi.org/10.1212/01.wnl.0000244468.22377.6b

83. Koga M, Gilbert M, Li J et al (2005) Antecedent infections in Fisher syndrome: a common pathogenesis of molecular mimicry. Neurology 64:1605–1611. https://doi.org/10.1212/01.WNL.0000160399.08456.7C

84. Houliston RS, Koga M, Li J et al (2007) A Haemophilus influenzae strain associated with Fisher syndrome expresses a novel disialylated ganglioside mimic. Biochemistry 46:8164–8171. https://doi.org/10.1021/bi700685s

85. Gilbert M, Karwaski M-F, Bernatchez S et al (2002) The genetic bases for the variation in the lipo-oligosaccharide of the mucosal pathogen, Campylobacter jejuni. Biosynthesis of sialylated ganglioside mimics in the core oligosaccharide. J Biol Chem 277:327–337. https://doi.org/10.1074/jbc.M108452200

86. Koga M, Gilbert M, Takahashi M et al (2006) Comprehensive analysis of bacterial risk factors for the development of Guillain-Barre syndrome after Campylobacter jejuni enteritis. J Infect Dis 193:547–555. https://doi.org/10.1086/499969

87. Koga M, Takahashi M, Masuda M et al (2005) Campylobacter gene polymorphism as a determinant of clinical features of Guillain-Barré syndrome. Neurology 65:1376–1381. https://doi.org/10.1212/01.wnl.0000176914.70893.14

88. Susuki K, Baba H, Tohyama K et al (2007) Gangliosides contribute to stability of paranodal junctions and ion channel clusters in myelinated nerve fibers. Glia 55:746–757. https://doi.org/10.1002/glia.20503

89. Uncini A (2023) Autoimmune nodo-paranodopathies 10 years later: clinical features, pathophysiology and treatment. J Peripher Nerv Syst 28(Suppl 3):S23–S35. https://doi.org/10.1111/jns.12569

90. Chiba A, Kusunoki S, Obata H et al (1997) Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. Brain Res 745:32–36. https://doi.org/10.1016/s0006-8993(96)01123-7

91. Koga M, Yoshino H, Morimatsu M, Yuki N (2002) Anti-GT1a IgG in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 72:767–771. https://doi.org/10.1136/jnnp.72.6.767

92. Kaymakamzade B, Selcuk F, Koysuren A et al (2013) Pupillary involvement in Miller Fisher Syndrome. Neuroophthalmology 37:111–115. https://doi.org/10.3109/01658107.2013.792356

93. Lee S-U, Kim H-J, Choi J-Y, Kim J-S (2019) Anti-ganglioside antibody-associated acute unilateral peripheral vestibulopathy. J Neurol 266:250–252. https://doi.org/10.1007/s00415-018-9109-z

94. Jung I, Kim H-J, Kim J-S (2017) Fluctuating ataxia and nystagmus in association with anti-GQ1b antibody in HIV infection. J Neurol Sci 382:123–125. https://doi.org/10.1016/j.jns.2017.09.044

95. Zaro-Weber O, Galldiks N, Dohmen C et al (2008) Ocular flutter, generalized myoclonus, and trunk ataxia associated with anti-GQ1b antibodies. Arch Neurol 65:659–661. https://doi.org/10.1001/archneur.65.5.659

96. Saito K, Shimizu F, Koga M et al (2013) Blood-brain barrier destruction determines Fisher/Bickerstaff clinical phenotypes: an in vitro study. J Neurol Neurosurg Psychiatry 84:756–765. https://doi.org/10.1136/jnnp-2012-304306

97. Faraci FM, Choi J, Baumbach GL et al (1989) Microcirculation of the area postrema. Permeability and vascular responses. Circ Res 65:417–425. https://doi.org/10.1161/01.res.65.2.417

98. Van Breemen VL, Clemente CD (1955) Silver deposition in the central nervous system and the hematoencephalic barrier studied with the electron microscope. J Biophys Biochem Cytol 1:161–166. https://doi.org/10.1083/jcb.1.2.161

99. Odaka M, Yuki N, Tatsumoto M et al (2004) Ataxic Guillain-Barré syndrome associated with anti-GM1b and anti-GalNAc-GD1 antibodies. J Neurol 251:24–29. https://doi.org/10.1007/s00415-004-0259-9

