Bickerstaff's Brainstem Encephalitis: A Case Study

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Key words: Bickerstaff's Brainstem Encephalitis (BBE), Guillain-Barré Syndrome (GBS), Innocent Bystander Theory, Anti-GQ1b Antibody

Abstract

Introduction: Bickerstaff's Brainstem Encephalitis is the rarest form of the Anti-Gq1b Antibody Syndromes, and it is characterized with acute ophthalmoplegia, ataxia, and altered sensorium.

Case Presentation: A 72-year-old female patient with a past medical history of migraines, hypertension, and hyperlipidemia presented to the neurology office complaints of difficulty walking for the past six weeks. In addition, she felt a left-sided weakness and eventually developed a left facial droop.

Management and Outcome: The MRI brain scan showed T2 hyperintensities in the brainstem. Analysis of the CSF profile revealed a low white blood count, high protein count, and a high angiotensin converting enzyme (ACE) level. Such results confirmed the presence of BBE. In order to treat this condition, the patient was given five cycles of plasma exchange and after the third dose, she started to make improvements.

Discussion: This case demonstrates a classical presentation of Bickerstaff's Brainstem Encephalitis. The reasons for the emergence of this autoimmune disorder are unclear, but the Molecular Mimicry Theory and Innocent Bystander Theory provide possible explanations.

Introduction

Bickerstaff's Brainstem Encephalitis is the rarest form of the Anti-Gq1b Antibody Syndromes. Discovered in 1951 by Bickerstaff and Cloake, this condition was closely associated with Guillain-Barré Syndrome (GBS) due to its classification as an autoimmune disease (Shahrizaila et al, 2010). However, unlike GBS, Bickerstaff's Brainstem Encephalitis affects the central nervous system, leading to more serious complications and even potential death.

Because of the rarity of BBE, the incidence and prevalence of this condition around the world is unknown. However, studies have shown that BBE is more prevalent in Asian countries than in the rest of the world (Shameem et. al, 2013). As of now, there are no clear explanations to support this trend. To learn more about this rare disease, this condition will be explored in depth by analyzing the case of a patient suffering from BBE.

Case Presentation

This is a case report over a 72-year-old female patient with a past medical history of migraines, hypertension, and hyperlipidemia. She presented to the neurology office complaints of difficulty walking for the past six weeks. In addition, she felt a left-sided weakness and upon physical examination, it was detected that she was leaning slightly to the left. Two weeks after the onset of symptoms, the patient developed a left facial droop and went to the emergency room to be evaluated.

While in the emergency room, she had a magnetic resonance imaging (MRI) brain scan done and it showed hyperintensity on the T2 imaging in the brainstem, more specifically in the midbrain and the pons with extension into the bilateral thalamus. There was no enhancement on the MRI brain scan, and she was sent home to follow up with a neurologist.

In the three weeks prior to seeing a neurologist, the patient started experiencing dysarthric speech, double vision, and dysphagia. In addition, her gait progressively worsened. Five weeks after the onset of her symptoms, the patient was readmitted into the hospital.

Management and Outcome

While at the hospital, the patient received another MRI brain scan with and without contrast, magnetic resonance angiogram (MRA) of the head and neck, and a lumbar puncture. The MRI brain scan showed the continued presence of the T2 hyperintensities in the brainstem. The MRA of the head and neck was normal and did not show any vessel stenosis.

