Published in final edited form as:

J Clin Neuromuscul Dis. 2013 March ; 14(3): 110–113. doi:10.1097/CND.0b013e3182852542.

Difference in Central and Peripheral Recovery in a Patient With Severe Axonal Motor Neuropathy and Central Nervous System Involvement and Review of Literature

Shade' B. Moody, MD^{*,†}, Ruchi J. Wanchoo, MD^{*}, Giridhar P. Kalamangalam, MD, DPhil^{*}, Ernesto Infante, MD^{*}, and Kazim A. Sheikh, MD^{*}

^{*}Department of Neurology, Department of General Pediatrics, University of Texas Medical School at Houston, Houston, TX

[†]Division of Child & Adolescent Neurology, Department of General Pediatrics, University of Texas Medical School at Houston, Houston, TX

Abstract

In the literature, the term fulminant Guillain–Barré syndrome is used to refer to patients with Guillain–Barré syndrome with rapidly progressive and severe weakness and/or comatose state mimicking brain death. We present the case of a 53-year-old man with fulminant Guillain–Barré syndrome with discrepancy in central nervous system and peripheral nervous system recovery. Our review of literature confirms that these patients often have good and relatively rapid recovery of central nervous system function, whereas peripheral nervous system function is relatively delayed and often incomplete.

Keywords

fulminant Guillain–Barré syndrome; Bickerstaff brain stem encephalitis; brain death; brain stem reflexes

INTRODUCTION

The term fulminant Guillain–Barré syndrome (FGBS) is used in the literature to denote patients with Guillain–Barré syndrome (GBS) and central nervous system (CNS) dysfunction, manifesting as altered consciousness and loss of brain stem reflexes, which can simulate brain death or with rapidly progressive severe weakness.^{1–3} The basis of unresponsiveness and loss of brain stem function in such cases is not completely known. Both central and peripheral mechanisms are invoked. Involvement of the CNS is supported by the frequent association of Bickerstaff brain stem encephalitis (BBE) with GBS and the abnormal electroencephalographic (EEG) finding of alpha coma pattern.^{2–5} Review of these cases indicates that the majority of patients with FGBS have relatively rapid, and often

Reprints: Kazim A. Sheikh, MD, Department of Neurology, University of Texas-Medical School at Houston, 6431 Fannin, St, Houston, TX 77030, (kazim.sheikh@uth.tmc.edu).

The authors have no conflicts of interest or funding to disclose.

complete, recovery of central function with significant residual peripheral nerve damage. The basis for this disparity in CNS and peripheral nervous system (PNS) recovery is unknown. With this background in mind, we present our case and review similar cases published in the literature.

CASE REPORT

A 53-year-old man presented with a 6-hour history of weakness and unsteadiness. He had no preceding infections or illnesses. Initial neurological examination showed normal level of arousal, right-sided weakness and hyporeflexia, and a right-sided Babinski sign. Four hours later, he developed respiratory failure requiring intubation. On day 2, he was noted to be areflexic and quadriplegic with left-sided ptosis and autonomic dysfunction. By day 3, he had dilated nonreactive pupils, loss of corneal, gag, and oculoccephalic reflexes, and no response to cold caloric testing.

Computed tomography of the head (day 1), 2 brain magnetic resonance imaging studies (day 3 and day 22), and a cerebral perfusion study were normal. Serial EEGs showed an alpha coma pattern that normalized subsequently. Routine blood parameters and anti-GQ1b, anti-GD1a, anti-GM1, and acetylcholine receptor antibodies were all normal or negative. Cerebrospinal fluid sampling (day 3 and day 25) was acellular, showing mildly elevated protein (46.6 mg/dL) in the second study. Cerebrospinal fluid infection screen was negative. Nerve conduction studies performed on day 3 revealed no evoked motor responses from the left median or left peroneal nerve. Motor conduction of the left ulnar nerve showed a distal latency of 3.9 milliseconds (ms), amplitude of 0.8 mV, and conduction velocity (CV) of 60 m/second. Sensory nerve conduction study (SNCS) of the left median nerve showed a peak latency of 3.1 ms, amplitude of 21 μ V and CV of 54 m/second. SNCS of the left ulnar nerve showed a peak latency of 3.1 ms, amplitude of 10 μ V, and CV of 38 m/second. Screening for neuromuscular junction defects was negative. Repeat nerve conduction study and electromyography performed on day 31 showed no evoked motor responses in median and ulnar nerves with preserved SNCS. There was evidence of active denervation in the tested muscles on electromyography. These findings were most consistent with the motor axonal variant of GBS.