100. Yuki N, Susuki K, Hirata K (2000) Ataxic form of Guillain-Barré syndrome associated with anti-GD1b IgG antibody. J Neurol Neurosurg Psychiatry 69:136–137. https://doi.org/10.1136/jnnp.69.1.136

101. Mao L, Jin H, Wang M et al (2020) Neurologic manifestations of hospitalized patients with Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol 77:683–690. https://doi.org/10.1001/jamaneurol.2020.1127

102. Maury A, Lyoubi A, Peiffer-Smadja N et al (2021) Neurological manifestations associated with SARS-CoV-2 and other coronaviruses: a narrative review for clinicians. Rev Neurol (Paris) 177:51–64. https://doi.org/10.1016/j.neurol.2020.10.001

103. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E et al (2020) Neurologic manifestations in hospitalized patients with COVID-19: the ALBACOVID registry. Neurology 95:e1060–e1070. https://doi.org/10.1212/WNL.0000000000009937

104. Aladawi M, Elfil M, Abu-Esheh B et al (2022) Guillain Barre Syndrome as a complication of COVID-19: a systematic review. Can J Neurol Sci 49:38–48. https://doi.org/10.1017/cjn.2021.102

105. Dang YL, Bryson A (2021) Miller-Fisher Syndrome and Guillain-Barre syndrome overlap syndrome in a patient post Oxford-AstraZeneca SARS-CoV-2 vaccination. BMJ Case Rep 14:e246701. https://doi.org/10.1136/bcr-2021-246701

106. Nishiguchi Y, Matsuyama H, Maeda K et al (2021) Miller Fisher syndrome following BNT162b2 mRNA coronavirus 2019 vaccination. BMC Neurol 21:452. https://doi.org/10.1186/s12883-021-02489-x

107. Neophytou P, Artemiadis A, Hadjigeorgiou GM, Zis P (2023) Miller Fischer syndrome after COVID-19 infection and vaccine: a systematic review. Acta Neurol Belg. https://doi.org/10.1007/s13760-023-02336-5

108. Monte G, Pro S, Ursitti F et al (2022) Case report: a pediatric case of Bickerstaff brainstem encephalitis after COVID-19 vaccination and Mycoplasma pneumoniae infection: looking for the culprit. Front Immunol 13:987968. https://doi.org/10.3389/fimmu.2022.987968

109. Finsterer J, Matovu D (2022) Do not miss Bickerstaff encephalitis as a complication of SARS-CoV-2 vaccines. Radiol Case Rep 17:2824–2825. https://doi.org/10.1016/j.radcr.2022.05.044

110. Nishimoto Y, Odaka M, Hirata K, Yuki N (2004) Usefulness of anti-GQ1b IgG antibody testing in Fisher syndrome compared with cerebrospinal fluid examination. J Neuroimmunol 148:200–205. https://doi.org/10.1016/j.jneuroim.2003.11.017

111. Kusunoki S, Shimizu J, Chiba A et al (1996) Experimental sensory neuropathy induced by sensitization with ganglioside GD1b. Ann Neurol 39:424–431. https://doi.org/10.1002/ana.410390404

112. Liu J-X, Willison HJ, Pedrosa-Domellöf F (2009) Immunolocalization of GQ1b and related gangliosides in human extraocular neuromuscular junctions and muscle spindles. Invest Ophthalmol Vis Sci 50:3226–3232. https://doi.org/10.1167/iovs.08-3333

113. Kusunoki S, Chiba A, Kanazawa I (1999) Anti-GQ1b IgG antibody is associated with ataxia as well as ophthalmoplegia. Muscle Nerve 22:1071–1074. https://doi.org/10.1002/(sici)1097-4598(199908)22:8%3C1071::aid-mus10%3E3.0.co;2-0

114. Vajn K, Viljetić B, Degmečić IV et al (2013) Differential distribution of major brain gangliosides in the adult mouse central nervous system. PLoS ONE 8:e75720. https://doi.org/10.1371/journal.pone.0075720

115. Chiba A, Kusunoki S, Obata H et al (1993) Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome: clinical and immunohistochemical studies. Neurology 43:1911–1917. https://doi.org/10.1212/wnl.43.10.1911

116. Susuki K, Yuki N, Hirata K (2001) Fine specificity of anti-GQ1b IgG and clinical features. J Neurol Sci 185:5–9. https://doi.org/10.1016/s0022-510x(01)00464-6

117. Fukami Y, Wong AHY, Funakoshi K et al (2016) Anti-GQ1b antibody syndrome: anti-ganglioside complex reactivity determines clinical spectrum. Eur J Neurol 23:320–326. https://doi.org/10.1111/ene.12769

