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CASE REPORT

Severe Bickerstaff Brainstem Encephalitis in a Young Adult Male: Delayed Recovery Despite Early Immunotherapy

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ABSTRACT

Bickerstaff brainstem encephalitis (BBE) is a rare post-infectious autoimmune disorder within the anti-GQ1b antibody spectrum, commonly presenting with ophthalmoplegia, ataxia, and impaired consciousness. Diagnosis is typically delayed because early symptoms are non-specific, and initial imaging often appears normal. We report a case of a 19-year-old male who initially presented with fever, limb weakness, and slurred speech. Within days, he deteriorated rapidly, requiring intubation. Initial imaging and cerebrospinal fluid analysis (CSF) were inconclusive. However, later serological studies revealed the presence of anti-GQ1b antibodies. Although MRI results were normal, the clinical picture was consistent with BBE. He underwent plasma exchange in the third week of illness. His recovery was complicated by hospital-acquired infection and barotrauma. His neurological recovery was slow. At the time plasma exchange was initiated (Day 21 of admission), the patient remained unresponsive with a Glasgow Coma Scale (GCS) of E1VTM1. By the sixth week of admission, his GCS had improved to E4V5M6, reflecting significant neurological recovery. With multidisciplinary rehabilitation, he eventually regained the ability to ambulate independently within 6 months. This case highlights the importance of considering BBE early in young patients presenting with acute brainstem dysfunction, even when initial imaging is unremarkable.

Keywords: *Bickerstaff brainstem encephalitis, anti-GQ1b antibodies, autoimmune encephalitis, plasma exchange, neurorehabilitation*

INTRODUCTION

Bickerstaff brainstem encephalitis (BBE) is a rare autoimmune neurological condition that mainly affects the brainstem. The typical clinical manifestations include ophthalmoplegia, ataxia and altered consciousness (Zoghaib et al., 2021). It is considered part of the anti-GQ1b antibody-associated spectrum of post-infectious disorders, which also includes Miller Fisher syndrome and Guillain–Barré syndrome (Nayak et al., 2024). It often follows a viral illness and may present with subtle or even normal neuroimaging findings, making diagnosis challenging (Abide et al., 2023). Other reports described cases with initially normal neuroimaging, only later to reveal subtle midbrain or pontine signal changes on repeat MRI, reinforcing the importance of serological testing in the diagnostic process (Mathur et al., 2023).

There are several case reports highlighting the diagnostic and therapeutic challenges of BBE. In some patients, presentations mimicked brainstem stroke or infectious meningoencephalitis, leading to delayed recognition until anti-GQ1b antibodies were identified (Hamza Ahmed et al., 2025). Although many patients respond to treatment, outcomes can vary significantly, and patients may experience delayed neurological improvement despite early immunotherapy. Severe presentations requiring mechanical ventilation have also been documented. In such cases, immunotherapy with intravenous immunoglobulin (IVIG) or plasma exchange has been associated with gradual recovery, although the timeline varies across individuals (Giaccari et al., 2024). These reports collectively emphasise the heterogeneity of BBE in its clinical course and in treatment response, making timely recognition and tailored management crucial.

CASE PRESENTATION

A 19-year-old previously healthy male, who recently completed pre-university studies, presented to Labuan Hospital with a two-day history of fever, generalised body weakness, and slurred speech. On admission, his neurological examination revealed hyperreflexia and a positive Romberg sign, but no cranial nerve deficits. Initial laboratory investigations revealed a mildly elevated white cell count of 14 × 103/µL, with otherwise regular renal and liver function tests (Table 1). A diagnosis of possible central nervous system infection or inflammatory demyelinating disorder was considered.

On the third day of admission (July 12, 2024), the patient experienced a sudden drop in consciousness, with GCS declining from E4V2M6 to E2V2M5, necessitating intubation for airway protection. Bilateral lower limb jerky movements were observed at the time, suggestive of seizure activity, although these were not aborted by diazepam and did not recur. A CT scan of the brain and a subsequent contrast-enhanced CT scan of the brain

Table 1: Key laboratory investigations during admission.

Test	Result	Reference	Comment
WBC	13.7 × 109/L	4.0 – 10.0	Mild leukocytosis
Sodium	131 mmol/L	135 – 145	Mild hyponatremia
CRP	2.8 mg/L	<5	Not elevated
Procalcitonin	0.11 ng/mL	<0.5	Not elevated
Serology	HIV, HBsAg, Anti-HCV, dengue, leptospira all negative		
Blood cultures	No growth	-	Negative
Anti-ganglioside antibodies (serum)	Positive GQ1b IgG	Negative	Supports diagnosis of BBE

were reported as usual. A lumbar puncture performed on day 4 revealed an opening pressure of 34 cmH2O, with cerebrospinal fluid (CSF) protein of 0.6 g/L and glucose of 3.89 mmol/L (glucose ratio: 0.62) (Table 2). Cultures and viral PCR screening were negative.

