

Anti-GM2 IgG-positive autoimmune brainstem encephalitis presenting as a stroke mimic: a case report and literature review

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Case Report

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Abstract

Background

Autoimmune encephalitis involving the brainstem is uncommon and may present with acute focal neurological deficits that closely resemble cerebrovascular disease. GM2 antibody–associated autoimmune encephalitis is rare, and its clinical characteristics remain incompletely understood.

Case Presentation:

We report a case of a 28-year-old male who presented with acute onset of vertigo, diplopia, right-sided facial numbness, and gait ataxia. Neurological examination localized the lesion to the brainstem and cerebellum. Brain magnetic resonance imaging and computed tomography angiography revealed no corresponding abnormalities. Cerebrospinal fluid analysis showed mildly elevated protein and immunoglobulins. Serum testing demonstrated positivity for anti-GM2 IgG antibodies, while other autoimmune, demyelinating, paraneoplastic, and infectious evaluations were negative. The patient demonstrated significant clinical improvement following intravenous corticosteroid therapy.

Conclusion

This case highlights the importance of considering autoimmune brainstem encephalitis in young patients with stroke-like presentations and emphasizes the diagnostic value of antibody testing when imaging findings are incongruent with clinical manifestations.

Background

Brainstem encephalitis is an inflammatory disorder affecting the brainstem, which can result from infectious, autoimmune, or paraneoplastic etiologies[1]. Among autoimmune causes, anti-ganglioside antibody-associated diseases have gained increasing recognition over the past decades. Gangliosides are sialic acid-containing glycosphingolipids abundantly expressed in the nervous system, playing crucial roles in cell signaling, neuronal development, and synaptic transmission[2].

GM2 gangliosides are glycosphingolipids widely expressed in neuronal membranes[3]. Antibodies against GM2 have been reported mainly in peripheral nervous system disorders and, less frequently, in central nervous system inflammatory diseases[4, 5].

Herein, we report a case of a young male presenting with acute brainstem syndrome who was found to have positive serum GM2 antibody and responded favorably to corticosteroid therapy. In addition, we review the relevant literature to further delineate the clinical features, diagnostic considerations, and potential pathophysiological mechanisms of this rare condition.

Case Presentation

A 28-year-old previously healthy male presented with a 2-day history of acute vertigo, diplopia, and right-sided numbness. Symptoms began suddenly upon awakening and progressively worsened over several hours. He denied preceding infection, fever, or systemic symptoms.

On neurological examination, findings were consistent with brainstem and cerebellar involvement, including bilateral abducens nerve palsy, right trigeminal sensory impairment, and limb ataxia. Motor strength and deep tendon reflexes were preserved.

Brain magnetic resonance imaging, including T1-, T2-flair, and diffusion-weighted sequences, showed no abnormalities corresponding to the clinical findings (Fig. 1A–F). Computed tomography angiography demonstrated patent intracranial and

cervical vessels without stenosis or occlusion (Fig. 1G). Notably, the severity of neurological deficits was disproportionate to the unremarkable neuroimaging findings.

(A-B) Diffusion-weighted imaging (DWI) at different axial levels showing no diffusion restriction in the brainstem or cerebellum, showing no evidence of acute infarction on DWI, (C–D) T2-FLAIR images demonstrating no abnormal hyperintensity in the brainstem or cerebellum, (E–F) T1-weighted images showing no structural abnormalities, (G) Three-dimensional CT angiography (CTA) revealing patent intracranial and cervical vessels without stenosis or occlusion.

Lumbar puncture was performed and key diagnostic findings included mildly elevated CSF protein, increased LDH levels, slight elevations in IgG and IgA, and positive serum anti-GM2 IgG antibodies (Table 1).

Table 1
Key Diagnostic Findings

Category	Parameter	Result	Reference Range
Cerebrospinal Fluid	Protein	0.46 g/L	0.15–0.45 g/L
	Lactate dehydrogenase (LDH)	71 U/L	0–40 U/L
	IgG	40.44 mg/L	10–40 mg/L
	IgA	5.59 mg/L	0–5 mg/L
Autoantibody	Anti-GM2 IgG	Positive (30 AU)	Negative

Antibodies associated with Miller Fisher syndrome (anti-GQ1b), demyelinating disorders (MOG-IgG, AQP4-IgG), autoimmune encephalitis (NMDAR, LGI1, CASPR2), and paraneoplastic syndromes were all negative. Extensive infectious workup, including serologic testing for EBV, CMV, HSV, and toxoplasma, as well as CSF Gram stain, bacterial culture, and viral PCR panel, was negative.

Electrophysiological studies showed no significant abnormalities, except for mildly reduced CMAP amplitude in the right ulnar nerve. Somatosensory evoked potentials and EEG were unremarkable. Systemic screening revealed no evidence of malignancy.