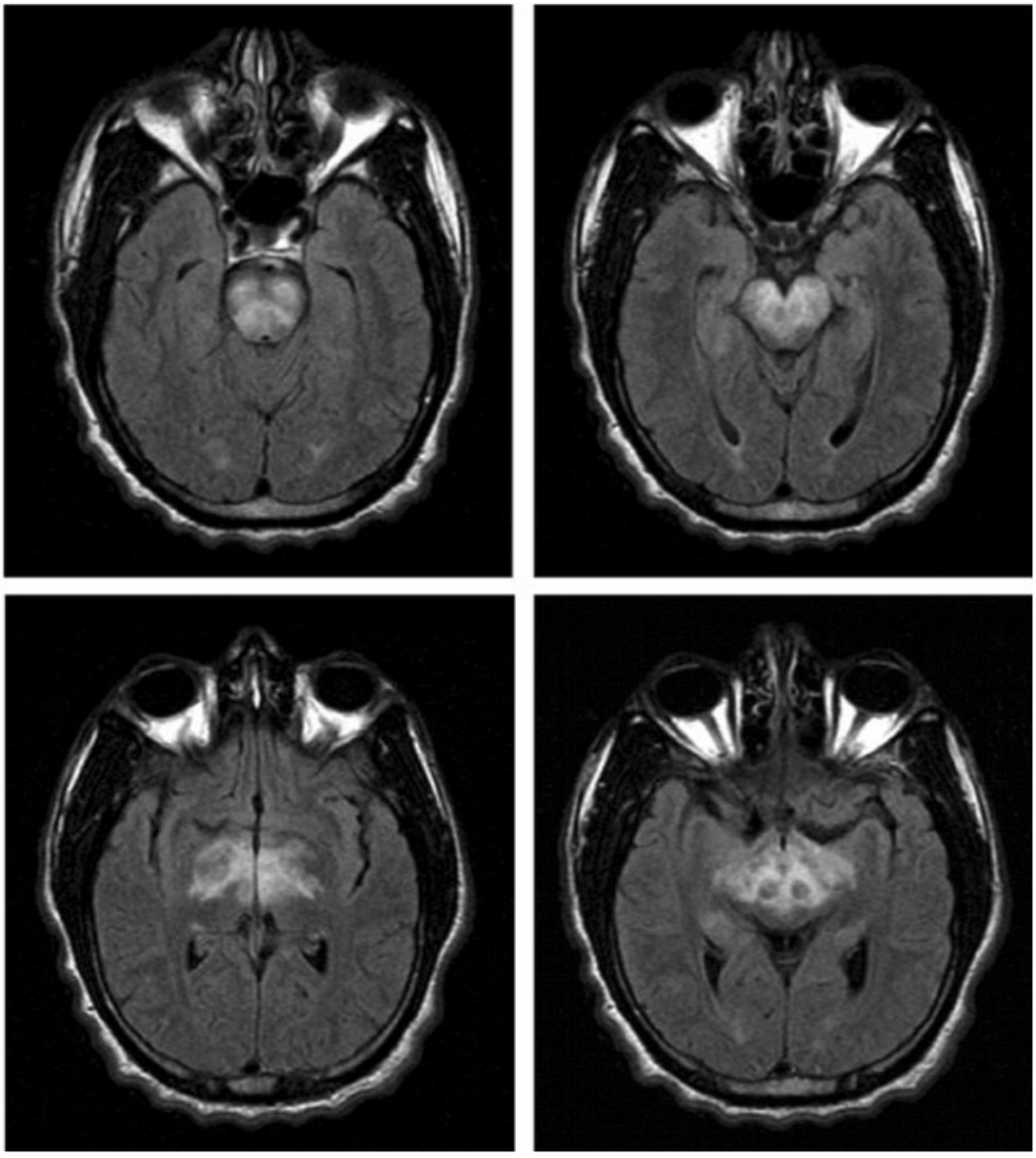

Figure 1 (above): This MRI brain scan shows hyperintensities in the brainstem, as witnessed by the areas with increased brightness.

In addition to an MRI brain scan, a lumbar puncture was also performed. Analysis of the CSF profile showed a white blood count of 20, high protein count of 86, and a high angiotensin converting enzyme (ACE) level. The rest of the cell count was normal. Several serological and CSF analyses were done, and the results are listed in the tables below.

