Fulminant Guillain Barre Syndrome AMSAN variant mimicking brain death: A lesson in persistence

.

ABSTRACT

Guillain-Barre syndrome (GBS) is the most common cause of acute flaccid paralysis. It commonly presents as acute symmetric ascending lower motor neuron palsy which typically occurs about one to three weeks following either a gastrointestinal or upper respiratory tract infection. GBS is termed fulminant when associated with rapid deterioration with flaccid quadriparesis, absent brainstem reflexes, and ventilator requirement.

Here, we report a case of a female in her twenties who presented with a history of weakness and sensory loss a few days after recovering from a diarrheal illness. She developed progressive ascending paralysis of her muscles within 24 hours and was intubated anticipating respiratory failure. Initial examination revealed dilated pupils and the presence of ocular movements, as well as bilateral facial nerve involvement. Investigative findings were consistent with GBS and intravenous immunoglobulin (IVIg) treatment was promptly initiated. Despite this, the patient deteriorated further and lost brainstem reflexes and failed to demonstrate spontaneous breaths. EEG indicated a deep coma.

Wecontinued with supportive care and physiotherapy and, after approximately 10 days of no initial response, our patient remarkablyregained muscle power and sensations. She was eventually weaned off ventilation and has since returned to full functional status.

This case report highlights the importance of persistence in treatment despite atypical presentations and initial clinical deterioration. Further, this case of fulminant GBS, AMSAN variant, involving the short ciliary nerve and mimicking brain death is a rare entity in clinical literature.

Keywords: Guillain-Barre, fulminant, brain-death, AMSAN, posterior ciliary nerve

1. INTRODUCTION

Guillain Barré Syndrome (GBS) is an acquired neuropathy that presents clinically as rapidly progressing paralysis, loss of tendon reflexes, and albumino-cytological dissociation. The history and examination of patients with GBS often results in a high degree of diagnostic suspicion that may be verified by further laboratory and electrodiagnostic testing (1) Despite its low incidence, it is still the most common cause of non-trauma-related acute neuromuscular paralysis. Campylobacter jejuni, Mycoplasma pneumoniae, Influenza virus, Epstein–Barr virus, and HIV are some of the common causative agents associated with GBS(2).GBS has several subtypes, one of which is AMSAN, which is characterized by the presence of damage of both sensory and motor axonal nerves (3).AMSAN has a rapid onset, and more severe symptoms, which causes significant functional limitationsin the patient(2).It has been found to have delayed recovery when compared to the demyelinating subtype of GBS (Acute inflammatory demyelinating polyneuropathy (AIDP)) (4). Fulminant GBS is a rare and severe entity with patients requiring long periods of hospitalization and long-term follow-up (5).It is more commonly seen in settings of axonal damage (6). Diagnosing cases of fulminant GBS is particularly challenging, especially when patients

present during the coma period with insufficient prior history.(7). Patients with fulminant GBS can often enter a clinical state resembling brain death- impaired consciousness and loss of brainstem reflexes. The exact mechanism behind this is yet to be explored (8). Very rarely, the demyelinating process in GBS can involve the ciliary ganglion or postganglionic branch of ciliary nerve, leading to loss of parasympathetic supply to the pupils. This manifests as bilateral tonic pupils (9).Investigations such as nerve conduction studies and CSF analysis may be used to confirm the diagnosis and delineate the variant.Treatment remains the same, which is by intravenous immunoglobulin (IVIg) or plasma exchange (10).Patients with fulminant GBS are at a potential risk for premature withdrawal of life-supporting measures, however it is imperative to recognize that such hasty clinical decisions could jeopardize full recovery in such patients. The continuation of treatment alongside aggressive support measures is crucial to optimize recovery(8).