Based on the clinical presentation, exclusion of alternative etiologies, and positive anti-GM2 antibody, anti-GM2 IgG-positive probable autoimmune brainstem encephalitis was considered.

The patient was treated with intravenous methylprednisolone (80 mg/day for 3 days) followed by oral corticosteroid tapering. Marked clinical improvement was observed, with resolution of vertigo and sensory symptoms and significant recovery of ocular movements and coordination.

Discussion and Conclusions

Autoimmune encephalitis involving the brainstem presents a diagnostic challenge due to its overlap with cerebrovascular, infectious, and demyelinating disorders[6]. In this report, the patient developed acute-onset diplopia, ataxia, and focal sensory deficits suggestive of posterior circulation stroke. However, neuroimaging failed to identify corresponding lesions, highlighting a marked clinic radiologic dissociation. This discrepancy prompted consideration of alternative etiologies and ultimately led to the diagnosis of anti-GM2 antibody–associated brainstem encephalitis.

Anti-GM2 antibody–associated central nervous system involvement has only rarely been reported. As summarized in Table 2, previously reported cases suggest that anti-GM2 antibodies may be associated with a spectrum of brainstem-predominant neurological disorders, including rhombencephalitis and Bickerstaff brainstem encephalitis (BBE)-like syndromes. Daponte et al. described anti-GM2–associated rhombencephalitis presenting with ocular flutter as the cardinal feature [10], while other reports have documented brainstem encephalitis with normal neuroimaging findings and favorable response to corticosteroid therapy. In addition, anti-GM2 antibodies have occasionally been identified in patients with BBE, either in combination with other antiganglioside antibodies or as isolated GM2 positivity [5]. Notably, although acute presentations have been reported,

our patient presented with a distinct stroke-like syndrome characterized by abrupt focal brainstem deficits, creating a strong clinical impression of acute cerebrovascular disease despite normal MRI and vascular imaging.

Table 2
Reported cases of anti-GM2 antibody–associated CNS involvement

Study (Year)	Age/Sex	Antibody	Clinical Presentation	MRI Findings	Diagnosis	Treatment	Outcome
Daponte et al. (2021) [10]	Adult / NA	Anti-GM2	Ocular flutter, brainstem symptoms	Not specified	Rhombencephalitis	Immunotherapy	Improved
Hong et al. (2023) [7]	17 / F	Anti-GM2 IgM	Vertigo, limb weakness, ataxia	Normal	Brainstem-cerebellar encephalitis	IVIG	Recovered
Giacconi et al. (2025) [5]	Child	Anti-GM1 + GM2	Ophthalmoplegia, ataxia	Not specified	BBE	IVIG	Improved
Nokura et al. (2020) [11]	Adult	GM2 + multiple antibodies	Cerebellar + limbic + brainstem involvement	Not specified	Paraneoplastic encephalopathy	Oncologic + immunotherapy	Variable
Present case	28 / M	Anti-GM2 IgG	Stroke-like onset, diplopia, ataxia	Normal	Brainstem encephalitis	Corticosteroids	Improved

Antiganglioside antibodies are autoantibodies targeting gangliosides—sialic acid–containing glycosphingolipids abundantly expressed in nervous tissue—and have been increasingly recognized in the pathogenesis of autoimmune neurological disorders[8]. While well-characterized antiganglioside antibodies, such as anti-GQ1b, are strongly associated with Miller Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE) [9], the clinical significance of rarer subtypes, including anti-GM2, in central nervous system (CNS) disease remains poorly defined. Although most existing literature on anti-GM2 antibodies pertains to peripheral neuropathies, sporadic reports have documented CNS manifestations in patients with positive anti-GM2 serology, lending biologic plausibility to a potential central pathogenic role[5, 10, 11].

The mechanisms underlying antiganglioside antibody–mediated CNS injury are incompletely understood. Gangliosides, including GM2, are integral components of neuronal membranes, and antibody binding has been shown to induce complement activation and immune-mediated neuronal dysfunction in peripheral nerve disorders. Similar mechanisms may operate within the CNS, potentially explaining severe neurological deficits in the absence of overt radiologic abnormalities[4, 12]. This clinicoradiologic discrepancy underscores the limitations of conventional neuroimaging in detecting antibody-mediated neuronal dysfunction [13].

Several differential diagnoses were systematically evaluated. Miller Fisher syndrome and Bickerstaff brainstem encephalitis were considered but deemed unlikely due to the absence of areflexia and negative anti-GQ1b antibodies. Demyelinating disorders, including multiple sclerosis and neuromyelitis optica spectrum disorder, were excluded based on negative disease-specific antibodies and unremarkable MRI findings. Infectious and paraneoplastic etiologies were also ruled out through comprehensive laboratory testing.

