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An Unusual Presentation of Bickerstaff Brainstem Encephalitis

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ABSTRACT

Bickerstaff brainstem encephalitis (BBE) is diagnosed by progressive, relatively symmetrical ophthalmoplegia, ataxia, disturbance of consciousness and/or hyperreflexia. Positive anti-GQ1b are found in 66% and abnormal brain MRI in 30% of patients. The classical triad seen in Fisher syndrome is ataxia, ophthalmoplegia and areflexia. If there is associated alteration in the level of consciousness and/or hyperreflexia, a diagnosis of Bickerstaff encephalitis is made due to possible involvement of the central nervous system. Here we report a case of BBE presenting with hyperreflexia without drowsiness as a sign of CNS involvement.

Keywords: Bickerstaff brainstem encephalitis, ophthalmoplegia, GQ1b

Bickerstaff brainstem encephalitis (BBE) is diagnosed by progressive, relatively symmetrical ophthalmoplegia, ataxia, disturbance of consciousness and/or hyperreflexia. Positive anti-GQ1b are found in 66% and abnormal brain magnetic resonance imaging (MRI) in 30% of patients. The classical triad seen in Fisher syndrome is ataxia, ophthalmoplegia and areflexia. If there is associated alteration in the level of consciousness and/or hyperreflexia, a diagnosis of Bickerstaff encephalitis is made due to possible involvement of the central nervous system (CNS). A Japanese survey estimated the annual incidence of Bickerstaff encephalitis as 0.078/1,00,000. The majority of case reports of Bickerstaff encephalitis have described the typical features of confusion or drowsiness as a sign of CNS involvement. However, this is the case report of a patient with BBE presenting with hyperreflexia without drowsiness as a sign of CNS involvement.

CASE REPORT

A 22-year-old male patient presented with history of headache and fever 7 days before admission. Fever recovered in next 2 days and was followed by acute onset double vision. Double vision was present in all the directions. Attendants noticed history of diminished movement of both eyeballs in all the directions. There was history of difficulty in walking in the form of swaying to either direction. There was no history of altered sensorium, drooping of eyelids, facial numbness or weakness, swallowing difficulty, sensory symptoms or weakness.

On examination, patient was conscious, oriented, speech was normal, pupils bilateral dilated and nonreactive with restricted extraocular movements in all directions. Other cranial nerves were normal. Motor system - bulk, tone, power - normal, deep tendon reflexes (DTR) were brisk, plantar extensor bilaterally; sensory system - normal, ataxia on tandem gait, extrapyramidal and peripheral nerves were normal, no signs of meningeal irritation, no involuntary movements. In view of acute-onset progressive bilateral complete ophthalmoplegia with pupillary involvement, brisk DTR in all 4 limbs, and ataxia on tandem walking, possibilities of Bickerstaff encephalitis, atypical Miller-Fisher and botulism were considered. MRI brain was normal and nerve conduction studies (NCS) in all limbs were normal. Botulism was unlikely due to absence of gastrointestinal (GI) symptoms and bulbar affection and no increment on repetitive nerve stimulation test (RNST) >20 Hz. Cerebrospinal fluid (CSF) showed albuminocytological dissociation with raised proteins. CSF GQ1b was; however, negative in our patient. As NCS was normal, atypical Miller-Fisher syndrome (MFS) was unlikely. Diagnosis of Bickerstaff was satisfied in view of ataxia,

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ophthalmoplegia and hyperreflexia. Patient was given injection IVIG 0.4 mg/kg for 5 days and showed complete recovery at 1 month follow-up.

DISCUSSION

Bickerstaff encephalitis was described initially by Edwin Bickerstaff in 1950s with clinical features of ophthalmoplegia, ataxia and drowsiness, preceded by infection. Similarities with MFS and Guillain-Barré syndrome (GBS) include areflexia, ophthalmoplegia and a raised protein in the CSF. This shows a shared etiology of the common association with antecedent infection. Odaka et al proposed clinical diagnostic criteria for the purpose of distinguishing BBE and MFS. Bickerstaff encephalitis is diagnosed as ophthalmoplegia and ataxia with disturbed consciousness and/or pyramidal signs. MFS is diagnosed as acute ophthalmoplegia and ataxia with areflexia or hyporeflexia. Our patient presented with complaints of ataxia, ophthalmoplegia with pyramidal signs but without altered sensorium.

CNS manifestations include drowsiness (45%), stupor, semi-coma or coma (29%), hyperreflexia (34%), Babinski's sign (40%) and deep sensory impairment (16%). Other common neurological features included ptosis, mydriasis, facial weakness, bulbar palsy and nystagmus. In our patient, mydriasis was present. Patients with GBS, MFS and BBE contain antibodies against gangliosides in there serum. Anti-GQ1b antibodies are present in 60-70% of BBE and 83-100% of MFS patients. GBS is associated with anti-GM1 antibodies except in 8%, where it is associated with anti-GQ1b positive.

The GQ1b antigen is highly expressed in the oculomotor, trochlear and abducens nerves, muscle spindles in the limbs and reticular formation in the brainstem. Infection by microorganism having GQ1b epitope may induce production of immunoglobulin G (IgG) anti-GQ1b antibodies in susceptible patients. The binding of anti-GQ1b antibodies to GQ1b antigens expressed on the cranial nerves and muscle spindles induces Fisher syndrome. Whereas, sometimes, the anti-GQ1b antibodies may also enter the brainstem and bind to GQ1b, inducing BBE. A continuous spectrum exists between these conditions, presenting with variable CNS and peripheral nervous system (PNS) involvement. Our patient was anti-GQ1b negative with preserved reflexes, which is predictable in light of the above evidence.

Bickerstaff encephalitis is usually associated with antecedent pathogens like herpes simplex virus, cytomegalovirus, Epstein-Barr virus, varicella-zoster virus, measles virus, *Salmonella typhi*, *Mycoplasma pneumoniae* and *Campylobacter jejuni* enteritis, substantiating evidence that antiganglioside antibodies work through molecular mimicry with infectious agents.

In MFS patients, ataxia improves by 3-41 days after onset, at a median of 32 days and ophthalmoplegia (between 3 and 46 days) at a median of 88 days. In Bickerstaff encephalitis, most patients achieve complete remission by 6 months.

The majority of cases are self-limiting. A definitive treatment for BBE is yet to be found. The established treatment is the same as that used in GBS: IVIg and plasmapheresis, although more clinical trials are required to determine its effectiveness.

CONCLUSION

Bickerstaff encephalitis can be diagnosed clinically with the triad of ataxia, complete ophthalmoplegia and pyramidal signs of hyperreflexia without evidence of impaired consciousness.

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