2. PRESENTATION OF CASE

A female in her twenties presented to the outpatient department of a local hospital with symptoms of fatigue, high-grade fever associated with chills and rigors for 3-4 days. She was treated with antibiotics and improved significantly on treatment. However, her fatigue persisted. Approximately a month later, she developed severe diarrhea and vomiting, leading to hospitalization.About 3 days following hospitalization, she developed tingling in bilateral distal upper extremities. Within 24 hours, she developed difficulty standing, inability to move her lower limbs, and eventually could not hold objects or lift her arms. An initial lumbar puncture and head CT were normal. She was intubated and shifted to the intensive care unit due to impending respiratory failure. Subsequently, she was referred to our tertiary care centre for further management. On examination, the patient was intubated, on controlled mode of ventilation, and hemodynamically stable. She was conscious, alert, and minimally oriented to time, place, and person, with a Glasgow Coma Scale of E4VTM5. Her pulse was 96 beats per minute, blood pressure 120/70 mmHg, respiratory rate 18 breaths/min, and oxygen saturation 98%. She was poorly built, and nourished, and conjunctival pallor was present. Neurological examination revealed normal ocular movements, dilated pupils, and bilateral lower motor neuron facial palsy. The lower limbs were abducted and externally rotated bilaterally. Motor examination showed a power of 3/5 in the right upper limb and 2/5 in all other limbs. Muscle tone was decreased, deep tendon reflexes were absent, and the plantar reflex was negative. Neck flexion and extension power were also reduced.Routine investigations were as detailed in Table 1. Inflammatory markers were elevated.

Table.1RELEVANT INVESTIGATIONS

Test	Result	Normal
CSF- Initial analysis	Protein 75, Cells 3 (Lymphocytes)	Protein: 15-60 mg/dL Cells: <5/mm^3
Anti Ganglioside antibodies	GM1 –weak positive	Negative
Hemoglobin	9.9 g/dL	12-14 g/dL
Potassium	4 mmol/L	3.5-4.5 mmol/L
Sodium	126 mmol/L	135-145 mmol/L

Our initial differentials included Botulism,Miller Fischer syndromeand Guillain Barre syndrome. The first two contenders were ruled out due to the pattern of progression (ascending palsy, with late ocular involvement).Further, suspecting Guillain Barre Syndrome, a nerve conduction study was performed, which revealed axonal and demyelinating motor and sensory neuropathy, and a repeat lumbar puncture revealed albumino-cytological dissociation, which led to the diagnosis of GBS. Intravenous immunoglobulins were started immediately for the same. However, the patient deteriorated further despite this. Aftera period of 24 hours, ocular movements and brainstem reflexes were lost with power worsening to 0 and no response to pain. To investigate the cause for worsening, blood tests and brain MRI were done, which showed normal findings, and EEG showed severe encephalopathy with theta waves, suggesting deep coma. Even on completion of intravenous immunoglobulin therapy, patient remained comatose with a Glasgow Coma Scale of E1VTM1 with dilated and fixed pupils. Her blood tests also revealed positivity for antibodies to GM1 ganglioside, and the patient was hence opined to have Fulminant Guillain Barre Syndrome.

A week later, the patient was tracheostomized owing to prolonged ventilation, and given supportive measures in the form of deep vein thrombosis prophylaxis, ventilation, and correction of electrolyte abnormalities. Rigorous physiotherapy was initiated at the earliest (Table 2), and passive music therapy was given. After about 10 days, slight movement of lips was noted, following which she regained sensations and power in a descending pattern. She also started taking spontaneous breaths, and hence, the mode of ventilation was shifted from controlled to synchronized intermittent mandatory ventilation, followed by an intermittent BiPap trial, and then tapered. Measurement of serum electrolytes then revealed hyponatremia, which was attributed to hypovolemia. She also developed a few complications owing to prolonged ICU stay, which were managed as described in Table 3.

DAY OF HOSPITALISATION	PHYSIOTHERAPY EXERCISES
Day 4	Passive Range of Motion B/L upper limbs and lower limbs
Day 22	Joint approximation
Day 28	Active assisted Range of Motion of B/L upper limbs and lower limbs
Day 32	High sitting for 5 min
Day 33	Neck control – initiation and maintenance for 3-4 seconds 20% manual resistance exercise for upper limbs Grips and pinches
Day 42	Shoulder shrugs
Day 47	Segmental and diaphragmatic facilitation Weight shifts in edge of bed sitting
Day 49	Chair sitting, abduction and adduction of shoulder and hips
Day 66	Standing with 3-person support
Day 71	Wheelchair mobilisation
Day 76	Active Range of Motion of B/L upper limbs and lower limbs