Even after stopping sedation on day 5, he remained unresponsive with a GCS of E1VTM1. He was transferred to Queen Elizabeth Hospital, Kota Kinabalu, for neurology input. A repeat lumbar puncture on day 16 showed a normal opening pressure, clear and acellular CSF (Table 2). Importantly, serum tested positive for anti-GQ1b IgG antibodies, confirming Bickerstaff brainstem encephalitis (Islam et al., 2024). An MRI brain scan performed on day 15 showed no abnormalities or contrast enhancement (Figure 1). However, the clinical picture and serological findings supported a diagnosis of autoimmune brainstem encephalitis (Giaccari et al., 2024). No follow-up MRI was performed, as the patient demonstrated progressive neurological recovery following treatment.

Between day 21 and day 29, he received five sessions of plasma exchange (PLEX) every other day. Each session replaced approximately 2.4 L of his plasma with 5% human albumin and 0.5% saline, along with pre- and post-treatment calcium gluconate infusions. During this time, he developed features of sepsis, with elevated inflammatory markers. A diagnosis of hospital-acquired pneumonia was made, and blood cultures were negative. He was treated with intravenous piperacillin-tazobactam followed by amoxicillin-clavulanate. CSF culture revealed the presence of Acinetobacter baumannii and Bacillus altitudinis, both of which were sensitive to appropriate antibiotics and were successfully treated.

On day 22, a CT pulmonary angiogram was performed to investigate persistent tachypnea and rising ventilator settings, with markedly elevated D-dimer. The scan excluded pulmonary embolism but incidentally revealed pneumomediastinum, pneumopericardium, and left dominant pneumothorax. These findings were attributed to barotrauma secondary to mechanical ventilation. Cardiothoracic and respiratory input recommended conservative management.

Table 2: Key laboratory investigations during admission.

Parameter	First LP (13/07/2024)	Second LP (25/07/2024)	Reference Range	Remarks
Appearance	Clear, colourless	Clear, colourless	Clear	Normal both
WCC	0 cells/mm3	0 cells/mm3	0-5 cells/mm3	No pleocytosis
Glucose (CSF:serum ratio)	3.9 mmol/L (0.62)	5.3 mmol/L (0.62)	Ratio >0.6	Normal
Protein	0.61 g/L	0.70 g/L	0.15 – 0.45 g/L	Mild elevation both
Gram stain/ Culture	No growth	Acinetobacter baumannii & Bacillus altitudinis	Negative	Likely contaminants (no pleocytosis)
AFB smear	Negative	Negative	Negative	Tuberculosis excluded
Cryptococcal Ag	Negative	-	Negative	Excluded
Viral PCR (JE, HSV)	Negative	-	Negative	Excluded
Autoimmune (NMDAR)	Negative	-	Negative	Excluded

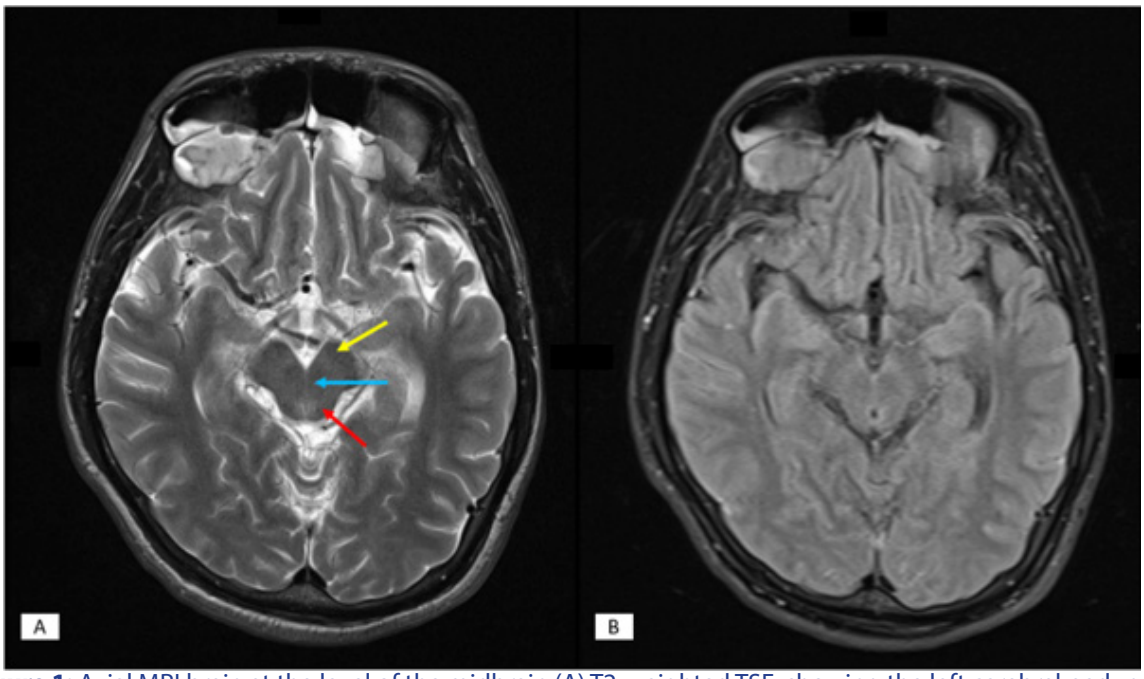

Figure 1: Axial MRI brain at the level of the midbrain (A) T2-weighted TSE, showing the left cerebral peduncle (yellow), the aqueduct of Sylvius (blue), and the left superior colliculus (red). (B) Corresponding FLAIR sequence. Both sequences demonstrate no abnormal signal changes in the brainstem or surrounding structures.

