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CASE REPORT

Rehabilitation of a patient with overlap of acute transverse myelitis and Bickerstaff's brainstem encephalitis: a case report

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We report on one patient with Bickerstaff's brainstem encephalitis (BBE) and associated flaccid weakness. Counter to previous studies with BBE which indicate weakness due to Guillain–Barre syndrome, our patient's presentation of paraplegia following BBE is consistent with concomitant acute transverse myelitis. Her findings of BBE largely resolved, although she remained with T6 American Spinal Injury Association (ASIA) A paraplegia. Motor functional impairment measure scores improved from 20 at admission to 66 before discharge home with assistance. This case presents the first potential overlapping case of acute transverse myelitis with BBE and describes how acute inpatient rehabilitation can be effective in facilitating transition back to independence following tetraplegia with BBE.

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Bickerstaff's brainstem encephalitis (BBE) is a rare, autoimmune mediated inflammatory condition, which is associated with opthalmoplegia, altered mental status and ataxia.[1–3] Flaccid weakness and areflexia are also variably found, and BBE has classically been implicated following antecedent *Campylobacter jejuni* infection (23%).[2] Although some argue that BBE lies on a spectrum with other immunologically driven neurologic syndromes such as Miller–Fisher, polyneuritis cranialis and Guillain–Barre syndrome (GBS), population studies have demonstrated an overlap of patients who appeared to have BBE as well as flaccid limb weakness (assumed to be acute motor axonal neuropathy variant of GBS).[3] Over time, patients with this constellation of findings had significantly worse long-term mean disability scores than either alone,[4] with previous case series documenting some degree of eventual improvement (although full details of what this functionally meant are not available). Limited details are currently published in literature to our knowledge in regards to the rehabilitation time course or specific functional expectations regarding BBE with associated flaccid weakness. In addition, there have been no reports of overlap between BBE and acute transverse myelitis.

A 46-year-old previously healthy woman presented to the Emergency Department with 6 days of nausea, diarrhea, fever to 39.4 °C, altered mental status, ataxia and progressive generalized weakness. She quickly developed urinary retention, severe headache, diplopia, new onset generalized tonic-clonic seizures, flaccid paralysis and was intubated for airway protection. Extensive testing was done for central nervous system infection (Lyme's, Dengue, West Nile, cytomegalovirus, varicella virus, Epstein–Barr virus, herpes simplex virus, John Cunningham polymovirus, rabies, arbovirus, Rocky mountain spotted fever, toxoplasmosis, bacterial, atypical bacterial, tuberculosis and fungal) and *N*-methyl-D-aspartate receptor antibody (Ab), all of which were negative. Cerebrospinal fluid (CSF) from repeat lumbar punctures on hospital days 0, 2 and 7 showed minimally decreased glucose, pleocytosis without oligoclonal bands and increased protein without albuminocytologic dissociation. Serum titers for *C. jejuni* were marginally positive and anti-GQ1b Ab was negative. Magnetic resonance imaging (MRI) of patient's neuroaxis demonstrated diffusion restriction involving the splenium of corpus callosum, which resolved on repeat imaging 3 days later. There was additionally, persistent lack of fluid-attenuated inversion recovery (FLAIR) suppression within sulci in supratentorial fossa and within folia of posterior fossa without any evidence of cerebral demyelinating lesions. Leptomeningeal enhancement was diffusely present throughout the brainstem, spinal cord (continuous down to T5), and was noted along the surface of the conus medularis without any evidence of demyelinating lesions. Increased T2 signal was present within the substance of the spinal cord from T2 to T5 on MRI, without evidence of cord compression or abnormal flow voids. Magnetic resonance angiography was not completed, although suspicion for cord infarct was low, given lack of ischemic evolution on repeated MRI.

The patient initially was treated with 5 days of intravenous immunoglobulin (initiated before hospital day 3) for suspected GBS followed by 6 days of 1 g methylprednisolone per day before an extended prednisone taper for suspected acute transverse myelitis. Clinical seizures resolved within 1 week of initial presentation, and patient's vision improved, although she continued to have end gaze nystagmus. Convalescent serum samples demonstrated continued marginally positive *C. jejuni* titers. This, grouped with MRI and clinical findings, lead to the diagnosis of BBE being made. Electrodiagnostics were not done at the outside hospital as she was felt clinically to have a GBS variant.

Thirty-six days after initial presentation, the patient presented to acute inpatient rehabilitation with flaccid tetraplegia, urinary retention, dysphagia with percutaneous endoscopic gastrostomy tube in place and on a ventilator with tracheostomy. Admission American Spinal Injury Association (ASIA) exam showed C5 ASIA impairment scale A tetraplegia with a zone of partial preservation of bilateral sensory/motor levels to T4. Patient underwent extensive therapy, was weaned off the ventilator on day 6 and

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had her tracheostomy decannulated on day 15. Her severe oropharyngeal dysphagia slowly resolved and she progressed to tolerate a general texture diet. Patient was further noted to have decreased articulatory precision of lingual sounds, which improved moderately, although remained at the time of discharge. Patient initially had autonomic instability and had several instances of low-grade autonomic dysreflexia, which resolved with draining a large amount of urine with a straight catheter. Upper extremity strength improved to 5/5 on manual muscle testing and full sensation reappeared to T6 with a broad area of constrictive transitional zone pain extending to T12 (treated with minimal success initially with gabapentin and then pregabalin). Lower extremities remained largely flaccid with absent deep tendon reflexes and Babinski reflexes bilaterally. Discharge ASIA exam demonstrated T6 ASIA impairment scale A paraplegia. Patient was, however, able to reflexively complete bowel care with self-initiated digital stimulation and developed tense rectal tone. She continued to have neurogenic bladder and was trained on scheduled intermittent self-catheterization. Motor functional independence measure (FIM) scores improved from 20 at admission to 66 at discharge and patient was able to return home with family and home therapies 96 days after initial presentation to the outside hospital.