Table 2: Physiotherapy exercise schedule

Sl. no	Complication	Symptoms	Cause/Agent	Treatment
1	Urinary tract infection	Recurrent fever	*Escherichia Coli*	Fosfomycin
2	Ventilator-Associated Pneumonia	Increased secretions	*Pseudomonas*	Ciprofloxacin
3	Corneal Opacity		Loss of extraocular movements for a prolonged period	Lubricating Eye drops, lid taping
4	Paralytic Ileus		Hypokalemia	Conservative management
5	Hyponatremia		Hypovolemia	Intravenous Fluid Administration

Table 3: Complications

Swallowing exercises were started and continued andsemisolid feeds were initiated. Intermittent corking of the tracheostomy tube was advised, and the patient was decannulated on follow-up two weeks later.The patient has since been on regular follow up and is currently back to her full functional status and has no residual deficits despite having had the fulminant form of the disease.

The chain of events from her admission to discharge have been pictorially represented in Figure 1.

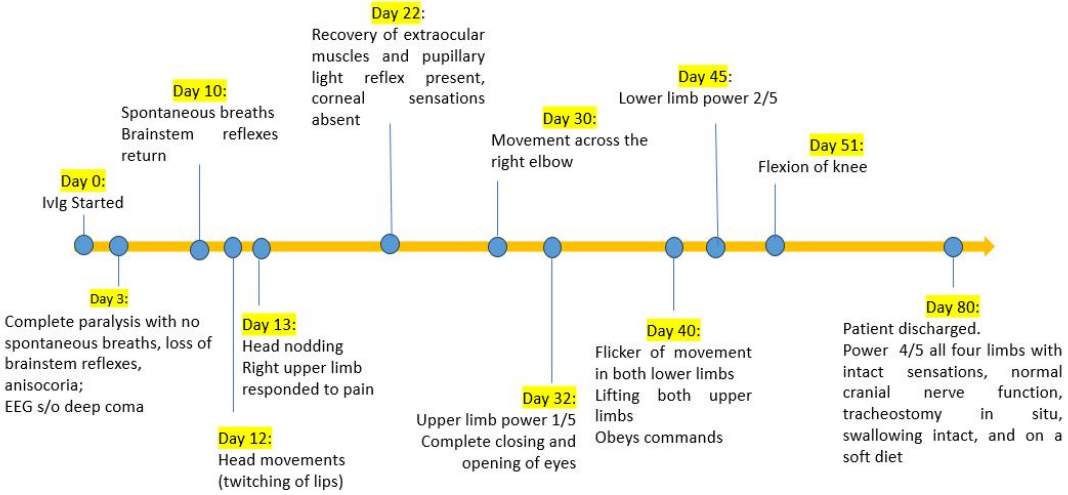

Figure 1: Timeline of events

3. DISCUSSION

GuillianBarréSyndrome (GBS), the commonest cause of acute generalized paralysis worldwide, is a rare and severe polyradiculoneuropathy clinically manifesting as acute onset and rapidly progressing ascending paralysis, loss of tendon reflexes and the classical finding of elevated cerebrospinal fluid (CSF) protein without pleocytosis(11).GBS is termed as fulminant when the patient rapidly deteriorates, showing severe symptoms, such as absent brainstem reflexes, complete quadriplegia as well as ventilator requirement, as seen in our patient (12). Fulminant GBS has a mortality rate of 20%, in contrast with Classical GBS, which has a rate of 3-10%, as well as a poorer recovery rate (13). It also leaves patients with long-term functional impairment. Alain Rouge et. al. reported a case of Fulminant GBS mimicking brain death which was followed up for 9 years. In that case, the patient's quality of life was severely impacted due to his disability despite regular physiotherapy and follow-up (5). Our patient was back to her full functional status within 2 months following her discharge.

There have been very few reports of patients with fulminant GBS entering a clinical state mimicking brain death (4). These patients have a poor rate of recovery and high mortality, especially in the presence of dysautonomia. To declare brain death, one must rule out reversible causes and identify an etiology that explains the clinical picture (6). Hence, our patient was not declared brain dead and was identified to have a syndrome 'mimicking' it.