He received 2 courses (2 gm/kg each) of intravenous immunoglobulin during the first and third weeks of his illness without improvement. He began to recover 8 weeks after symptom onset, by which stage he had received tracheostomy and a percutaneous endoscopic gastrostomy tube. He was gradually weaned from ventilator support. He was moving his upper extremities against gravity before his placement in a long-term facility 8 months after the onset of initial symptom.

Nearly 28 months after the symptom onset, he is still living in a nursing home. He is able to talk, drink liquids, and eat a soft diet. He has some use of arms and is able to use a remote control to change the channels on the television and adjust the height of his bed. He is able to lift his arms enough to touch his face but is unable to feed himself. He is still wheelchair bound with no movement in his right leg and less than antigravity strength in his left leg. He

has no cognitive deficits. He has no recollection of the events that occurred while he appeared clinically “brain dead.”

RESULTS

The search terms “fulminant Guillain–Barré syndrome, Guillain–Barré syndrome and brain death, Bickerstaff brain stem encephalitis, and Bickerstaff brain stem encephalitis and brain death” were used in the PubMed, and cases that simulated brain death and had GBS were collated.^{1–20} Of 23 published cases, 22 patients had usable information about central and peripheral recovery. A case report that did not clearly detail the length of “brain death” in a patient with full recovery was not included. Our review of these 22 cases with loss of brain stem reflexes and a comatose state mimicking brain death in patients with GBS revealed that the majority of these patients had better CNS compared with PNS recovery, as in our case. Eighteen of the 22 patients included in the review had better CNS recovery than PNS recovery.^{1–14} The CNS recovery in these cases ranged from 5 days to 8 months with the majority of patients recovering in 1–6 weeks. Another patient had full CNS recovery by day 18 but died from a fatal arrhythmia.¹⁷ Majority of these patients with CNS dysfunction have nonspecific EEG abnormalities with 7 of 22 showing alpha coma pattern.^{2,4–6,12,14,18} In contrast, PNS recovery was significantly delayed and incomplete compared with CNS recovery with some patients still having significant motor deficits more than 12 months after the onset of illness. One patient had “full recovery” of motor function, and another was able to “walk unaided” at 6 months.^{16,18} Motor function was not clearly documented in another patient.¹⁹

In comparison, our patient’s level of consciousness had returned to a level that allowed him to participate in bedside neurological testing at 8 weeks after the symptom onset, but at 8 months after the symptom onset, he still had significant residual PNS deficits manifesting as severe atrophy and weakness of facial, bulbar, and extremity muscles from severe axonal injury. Currently, the patient is cognitively intact and has normal speech and language functions, despite severe residual weakness.

DISCUSSION

Our case emphasizes the fact that CNS recovery generally greatly exceeds and precedes PNS recovery in patients with FGBS associated with CNS dysfunction. The current thinking about GBS and BBE would favor the notion that patients with FGBS have GBS overlap with BBE.^{21–23} The reasons for the differential CNS and PNS recovery in FGBS are not known. This case raises the possibility that PNS and CNS have different mechanisms of injury and/or repair if common immune effectors are involved in CNS and/or PNS injury in this disorder. Alternatively, different immune effectors could induce PNS and CNS injuries, which could explain the disparity in recovery. The lack of obvious magnetic resonance imaging structural abnormalities in our case suggests that CNS involvement comprises a physiological/functional injury of central pathways rather than a structural disruption. Whether immune effectors such as autoantibodies or sodium channel blocking peptides, which have been reported to be present in a proportion of patients with GBS and BBE and experimentally shown to disrupt nodal function, are involved in CNS dysfunction remains

conjectural.²⁴⁻²⁸ Some have suggested the possibility that the apparent CNS dysfunction may be due to severe deafferentation rather than actual altered consciousness, a fact that may be supported by the normal EEGs seen in some patients. However, in cases with predominantly motor nerve involvement, deafferentation alone does not explain the abnormal EEGs or altered consciousness. Understanding the pathophysiology of CNS dysfunction in this condition can have translational implications.