Table 1

Aspergillus Antibody	Latest Ref Range: <1:8	<1:8
Blastomyces Antibody	Latest Ref Range: <=0.9 IV	0.0
Coccidioides Antibody	Latest Ref Range: <1:2	<1:2
CMV Antibody, IgM	Latest Ref Range: <=29.9 AU/mL	<8.0
Histoplasma Mycelia Antibody	Latest Ref Range: <1:8	<1:8
Histoplasma Yeast Antibody	Latest Ref Range: <1:8	<1:8

Table 2

	Ref. Range	
TB GOLD	Unknown	NEGATIVE
Mitogen-NIL	Latest Units: IU/mL	>10.00
TB1 Minus NIL	Latest Ref Range: 0.00 - 0.34 IU/mL	0.00
TB2 Minus NIL	Latest Ref Range: 0.00 - 0.34 IU/mL	0.01
NIL	Latest Units: IU/mL	0.02
(1,3)-beta-D-glucan	Latest Units: pg/mL	<31
(1,3)-beta-d-glucan interpretation	Latest Ref Range: Negative	Negative

Table 3

	Ref. Range	
Tube Number, CSF	Unknown	4.0
Total Volume, CSF	Latest Units: mL	10.0
Color, CSF	Latest Ref Range: Colorless	Colorless
Clarity, CSF	Latest Ref Range: Clear	Clear
RBC, CSF	Latest Ref Range: <=0 /uL	6 (H)
WBC, CSF	Latest Ref Range: 0 - 5 /uL	2 (C)
Lymphocyte, CSF	Latest Ref Range: 28 - 96 %	90
Monocyte, CSF	Latest Ref Range: 15 - 45 %	10 (L)
Protein, CSF	Latest Ref Range: 15.0 - 40.0 mg/dL	82.2 (H)
Glucose, CSF	Latest Ref Range: 40 - 70 mg/dL	61
ACE, CSF	Latest Ref Range: 0.0 - 2.5 U/L	**3.2 (H)**
B. burgdorferi (Lyme) Ab, tot, CSF	Latest Ref Range: <=0.99 LIV	0.17
IgG, CSF	Latest Ref Range: 0.48 - 5.86 mg/dL	8.69 (H)
Albumin, CSF	Latest Ref Range: 13.80 - 24.60 mg/dL	47.40 (H)
IgG, serum	Latest Ref Range: 751 - 1,560 mg/dL	794

IgG Index, CSF	Latest Ref Range: 0.28 - 0.66 ratio	0.83 (H)
IgG Synthesis, CSF	Latest Ref Range: 0.0 - 8.0 mg/d	17.5 (H)
Albumin Index	Latest Ref Range: 0.0 - 9.0 ratio	13.2 (H)
IgG/Albumin Ratio, CSF	Latest Ref Range: 0.09 - 0.25 ratio	0.18
Albumin, serum (IgG Synthesis)	Latest Ref Range: 3,660 - 5,100 mg/dL	3,580 (L)

Table 4

	Ref. Range	
TSH	Latest Ref Range: 0.500 - 8.900 uIU/mL	3.053
Vitamin B1, whole blood	Latest Ref Range: 70 - 180 nmol/L	76
Vitamin B12	Latest Ref Range: 213 - 816 pg/mL	352
Angiotensin Converting Enzyme	Latest Ref Range: 9 - 67 U/L	<5 (L)

The following results confirmed that the patient was suffering from BBE. In order to treat the this condition, the patient was given five cycles of plasma exchange and after the third dose, she started to improve in regards to eye movement. Her speech also improved and she was able to speak more clearly. By day 8 of her admission into the hospital, the patient was able to begin ambulating with a cane. She is expected to make a full recovery within two years.

Discussion

Bickerstaff's Brainstem Encephalitis (BBE) is an autoimmune disorder that causes inflammation of the central nervous system, specifically the brainstem. The central nervous system is responsible for communicating signals between the brain and the spinal cord, and thus disorders that affect this part of the neural network have the potential to affect all other parts of the body, including the peripheral and autonomic nervous systems. Because BBE affects the brain stem, which is responsible for basic functions such as breathing, blood pressure regulation, heart rate, and swallowing, many patients end up paralysed and on life support (Tyrakowska et al, 2016).

Unlike Guillain-Barré Syndrome (GBS), symptoms of BBE are not acute-onset. Thus, BBE progresses slowly. As a result, it is difficult for physicians to diagnose this condition, for there are many differential diagnoses such as Wernicke's Encephalopathy, Bell's Palsy, and diplopia. Nonetheless, the symptoms of BBE are quite similar to Guillain-Barré Syndrome: patients are characterized with acute ophthalmoplegia, ataxia, and altered sensorium (Shahrizaila et al, 2010). The biggest difference between the two conditions is that unlike GBS, patients with BBE experience disturbances in their consciousness.