GBS is a heterogeneous condition with several variants which can fall into either of the two subtypes: axonal or demyelinating. While 85-90% of the cases of GBS are of the AIDP variant, the axonal variants – acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy(AMSAN) are lesser known and more severe (14). In hyperacute cases, axonal degeneration can occur secondary to demyelination (15). Severe degeneration of axons, whether a primary event or secondary to AIDP, is associated with worse clinical outcomes. Axonal forms of GBS are associated anti-GM1 ganglioside antibodies, as seen in our patient (6). These antibodies are linked to antecedent *Campylobacter jejuni* infection (16), which is presumed to be the cause of diarrhea in our patient prior to presentation.

Very few cases exist in medical literature of patients with GBS developing bilateral mydriasis (5). The preganglionic sympathetic and parasympathetic nerve fibres of the short ciliary nerve are surrounded by a thin myelin sheath (17) The demyelination of these fibres leads to bilateral tonic pupils in GBS. This can also exist independently of external ophthalmoplegia (9). Miller-Fischer Syndrome is a variant of GBS that exhibits the triad of – external ophthalmoplegia, ataxia, and areflexia. Patients with MFS present with diplopia first, due to external ophthalmoplegia (13). Our patient also had external ophthalmoplegia. However, since it was not the first presentation and she developed sensory involvement along with an ascending pattern of paralysis, it was ruled out.

Either plasma exchange (200-250 ml plasma/kg body weight in five sessions) or intravenous immunoglobulin (0.4 g/kg body weight daily for five days), which is the standard treatment for GBS, also applies to fulminant GBS. There are no studies showing either of these methods to be superior to the other in the literature. IVIg is typically the preferred course of medication despite being more expensive as it is easy to administer and is usually more readily available than plasma exchange. Studies have failed to show that a combination of the two may be superior to either one alone (4) .It has been observed that, in the first four weeks after receiving conventional dosages of plasma exchange or IVIg, about 40% of patients do not improve [6]. Such a progression of the disease does not indicate treatment failure, as it limits the damage done by illness by preventing further injury to the nerves.

In cases of fulminant GBS, patients may require long-term supportive care and ICU care must be continued. Moreover, patients require to be constantly monitored, adequate nutrition, timely physiotherapy with passive movement of limbs, DVT prophylaxis, and tracheostomy (18).

It is prudent to consider fulminant GBS as a diagnosis in all patients with a rapid progression of disease, acute onset paralysis, and cranial nerve palsy. The CSF finding of albumino-cytologic dissociation, and electrophysiologic studies, and radiological investigations can prevent us from misdiagnosing this potentially fatal disease. Definitive treatment must be started at the earliest and supportive care must be continued even if signs of recovery are not appreciated or worsening clinical status is observed, as most patients have a slow course of recovery. and rapid improvement should not be expected.

4. CONCLUSION

In conclusion, fulminant GBS, albeit a rare entity, can pose significant diagnostic challenges. Clinicians must maintain a high index of suspicion to accurately diagnose and treat the same. Early intubation and initiation of IVIg treatment are of paramount importance for better outcomes. As demonstrated in this case, recovery can be slow, requiring persistence with supportive care and physiotherapy.

5. RECOMMENDATIONS

- Clinicians must not withdraw supportive care prematurely in cases of fulminant GBS.
- GBS should be considered as a differential diagnosis when confronted with a patient in a comatose state and clinicians must collect athorough and adequate history to rule out the same.
- Clinicians must be aware that short ciliary nerve involvement, manifesting as loss of extraocular movements, although rare, can occur in GBS.

6. LIMITATIONS

This case has limited generalizability due to the depiction of a rare occurrence.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

DrMeghnaSomaraj and Dr Arundhati Negi wrote the manuscript and performed literature searches. Dr Ranitha Gopi and Dr Weena Stanley were the lead clinicians in charge of the care for the patient. All authors read and approved the final manuscript.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

REFERENCES

1. Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, Cornblath DR, et al. Diagnosis and management of Guillain–Barré syndrome in ten steps. Nature Reviews Neurology 2019 15:11 [Internet]. 2019 Sep 20 [cited 2023 Aug 15];15(11):671–83. Available from: https://www.nature.com/articles/s41582-019-0250-9

2. Nazir Z, Habib A, Ali T, Kiran |, Khan S, Samar |, et al. Co-occurrence of Guillain-Barre syndrome and rheumatoid arthritis in a young female: A case report from a low middle-income country. Clin Case Rep [Internet]. 2024 [cited 2024 Aug 19];12:8481. Available from: https://doi.org/10.1002/ccr3.8481wileyonlinelibrary.com/journal/ccr3

