An Elderly Patient With Bickerstaff Brainstem Encephalitis and Transient Episodes of Brainstem Dysfunction

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Background: Bickerstaff brainstem encephalitis (BBE) is a rare inflammatory, demyelinating disease that generally has a good prognosis.

Objective: To describe the course of a patient with severe BBE and multiple medical complications.

Design: Case report.

Setting: Academic medical center.

Patient: An 81-year-old woman with BBE who fully recovered. The patient had transient and very frequent episodes of brainstem dysfunction during the recovery phase.

Main Outcome Measures: Clinical and biochemical evaluation with magnetic resonance imaging.

Conclusions: Bickerstaff brainstem encephalitis is a potentially reversible syndrome that needs early diagnosis (facilitated by magnetic resonance imaging) and prompt aggressive and supportive treatment. Frequent episodes of transient brainstem dysfunction occurred in our patient during recovery, possibly due to ephaptic transmission.

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Bickerstaff and Cloake first described the entity known as Bickerstaff brainstem encephalitis (BBE)\(^1\); however, the definition of BBE has evolved. In a recent review, Odaka et al\(^2\) defined BBE as a disorder with progressive ophthalmoplegia and ataxia and with features suggesting a central nervous system process, such as disturbed consciousness or hyperreflexia. In this report, we describe a patient who had BBE with a number of remarkable features. The diagnosis was made quickly, partly through the use of magnetic resonance imaging (MRI) studies. Methylprednisolone sodium succinate and prednisone were used as the only BBE treatment and led to a complete recovery, stressing the importance of early disease recognition and aggressive treatment—even in elderly patients such as ours. Of special interest was the development of very brief transient episodes of brainstem dysfunction that occurred hundreds of times a day during the recovery phase.

REPORT OF A CASE

An 81-year-old woman was admitted on April 2, 2006, because of progressively slurred speech, diplopia, clumsiness, and unsteady walking. One month before admission, the patient had developed a severe nonproductive cough that was diagnosed as interstitial pneumonitis and treated with moxifloxacin hydrochloride. The respiratory problems initially improved, but then the cough significantly worsened before the onset of neurological problems. Three days before admission, the patient developed dysarthria followed by diplopia, clumsiness, and ataxia.

On admission, the patient was afibrile with a mildly disturbed mental state and dysarthria. She exhibited incomplete horizontal eye movements with no ptosis or pupillary abnormalities. Results of the motor examination were unremarkable except for a questionable right Babinski sign and unsteady gait. The patient had dysmetria and slowed rapid alternating movements in the upper extremities. Results of the sensory examination were normal.

A chest radiograph showed an increase in interstitial markings and small right-sided effusion. A brain MRI showed increased signal on fluid-attenuated inversion recovery image sequences, with gadolinium enhancement in the brainstem (Figure). A magnetic resonance angiogram showed no abnormalities. Analy-
sis of the cerebrospinal fluid showed a white blood cell count of 2/µL, a glucose level of 58 mg/dL, and a protein level of 26 mg/dL; no oligoclonal bands or elevation of IgG, IgG index, or IgG synthesis; and negative polymerase chain reaction results for herpes simplex virus and varicella-zoster virus genome. Blood study results showed no elevation of antibodies to neurotropic viruses, Brucella, or Mycobacterium tuberculosis. Results of other blood studies, including SSA (Ro) and SSB (La) antibodies, DNA double-stranded antibody, antinuclear antibody, and paraneoplastic antibody panel, were unremarkable. Results of serological studies on a variety of respiratory pathogens showed no elevations that would suggest a recent infection.

A tentative diagnosis of BBE was made, and the patient was transferred to the neurological intensive care unit. A regimen of acyclovir, doxycycline, a combination of sulfamethoxazole and trimethoprim, and methylprednisolone sodium succinate, 1 g/d, was begun. The patient quickly developed dysphagia and hyperactive reflexes, as well as cardiac arrhythmias and signs of acute kidney injury. On April 5, acyclovir administration was discontinued and mechanical ventilation for airway protection and hemodynamic stabilization was started. Episodes of agitation prompted treatment with haloperidol and midazolam and a decrease in methylprednisolone sodium succinate to 500 mg/d. On April 6, the patient was noted to have bilateral Babinski signs with unsustained ankle clonus; she became more difficult to arouse, with extensor posturing on the right side. A second MRI showed extension of the brainstem involvement without new lesions. A cervical spine MRI showed no abnormalities. An electroencephalogram showed marked generalized slowing in the theta range, suggestive of an encephalopathy. Results of a second lumbar puncture on April 7 were normal. On April 9, an MRI showed no change and no gadolinium enhancement, and the methylprednisolone sodium succinate dosage was lowered to 60 mg/d given intravenously. On April 10, the patient was more responsive and a tetraparesis became apparent. The examination on April 11 showed horizontal gaze abnormalities, ptosis, seventh nerve palsies, and increased strength. Over the next several days, the patient improved in mental state, ptosis, eye movements, and renal function and was therefore extubated. Prednisone therapy was begun. The patient’s speech became clearer.