The rapid and sustained clinical improvement following corticosteroid therapy strongly supports an immune-mediated pathophysiology. Although standardized treatment strategies for antiganglioside antibody–associated encephalitis have not been defined, current consensus recommendations for autoimmune encephalitis emphasize early initiation of immunotherapy—including corticosteroids, intravenous immunoglobulin, and plasmapheresis—to optimize neurological outcomes[14].

This case highlights several important clinical implications. Autoimmune brainstem encephalitis should be considered in young patients presenting with acute, stroke-like neurological deficits when neuroimaging findings are discordant with clinical localization. Furthermore, expanded antibody testing, including antiganglioside panels, may yield diagnostic insight in atypical brainstem syndromes with otherwise unrevealing evaluations. Early recognition and prompt immunotherapy may lead to favorable outcomes and help avoid unnecessary interventions for presumed cerebrovascular disease[15].

In conclusion, this report expands the clinical spectrum of antiganglioside antibody–associated neurological disorders by describing a rare presentation of anti-GM2 antibody–associated brainstem encephalitis mimicking acute cerebrovascular disease. Increased awareness of rare antiganglioside antibody syndromes and judicious use of expanded antibody testing may facilitate earlier diagnosis and improved patient outcomes.

Abbreviations

AQP4
Aquaporin-4
BBE
Bickerstaff brainstem encephalitis
CMAP
Compound muscle action potential
CNS: Central nervous system
CSF
Cerebrospinal fluid
CTA
Computed tomography angiography
DWI
Diffusion-weighted imaging
EEG
Electroencephalography
IVIG
Intravenous immunoglobulin
LDH
Lactate dehydrogenase
MFS
Miller Fisher syndrome
MOG
Myelin oligodendrocyte glycoprotein
MRI
Magnetic resonance imaging
PCR
Polymerase chain reaction

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Huashan Hospital, Fudan University.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

All authors contributed to the study conception and design. TYS conceived the study, collected the clinical data, performed the literature review, and drafted the manuscript. HZ contributed to data acquisition, critically revised the manuscript, and supervised the study. All authors read and approved the final manuscript. All authors read and approved the final manuscript of “Anti-GM2 IgG-positive autoimmune brainstem encephalitis presenting as a stroke mimic: a case report and literature review”

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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Figures

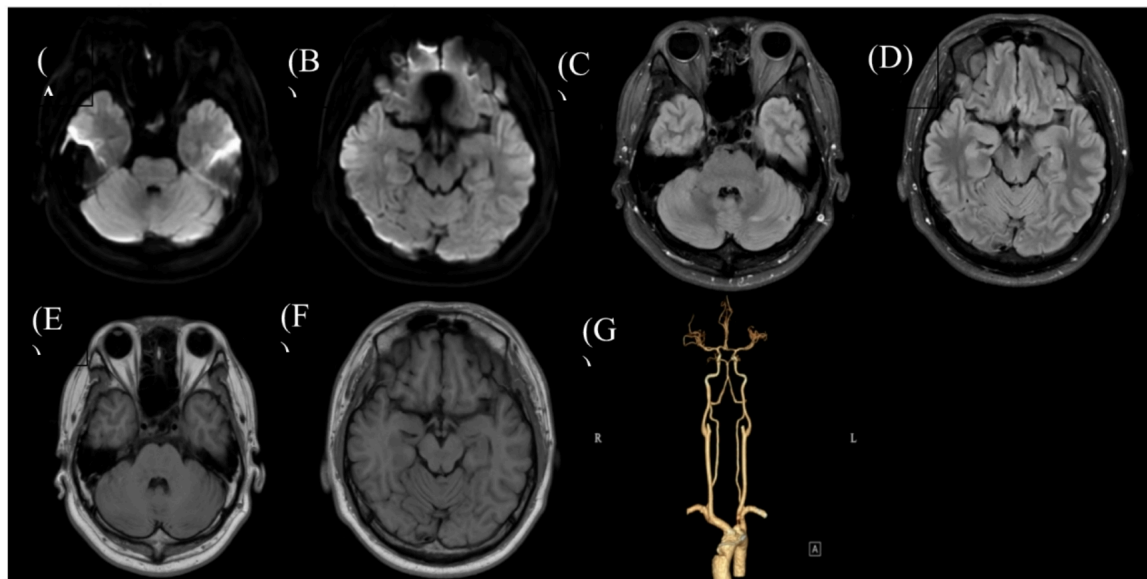


Figure 1

Neuroimaging findings

(A-B) Diffusion-weighted imaging (DWI) at different axial levels showing no diffusion restriction in the brainstem or cerebellum, showing no evidence of acute infarction on DWI, (C–D) T2-FLAIR images demonstrating no abnormal hyperintensity in the brainstem or cerebellum, (E–F) T1-weighted images showing no structural abnormalities, (G) Three-dimensional CT angiography (CTA) revealing patent intracranial and cervical vessels without stenosis or occlusion.