The alpha coma EEG pattern seen in our patient is classically seen in diffuse brain injury from anoxia, toxic, metabolic, or other factors.²⁹ However, an alpha coma-like pattern also occurs in deafferentated states from brain stem lesions, where in fact the patient is locked in, rather than comatose. However, rather than the posterior-dominant reactive rhythm that characterizes the normal alpha rhythm in wakefulness, our patient had an unvarying, widely distributed alpha rhythm pattern that suggested coma. Nevertheless, the alpha rhythm in deafferentation may lack both a posterior dominance and reactivity; equally, the alpha coma of diffuse brain injury may exhibit both posterior dominance and reactivity.²⁹ Notably, the electrical studies in our case showing predominant motor involvement would argue against peripheral (spinal and cranial nerve) deafferentation significantly contributing to the EEG abnormalities.

In summary, GBS with severe and rapidly progressive weakness associated with CNS dysfunction that can simulate brain death has been rarely reported in the literature. This poses a potential risk for premature withdrawal of life-supporting measures. The patients who have been reported in the literature had a relatively benign course relative to their CNS recovery but were often left with severe residual weakness. The reasons for such disparity are unclear, but the significant chance for full CNS recovery necessitates the use of aggressive supportive care in these patients.

REFERENCES

1. Bakshi N, Maselli R, Gospe SM, et al. Fulminant demyelinating neuropathy mimicking cerebral death. *Muscle Nerve*. 1997; 20:1595–1597. [PubMed: 9390675]
2. Friedman Y, Lee L, Wherrett J, et al. Simulation of brain death from fulminant deafferentation. *Can J Neurol Sci*. 2003; 30:397–404. [PubMed: 14672276]
3. Rigamonti A, Basso F, Stanzani L, et al. Guillain-Barré syndrome mimicking brain death. *J Peripher Nerv Syst*. 2009; 14:316–319. [PubMed: 20021574]
4. Hassan T, Mumford C. Guillain-Barré syndrome mistaken for brainstem death. *Postgrad Med J*. 1991; 67:280–281. [PubMed: 2062776]
5. Marti-Masso JF, Suarez J, Lopez de Munain A, et al. Clinical signs of brain death simulated by Guillain-Barré syndrome. *J Neurol Sci*. 1993; 120:115–117. [PubMed: 8289072]
6. Carroll WM, Mastaglia FL. Locked-in coma in postinfective polyneuropathy. *Arch Neurol*. 1979; 36:46–47. [PubMed: 217318]
7. Al-Din AN, Jamil AS, Shakir R, et al. Coma and brain stem areflexia in brain stem encephalitis (Fisher's syndrome). *BMJ*. 1985; 291:535–536. [PubMed: 3928039]
8. Tan A, Chee M. Fulminant Guillain-Barré syndrome with quadriplegia and total paresis of motor cranial nerves as a result of segmental demyelination. *J Neurol Sci*. 1995; 134:203–206. [PubMed: 8747867]
9. Bohlega S, Stigsby B, Haider A, et al. Guillain-Barré syndrome with severe demyelination mimicking axonopathy. *Muscle Nerve*. 1997; 20:514–516. [PubMed: 9121514]