Figure. Magnetic resonance imaging in an 81-year-old patient on admission (A-C) showing increased signal in the midbrain on fluid-attenuated inversion recovery (FLAIR) images (A and B), with gadolinium enhancement on a T1-weighted image (C), and 5 weeks later (D and E) showing significant resolution on FLAIR images.
and her reflexes more normal. On April 20, the patient was discharged to a rehabilitation facility while receiving prednisone, 40 mg/d, with a tapering regimen.

The patient noted continuing improvement at the rehabilitation facility and was discharged on May 17 while receiving prednisone, 10 mg/d. A few days later, she noticed very frequent, stereotypic episodes lasting 1 to 10 seconds and occurring throughout the day; these episodes consisted of transient diplopia accompanied by dysarthria (if talking) and gait imbalance (if walking). The episodes increased in frequency so that they occurred up to hundreds of times a day. The patient was witnessed to have multiple episodes of paroxysmal worsening of slurred speech and ataxia with diplopia. Between episodes, results of an examination showed minimal dysarthria, full eye movements, no ptosis, a questionable right Babinski sign, slight clumsiness, and a slow gait with a negative Romberg sign. Electroencephalograms and electrocardiograms showed no abnormalities during the episodes. Magnetic resonance imaging showed a decrease in the abnormal signal in the brainstem with no evidence of recent stroke (Figure, D and E). Prednisone was increased to 15 mg/d and then slowly tapered over more than a month. When seen by one of us (R.P.R.) on June 14, the patient continued to have these episodes on a very frequent basis although they no longer involved diplopia. On June 28, the episodes decreased in frequency to approximately only 2 per day. In addition to the episodes, the patient had minimal slurring of words when she first began to speak and a slight imbalance when she began to walk. Over the next few weeks, the episodes disappeared and the patient returned to her normal baseline condition. An anti-GQ1b antibody level measured months after admission was normal (<1:100).

COMMENT

The definition of BBE has evolved since the original description, partly as a result of a classification of similar and, at times, overlapping disease entities such as the Miller Fisher syndrome (MFS) (see Lo³ for a review), Guillain-Barré syndrome (GBS) (see Griffin and Sheikh4 for a review), and acute demyelinating encephalomyelitis (ADEM) (see Tenembaum et al5 for a review), and partly because of the availability of new diagnostic tools, including MRI and anti-GQ1b antibody testing. There are a number of features shared by BBE and MFS, a variant of GBS, including electrophysiological study results of these patients can suggest a motor axonal neuropathy, presumably representing an acute motor axonal neuropathy variant of GBS. One could also envision BBE as a brainstem-localized variant of ADEM, an immune-mediated inflammatory disease that usually affects the white matter of the brain and spinal cord and is often preceded by an infection. The similarities in BBE, MFS, GBS, and ADEM suggest their classification in a spectrum of autoimmune disorders that sometimes overlap. A number of different viral and bacterial infections have been implicated in the prodromal illness, including Campylobacter jejuni,6,8 raising the possibility that BBE can result from an autoimmune response to a number of different pathogens.

In our case, the presence of Babinski signs, a disturbed state of consciousness, and the dramatic MRI signal abnormalities in the brainstem indicated a diagnosis of BBE. The patient's weakness presumably resulted from the extensive brainstem lesion involving the corticospinal tracts and was not related to an associated GBS. The age of the patient was not at all typical for patients with BBE and contrasts with previously presented cases.2

A remarkable feature of our patient was the presence of brief paroxysmal episodes of brainstem dysfunction that appeared after recovery of much of her neurological function. During these episodes, the patient exhibited transient ataxia, diplopia, and dysarthria—deficits that had been seen on a continuous basis earlier in the disease course. For several weeks, the episodes occurred hundreds of times a day, lasting 1 to 10 seconds. They were not related to a seizure phenomenon or cardiovascular abnormality.

Episodes of sensory disturbance are not infrequent in demyelinating processes such as multiple sclerosis. Episodes that involve more complex abnormalities are not common but have been described. The episodes of brainstem dysfunction in our patient resembled similar events reported by Andermann et al10 and Espir et al.11 One of the 2 patients described by Andermann et al had as many as 200 attacks a day that lasted 10 to 15 seconds and subsided over months; these episodes were thought to result from a disturbance in the excitability of demyelinated axons. Our patient's episodes exhibited several brainstem abnormalities suggesting mass synchronous firing as a result of ephaptic transmission (see Smith and McDonald12 for a review). In this condition, neuronal excitability can spread laterally to adjacent axons that may have an abnormally lowered threshold for firing as a result of demyelination. Interestingly, axons that are experimentally demyelinated develop spontaneous activity with a lowered threshold for firing 1 week or more after the insult, possibly explaining the onset of these episodes during the patient's recovery.

The dramatic MRI abnormalities in our patient assisted us in making an early diagnosis, which allowed prompt treatment of BBE. Various treatments of BBE have been used in the past, including corticosteroids, intravenous immunoglobulin, and plasmapheresis. Our patient was treated with corticosteroids, which seemed to have a positive therapeutic effect. Additional treatment with intravenous immunoglobulin and plasmapheresis was not used because of concerns about our patient's renal and hemodynamic status. Despite the fact that this
elderly woman had significant neurological deficits and serious medical problems, she eventually returned to her baseline status, highlighting the importance of aggressive, supportive treatment in what can be a completely reversible process.2,13

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REFERENCES


Calendar of Events

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