BBE can impact virtually anyone regardless of age, gender, race, or family history, and it occurs most often after an antecedent infection or surgery. Culprit pathogens include viruses such as *Epstein-Barr* (mono virus), cytomegalovirus, and bacteria such as *Campylobacter Jejuni,* which cause a diarrheal disease. The flu vaccination has also been reported to cause this condition (Mazidi et al, 2013).

Although there is no exact explanation for why the antibodies begin attacking the nervous system, many medical professionals have generally developed a consensus around the Molecular Mimicry Theory and the Innocent Bystander Theory. The Molecular Mimicry Theory explains how viruses tend to have epitopes that are similar to and react with the host proteins; this can lead to the production of monoclonal, or asexually cloned, antibodies that react with these same proteins in uninfected cells (Fujinami et al, 2006). In terms of BBE, an infection can lead to the production of one antibody that attacks uninfected neurons with this certain protein, and as B-cells create antibodies, more of the faulty antibodies are manufactured. In the Innocent Bystander Theory, it is believed that viral infections cause antigen-presenting cells (APC) to

become activated. Antigen-presenting cells present antigen material on the surface of cell so that the T-cell knows to destroy that specific infected cell. In the case of BBE, the APC is presented on uninfected cells, and thus healthy neurons are destroyed.

The Anti-QG1b antibody is known to play a significant role in the development of BBE. This antibody works with the peripheral nerve ganglioside (GQ1b). Gangliosides are a group of complex lipids that are present in the gray matter of the brain (Odaka et al, 2011), and they can be found at neuromuscular junctions, sensory nerves, and cranial nerves. As a result, when the anti-GQ1b antibody binds to such sites, problems in consciousness, sensory performance, and motor control can arise. Nonetheless, the anti-GQ1b antibody is not expressed in the central nervous system, so most of the problems that arise from this antibody affect only the peripheral nervous system.

In order to test for the presence of the Anti-GQ1b antibody, electrophoresis can be used. Electrophoresis separates proteins by size, and when a certain fragment matches the measurement of an anti-GQ1b antibody, it can be concluded that the patient has this antibody. In addition to electrophoresis, there are multiple other methods that can be used to test for BBE.

A lumbar puncture can be done to evaluate protein and white blood cell count. The lumbar puncture is done by inserting a needle into the L3 or L4 lumbar spine interspace and collecting cerebrospinal fluid. The fluid is then analyzed for cell count and protein. In BBE, the white cell count is normal but the protein count is significantly elevated, leading to a term called cyto albumino dissociation (Soliven, 2008). However, before making a solid conclusion, it is prudent to check for other inflammatory syndromes such as HIV, Sjogrens, Lyme disease, Sarcoidosis, and Lupus.

MRI scans can also indicate whether a patient has BBE. T2 hyperintensities are often indicative of this condition.

Treating BBE is very similar to treating other anti-GQ1b antibody syndromes, such as GBS. Overall, there are two main treatments for this syndrome: plasmapheresis (PE) and intravenous immunoglobulin therapy (IVIg). Both of these treatments are quite effective as long as they are started within two weeks of the onset of the symptoms. During plasmapheresis, a process that is quite similar to dialysis, blood is filtered in order to remove the harmful antibodies. In immunoglobulin therapy (IVIg), injections of immunoglobulins, a natural protein that attacks infections, is given to patients. This treatment essentially dilutes the number of harmful antibodies with healthy antibodies, so the probability of the autoimmune mechanism occurring is much lower (Jolles et al, 2005). When steroids are given in conjunction with IVIg, recovery can be hastened.

In addition to acute care, rehabilitative care is also beneficial to patients who have lost their ability to move and perform daily activities. Through physical therapy, muscle contracture can be avoided and patients can regain full control of their bodies.

BBE is a fairly rare type of inflammation, and because of this, there is minimal information about this condition. In order to learn more about BBE, more research and clinical trials must be conducted.

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