3. Hu J, Luo X, Wang Y, Prado E, Fu Q, Shao A. Fulminant Guillain–Barré Syndrome and Spontaneous Intraventricular Hemorrhage: A Case Report and Literature Review. Front Neurosci [Internet]. 2020 Jun 30 [cited 2023 Aug 16];14. Available from: /pmc/articles/PMC7340086/

4. Ravikumar S, Poysophon P, Poblete R, Kim-Tenser M. A case of acute motor axonal neuropathy mimicking brain death and review of the literature. Front Neurol. 2016;7(APR).

5. Rouge A, Lemarie J, Gibot S, Bollaert PE. Long-term impact after fulminant Guillain-Barré syndrome, case report and literature review. Vol. 9, International Medical Case Reports Journal. Dove Medical Press Ltd; 2016. p. 357–63.

6. Nithyashree N, Dhanaraj M, Kumar S, Saraswathi MB. Factors predicting poor outcome in patients with fulminant Guillaine-Barré syndrome. Ann Indian Acad Neurol. 2014 Oct 1;17(4):463–5.

7. Snyder LA, Rismondo V, Miller NR. The Fisher variant of Guillain-Barré syndrome (Fisher syndrome). J Neuroophthalmol [Internet]. 2009 Dec [cited 2023 Aug 16];29(4):312–24. Available from: https://pubmed.ncbi.nlm.nih.gov/19952907/

8. Moody SB, Wanchoo RJ, Kalamangalam GP, Infante E, Sheikh KA. Difference in central and peripheral recovery in a patient with severe axonal motor neuropathy and central nervous system involvement and review of literature. J ClinNeuromuscul Dis [Internet]. 2013 Mar [cited 2023 Aug 16];14(3):110–3. Available from: https://pubmed.ncbi.nlm.nih.gov/23492462/

9. Hong SH, Byun SH, Hong EH, Lee YH, Moon JH. Bilateral tonic pupils and guillain-barre syndrome in a 6-year-old boy. Vol. 27, Annals of Child Neurology. Korean Child Neurology Society; 2019. p. 146–8.

10. Van Den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, Van Doorn PA. Guillain-Barré syndrome: Pathogenesis, diagnosis, treatment and prognosis. Vol. 10, Nature Reviews Neurology. 2014.

11. Vedanaryanan VV, Chaudhry V. Guillian Barre Syndrome - Recent advances. Indian J Pediatr [Internet]. 2000 [cited 2023 Aug 15];67(9):635–46. Available from: https://link.springer.com/article/10.1007/BF02762173

12. Nakamura Y, Motoki M, Hirose T, Hosokawa T, Ishida S, Arawaka S. Fulminant Guillain-Barré syndrome showing severe pharyngeal-cervical-brachial weakness in the recovery phase: A case report. BMC Neurol. 2019 Jun 28;19(1).

13. Rigamonti A, Basso F, Stanzani L, Agostoni E, Lauria G. Guillain-Barré syndrome mimicking brain death. Vol. 14, Journal of the Peripheral Nervous System. 2009. p. 316–9.

14. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barré syndrome: An update. Journal of Clinical Neuroscience. 2009 Jun 1;16(6):733–41.

15. Vital C, Vital A, Arne P, Hilbert G, Gruson D, Gbikpi-Benissan G, et al. Inexcitability of nerves in a fulminant case of Guillain-Barre syndrome. Journal of the Peripheral Nervous System. 2000 Jun;5(2):111–5.

16. Okuda B, Koga M, Katsuta T, Okamoto K, Yuki N. Fulminant Guillain-Barre Syndrome after Campylobacterjejuni Enteritis and Monospecific Anti-GTla IgG Antibody. Vol. 41, Internal Medicine. 2002.

17. Anzai T, Uematsu D, Takahashi K, Katayama T. Guillain-Barre Syndrome with Bilateral Tonic Pupils. Vol. 33, Internal Medicine. 1994.

18. Upadhyay P, Saroa R. A Stitch in Time Defeats the Landry-Guillain-Barré Strohl Syndrome. Cureus. 2022 Sep 11;