On day 31, he had a surgical tracheostomy and was gradually weaned off the ventilator. By week 7, his GCS improved to E4VTM6. Neurological examinations showed bilateral lower motor neuron facial weakness, upper limb power of 4/5, and lower limb power of 2/5. Physiotherapy, occupational therapy, and dietary support were initiated. He required wheelchair mobility and nasogastric tube feeding and was referred to social welfare services for home support.

A follow-up neurology outpatient assessment approximately 6 months after admission (January 13, 2025) showed remarkable progress. He was alert, cognitively intact, and communicating well despite persistent dysarthria. His facial weakness was improving. Upper limb strength had returned to normal, and lower limb strength improved to 3–4/5. Although still using a wheelchair, he was able to stand with assistance and was undergoing intensive neurorehabilitation. His tracheostomy was successfully closed 9 weeks post-tracheostomy, in October 2024. Further plans included ENT follow-up and orthotic support for bilateral foot drop.

DISCUSSION

BBE is a post-infectious autoimmune encephalitis characterised by brainstem dysfunction and strongly associated with anti-GQ1b antibodies. While usually self-limiting, its symptoms can range from mild ophthalmoplegia to deep coma (Lee et al., 2024). The presence of anti-GQ1b antibodies is a key diagnostic feature, particularly when neuroimaging is inconclusive (Koga et al., 2020). These antibodies are particular for BBE and related anti-GQ1b spectrum disorders (Giaccari et al., 2024).

Similar findings were reported by Cabral et al. (2023), who demonstrated that patients with classical BBE symptoms, such as drowsiness, ataxia, and ophthalmoplegia, frequently had normal imaging studies. This reinforces the importance of testing for anti-GQ1b antibodies in suspected cases, even when MRI findings are non-revealing.

Other differentials, including acute disseminated encephalomyelitis (ADEM), were considered, given the preceding fever

and altered consciousness. However, ADEM seemed unlikely due to the absence of multifocal demyelinating lesions on MRI and no inflammatory cells in the CSF (Finsterer & Iranpoor, 2022).

The patient's prolonged unconsciousness and slow initial response to treatment are less typical, though they have been reported before. Larger studies of BBE and overlapping syndromes have documented delayed recovery despite immunotherapy (Islam et al., 2024). Although IVIG remains the primary treatment, evidence supports plasma exchange as an effective alternative, particularly in severe presentations (Ban et al., 2022). Prior to PLEX, neither corticosteroids nor intravenous immunoglobulin (IVIG) were administered. In this case, the decision to initiate PLEX as the first-line immunotherapy on day 21 of admission was guided by the patient's prolonged unresponsiveness despite cessation of sedation. While IVIG is more commonly used in Bickerstaff encephalitis, PLEX was selected due to its potential to expedite the clearance of circulating pathogenic antibodies, such as anti-GQ1b, especially in severe presentations (Giaccari et al., 2024). This approach is supported by reports of PLEX being effective in severe or delayed presentations of Guillain-Barré spectrum disorders.

A similar case by Czempik et al. (2025) involved a 32-year-old man who developed Bickerstaff brainstem encephalitis following a febrile illness due to Influenza A. He rapidly deteriorated with impaired consciousness requiring intubation. His brain MRI was unremarkable, and he received five sessions of plasma exchange, with complete recovery reported at follow-up. While both patients had similar treatments and disease severity, our patient faced additional complications, including secondary infections and respiratory complications. In our case, the slow recovery and residual foot drop may be attributed to several contributing factors. Like other reports, this illustrates how BBE can vary significantly and that routine imaging does not necessarily rule out severe brain involvement. Plasma exchange and supportive care demonstrate that substantial recovery is possible even after prolonged periods of unconsciousness.

CONCLUSION

In summary, although Bickerstaff brainstem encephalitis typically presents with altered consciousness and cranial nerve problems, its onset may be subtle and imaging findings may be normal. This case highlights the importance of considering BBE in the differential diagnosis when evaluating patients with acute neurological deterioration following a febrile illness. Early serological testing for anti-GQ1b IgG antibodies is crucial, especially when conventional imaging is inconclusive. Although the patient's GCS remained low despite starting immunotherapy early, his eventual recovery shows that prolonged unconsciousness does not necessarily indicate a poor prognosis. Complications such as ventilator-associated pneumonia and barotrauma highlight the importance of supportive treatment throughout the disease course.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

CONSENTS

Written informed consent was obtained from the patient's guardian for publication of this case report and any accompanying images.

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