118. Kashihara K, Shiro Y, Koga M, Yuki N (1998) IgG anti-GT1a antibodies which do not cross react with GQ1b ganglioside in a pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 65:799. https://doi.org/10.1136/jnnp.65.5.799

119. Taphoorn MJ, Uitdehaag BM, Lanting P (1991) A brain-stem lesion in the Miller Fisher syndrome demonstrated by CT and MRI. J Neurol 238:243. https://doi.org/10.1007/BF00314791

120. Giroud M, Mousson C, Chalopin JM et al (1990) Miller-Fisher syndrome and pontine abnormalities on MRI: a case report. J Neurol 237:489–490. https://doi.org/10.1007/BF00314769

121. Garcia-Rivera CA, Rozen TD, Zhou D et al (2001) Miller Fisher syndrome: MRI findings. Neurology 57:1755. https://doi.org/10.1212/wnl.57.10.1755

122. Romano N, Federici M, Castaldi A (2021) Imaging presentation of Bickerstaff Brainstem Encephalitis. Neurohospitalist 11:370–372. https://doi.org/10.1177/1941874421993671

123. Hiew FL, Ramlan R, Viswanathan S, Puvanarajah S (2017) Guillain-Barré syndrome, variants & forms fruste: reclassification with new criteria. Clin Neurol Neurosurg 158:114–118. https://doi.org/10.1016/j.clineuro.2017.05.006

124. Wakerley BR, Kokubun N, Funakoshi K et al (2016) Clinical classification of 103 Japanese patients with Guillain-Barré syndrome. J Neurol Sci 369:43–47. https://doi.org/10.1016/j.jns.2016.08.002

125. Sauron B, Bouche P, Cathala HP et al (1984) Miller Fisher syndrome: clinical and electrophysiologic evidence of peripheral origin in 10 cases. Neurology 34:953–956. https://doi.org/10.1212/wnl.34.7.953

126. Fross RD, Daube JR (1987) Neuropathy in the Miller Fisher syndrome: clinical and electrophysiologic findings. Neurology 37:1493–1498. https://doi.org/10.1212/wnl.37.9.1493

127. Jamal GA, Ballantyne JP (1988) The localization of the lesion in patients with acute ophthalmoplegia, ataxia and areflexia (Miller Fisher syndrome). A serial multimodal neurophysiological study. Brain 111(Pt 1):95–114. https://doi.org/10.1093/brain/111.1.95

128. Dachy B, Deltenre P, Deconinck N, Dan B (2010) The H reflex as a diagnostic tool for Miller Fisher syndrome in pediatric patients. J Clin Neurosci 17:410–411. https://doi.org/10.1016/j.jocn.2009.06.014

129. Ogawara K, Kuwabara S, Yuki N (2002) Fisher syndrome or Bickerstaff brainstem encephalitis? Anti-GQ1b IgG antibody syndrome involving both the peripheral and central nervous systems. Muscle Nerve 26:845–849. https://doi.org/10.1002/mus.10246

130. Arai M, Susuki K, Koga M (2003) Axonal pharyngeal-cervical-brachial variant of Guillain–Barré syndrome without Anti-GT1a IgG antibody. Muscle Nerve 28:246–250. https://doi.org/10.1002/mus.10424

131. Kim JK, Kim B-J, Shin HY et al (2016) Acute bulbar palsy as a variant of Guillain-Barré syndrome. Neurology 86:742–747. https://doi.org/10.1212/WNL.0000000000002256

132. Yuki N, Uncini A (2014) Acute and chronic ataxic neuropathies with disialosyl antibodies: a continuous clinical spectrum and a common pathophysiological mechanism. Muscle Nerve 49:629–635. https://doi.org/10.1002/mus.24192

133. Kuwabara S, Asahina M, Nakajima M et al (1999) Special sensory ataxia in Miller Fisher syndrome detected by postural body sway analysis. Ann Neurol 45:533–536. https://doi.org/10.1002/1531-8249(199904)45:4%3C533::aid-ana19%3E3.0.co;2-h

134. Bergin PS, Bronstein AM, Murray NM et al (1995) Body sway and vibration perception thresholds in normal aging and in patients with polyneuropathy. J Neurol Neurosurg Psychiatry 58:335–340. https://doi.org/10.1136/jnnp.58.3.335