10. Hughes R, McGuire G. Neurologic disease and the determination of brain death: the importance of diagnosis. *Crit Care Med*. 1997; 25:1923–1924. [PubMed: 9366780]
11. Ragazzoni A, Grippo A, Tozzi F, et al. Event-related potentials in patients with total locked-in state due to fulminant Guillain-Barré syndrome. *Int J Psychophysiol*. 2000; 37:99–109. [PubMed: 10828378]
12. Vargas F, Hilbert G, Gruson D, et al. Fulminant Guillain-Barré syndrome mimicking cerebral death: case report and literature review. *Intensive Care Med*. 2000; 26:623–627. [PubMed: 10923739]
13. Joshi MC, Azim A, Gupta GL, et al. Guillain-Barré syndrome with absent brainstem reflexes—a report of two cases. *Anaesth Intensive Care*. 2008; 36:867–869. [PubMed: 19115659]
14. Rivas S, Douds L, Ost Dahl R, et al. Fulminant Guillain-Barré syndrome after closed head injury: a potentially reversible cause of an ominous examination. *J Neurosurg*. 2008; 108:595–600. [PubMed: 18312109]
15. Bernard V, Van Pesch V, Hantson P, et al. Guillain-Barré syndrome mimicking brain death pattern: a poorly reversible condition. *Acta Neurol Belg*. 2010; 110:93–96. [PubMed: 20514933]
16. Stojkovic T, Verdin M, Hurtevent JF, et al. Guillain-Barré syndrome resembling brainstem death in a patient with brain injury. *J Neurol*. 2001; 248:430–432. [PubMed: 11437171]
17. Fuller GN, Jacobs JM, Lewis PD, et al. Pseudoaxonal Guillain-Barre syndrome: severe demyelination mimicking axonopathy. A case with pupillary involvement. *J Neurol Neurosurg Psychiatry*. 1992; 55:1079–1083. [PubMed: 1469406]
18. Coad NR, Byrne AJ. Guillain-Barré syndrome mimicking brainstem death. *Anaesthesia*. 1990; 45:456–457. [PubMed: 2382803]
19. Drury I, Westmoreland B, Sharbough F, et al. Fulminant demyelinating polyradiculoneuropathy resembling brain death. *Electroencephalogr Clin Neurophysiol*. 1987; 67:42–43. [PubMed: 2439279]
20. Moussouttas M, Chandy D, Dyro F. Fulminant acute inflammatory demyelinating polyradiculopathy: case report and literature review. *Neurocrit Care*. 2004; 1:469–473. 2004. [PubMed: 16174952]
21. Odaka M, Yuki N, Yamada M, et al. Bickerstaff's brainstem encephalitis: clinical features of 62 cases and a subgroup associated with Guillain-Barré syndrome. *Brain*. 2003; 126:2279–2290. [PubMed: 12847079]
22. Ito M, Kuwabara S, Odaka M, et al. Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. *J Neurol*. 2008; 255:674–682. [PubMed: 18274803]
23. Susuki K, Johkura K, Yuki N, et al. Clinical Deterioration in Bickerstaff brainstem encephalitis caused by overlapping Guillain-Barré syndrome. *J Neurol Sci*. 2003; 211:89–92. [PubMed: 12767504]
24. Brinkmeier H, Aulkmeyer P, Wollinsky K, et al. An endogenous pentapeptide acting as a sodium channel blocker in inflammatory autoimmune disorders of the central nervous system. *Nature Med*. 2000; 6:808–811. [PubMed: 10888931]
25. Weber F, Rudel R, Aulkmeyer P, et al. The endogenous pentapeptide QYNAD induces acute conduction block in the isolated rat sciatic nerve. *Neurosci Lett*. 2002; 317:33–36. [PubMed: 11750990]
26. Willison HJ, Yuki N. Peripheral neuropathies and antiglycolipid antibodies. *Brain*. 2002; 125:2591–2625. [PubMed: 12429589]
27. Susuki K, Rasband MN, Tohyama K, et al. Anti-GM1 antibodies cause complement-mediated disruption of sodium channel clusters in peripheral motor nerve fibers. *J Neurosci*. 2007; 27:3956–3967. [PubMed: 17428969]
28. Yuki N. Fisher syndrome and Bickerstaff brainstem encephalitis (Fisher-Bickerstaff syndrome). *J Neuroimmunol*. 2009; 215:1–9. [PubMed: 19643503]
29. Chatrian, GE., Turella, GS. Electrophysiological evaluation of coma, other states of diminished responsiveness, and brain death. In: Ebersole, JS., Pedley, TA., editors. *Current Practice of Clinical Electroencephalography*. 3rd ed.. Lippincott Williams & Wilkins; Philadelphia, PA: 2003. p. 418-424.