At 1 and 3 months follow-up appointments, the patient continued to have flaccid lower extremity tone and a clear delineation of absent sensation to light touch and pin prick below T6. She also continued to experience transitional zone pain, although noted that it was decreasing when last seen in clinic. She continued to do intermittent self-catheterization, initiate her own bowel program and was functioning well at home.

BBE is a rare autoimmune mediated inflammatory condition, a subset of which has previously been associated with flaccid paralysis and assumed GBS. Here, we present findings of a 46-year-old female who had BBE with flaccid lower extremity paralysis. The diagnosis of BBE is often presumptively diagnosed when other possibilities have been exhausted. In addition to opthalmoplegia, and ataxia, altered mental status (74%),[2] bulbar palsy (34%)[1] and facial diplegia(45%)[2] have all also been noted in the literature. Albuminocytologic dissociation in CSF has been variably found, and in one study peaked at 46–55% by the third to fourth week in those individuals with BBE and associated limb weakness.[1] Anti-GQ1b Ab has been noted to be present in 68–70% of BBE.[1,2] On brain MRI, 23% were noted to have some abnormality,[2] whereas electroencephalogram (EEG) changes were seen in 57%.[1] In our patient, cognitive difficulties, diplopia and ataxia all resolved before discharge from acute inpatient rehabilitation. As has been previously seen in patients with BBE, our patient additionally had flaccid lower extremity paralysis, although no confirmatory electrodiagnostics were done to rule in or out GBS. In the absence of electrodiagnostic testing, the Brighton criteria have been developed for the diagnosis of GBS.[5] Despite our patient's rapid progression of flaccid weakness, respiratory muscle dysfunction, MRI enhancement of the conus and antecedent infection with *C. jejuni,* our patient does not meet any level of diagnostic certainty using the Brighton criteria. Instead, her presentation with acute onset paralysis, evidence of inflammation within the substance of her spinal cord on MRI without evidence of extra-axial compression, CSF pleocytosis, clearly delineated line of sensation (unchanged on follow-up testing 6 months after initial presentation), neurogenic bowel/bladder and autonomic dysreflexia/ instability are all supportive of acute transverse myelitis (ATM).[6] What's more, this patient also had chronic transitional zone pain, which commonly occurs following transverse myelitis. The presence of chronic lower motor neuron findings with ATM coincides with involvement of the anterior horn cells, as has been previously documented in other parainfectious ATM cases.[7] Odaka previously reported 37 cases of patients with BBE and associated limb weakness attributed to GBS.[2] Although electrodiagnostics were done in only a subset of this study population, findings were suggestive of a primarily motor axonal process occurring with sensory abnormalities not reported.

From limited studies, Bickerstaff brainstem encephalitis typically has a good recovery, although limited specific functional measures have been recorded in literature. When accompanied by flaccid weakness, recovery has been reported to be much slower and at times only partial.[2] Recovery from transverse myelitis is often incomplete, with 2/3 having moderate to severe residual disability. During her inpatient rehabilitation stay, our patient was able to resolve the majority of her bulbar symptoms and associated dysphagia (more characteristic of BBE), with FIM motor scores improving from 20 at initial presentation to 66 at discharge. Previous studies have noted that patients with non-traumatic spinal cord injuries have significantly lower FIM motor scores at discharge than their traumatically injured peers (44 vs 60).[8] This improvement for our patient above the expected FIM motor return was likely due in part to her extended stay in acute inpatient rehabilitation, but underscores the functional improvement that is possible with this constellation of syndromes. Based on this report, a broader differential diagnosis including ATM should be considered when encountering BBE with flaccid weakness. Long-term functional improvement with BBE and ATM overlap more closely aligns to that of ATM, and thus represents a significant clinical variant in terms of prognosis from BBE with flaccid weakness attributed to GBS.

This case describes how acute inpatient rehabilitation can be effective in facilitating transition back to independence following tetraplegia from BBE with clinical findings of flaccid paralysis. Although this flaccid paralysis has previously been described and attributed to GBS, we present potentially the first case of overlap between BBE and acute transverse myelitis.

COMPETING INTERESTS

The authors declare no conflict of interest.

REFERENCES

1 Ito M, Kuwabara S, Odaka M, Misawa S, Koga M, Hirata K *et al.* Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum. *J Neurol* 2008; **255**: 674–682.
2 Odaka M. Bickerstaff's brainstem encephalitis: clinical features of 62 cases and a subgroup associate with Guillain-Barre syndrome. *Brain* 2003; **126**: 2279–2290.
3 Lin J. Clinical variants of Guillain-Barré syndrome in children. *Pediatr Neurol* 2012; **47**: 91–96.
4 Overell JR, Hsieh S, Odaka M, Yuki N, Willison HJ. Treatment for Fisher syndrome, Bickerstaff's brainstem encephalitis and related disorders. *Cochrane Database Syst Rev* 2007; **1**: CD004761.
5 Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacombs BC. Diagnsosis of Guilllain-Barre syndrome and validation of the Brighton criteria. *Brain* 2014; **137**: 33–43.
6 Group TMCW. Proposed diagnostic criteria and nosology of acute transverse myelitis. *Neurology* 2002; **59**: 499.
7 Pradhan S, Kumar A. Lower motor neuron paralysis with extensive cord atrophy in parainfectious acute transverse myelitis. *Ann Indian Acad Neurol* 2014; **17**: 347–348.
8 McKinley WO, Seel RT, Hardman JT. Nontraumatic spinal cord injury: incidence, epidemiology, and functional outcome. *Arch Phys Med Rehabil* 1999; **80**: 619–623.