135. Kurihara T, Igarashi Y, Kobai K et al (2020) Diagnosis and prediction of prognosis for Bickerstaff's brainstem encephalitis using auditory brainstem response: a case report. Acute Med Surg 7:e517. https://doi.org/10.1002/ams2.517

136. Jacobs BC, O'Hanlon GM, Bullens RWM et al (2003) Immunoglobulins inhibit pathophysiological effects of anti-GQ1b-positive sera at motor nerve terminals through inhibition of antibody binding. Brain 126:2220–2234. https://doi.org/10.1093/brain/awg235

137. Mori M, Kuwabara S, Fukutake T, Hattori T (2007) Intravenous immunoglobulin therapy for Miller Fisher syndrome. Neurology 68:1144–1146. https://doi.org/10.1212/01.wnl.0000258673.31824.61

138. Hughes RAC, Swan AV, Raphaël J-C et al (2007) Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain 130:2245–2257. https://doi.org/10.1093/brain/awm004

139. Overell JR, Hsieh ST, Odaka M et al (2007) Treatment for Fisher syndrome, Bickerstaff's brainstem encephalitis and related disorders. Cochrane Database Syst Rev 2007:CD004761. https://doi.org/10.1002/14651858.CD004761.pub2

140. Kaida K, Kusunoki S, Kanzaki M et al (2004) Anti-GQ1b antibody as a factor predictive of mechanical ventilation in Guillain-Barré syndrome. Neurology 62:821–824. https://doi.org/10.1212/01.wnl.0000113718.27729.43

141. Hardy TA, Barnett MH, Mohamed A et al (2012) Severe Bickerstaff's encephalitis treated with Rituximab: serum and CSF GQ1b antibodies. J Neuroimmunol 251:107–109. https://doi.org/10.1016/j.jneuroim.2012.07.008

142. Halstead SK, Zitman FMP, Humphreys PD et al (2008) Eculizumab prevents anti-ganglioside antibody-mediated neuropathy in a murine model. Brain 131:1197–1208. https://doi.org/10.1093/brain/awm316

143. Fletcher DD, Lawn ND, Wolter TD, Wijdicks EFM (2000) Long-term outcome in patients with Guillain–Barré syndrome requiring mechanical ventilation. Neurology 54:2311–2315. https://doi.org/10.1212/WNL.54.12.2311

144. Heckmann JG, Dütsch M (2012) Recurrent Miller Fisher syndrome: clinical and laboratory features. Eur J Neurol 19:944–954. https://doi.org/10.1111/j.1468-1331.2011.03584.x

145. Vermeersch G, Boschi A, Deggouj N et al (2011) Recurrent Miller Fisher syndrome with vestibular involvement. Eur Neurol 66:210–214. https://doi.org/10.1159/000331486

146. Toru S, Ohara M, Hane Y et al (2012) Successful steroid treatment for recurrent Miller Fisher syndrome. Muscle Nerve 45:763–764. https://doi.org/10.1002/mus.23257

147. Grosso S, Verrotti A, Tei M et al (2014) Recurrent Miller Fisher syndrome in children. Pediatr Neurol 50:269–271. https://doi.org/10.1016/j.pediatrneurol.2013.10.016

148. Dong H, Liu Z, Tang Y et al (2011) Recurrent Fisher-Bickerstaff syndrome: report of a Chinese case. Chin Med J (Engl) 124:2786–2788

149. Sharma V, Chan YC, Ong null et al (2006) Bickerstaff's brainstem encephalitis: can it recur? J Clin Neurosci 13:277–279. https://doi.org/10.1016/j.jocn.2005.01.011

150. Chamsi Basha A, Kolko N, Santoro JD, Alomani H (2020) A probable case of recurrent Bickerstaff Brainstem Encephalitis with Fulminant Course in a Pediatric patient. Neurologist 25:14–16. https://doi.org/10.1097/NRL.0000000000000255

151. Ishii J, Yuki N, Kawamoto M et al (2016) Recurrent Guillain-Barré syndrome, Miller Fisher syndrome and Bickerstaff brainstem encephalitis. J Neurol Sci 364:59–64. https://doi.org/10.1016/j.jns.2016.03.008

152. Chida K, Nomura H, Konno H et al (1999) Recurrent Miller Fisher syndrome: clinical and laboratory features and HLA antigens. J Neurol Sci 165:139–143. https://doi.org/10.1016/s0022-510x(99)00095-7