Case Report

Bickerstaff's brainstem encephalitis (BBE)

Mohamed NA Idris, MD*, Maha A Zibair, MD*, Samira M Mirgani, MD**, Eedetal A Ibrahim, MD**, Rasha M Rida, MD**, Mohamed K Saeed, MD**, Moaz A Abdulatif, MD**, Hassab Al-Rasoul S Ali, MRCP*

Faculty of Medicine, University of Khartoum, Sudan*, Shaab Teaching Hospital, Khartoum, Sudan**

Abstract

Bickerstaff’s brainstem encephalitis is a rare disease. It has been documented to be associated with or follow various infections. However, association with malaria hasn’t been reported before. Our patient was 26-year-old Sudanese lady, had acute falciparum malaria based on positive blood film, clearance of fever in response to artesunate injection. However, one week later, she presented with multiple cranial nerve palsies, quadriplegia with extensor plantar responses. MRI brain showed T1 hypointense, T2 hyperintense signals in the medulla and pons. Routine investigations and screening for infections, vasculitis, SLE, HIV was negative. CSF analysis was normal with negative PCR for herpes simplex and tuberculosis. In response to IV methylprednisolone, she steadily had improved to go back to work; serial brain MRI scans showed complete resolution of the lesions. Our final diagnosis was Bickerstaff brainstem encephalitis following malaria.

Keywords: Bickerstaff’s brainstem encephalitis, malaria, corticosteroids, Sudan

Introduction

In 1951, Bickerstaff and Cloake described three cases of ophthalmoplegia under the title of “mesencephalitis and rhomboencephalitis” and suggested that the clinical features were due to a midbrain disturbance(4).

Five years later, Miller Fisher published his famous paper on a syndrome of ophthalmoplegia, ataxia, and areflexia(2) and suggested that this syndrome was an unusual variant of Guillain-Barré syndrome. The following year, Bickerstaff published an article entitled “further observations on a grave syndrome with benign prognosis” which he continued to regard as a form of encephalitis.

A subsequent publication from a group including Bickerstaff came down strongly on the side of encephalitis in a paper that described 18 patients with the syndrome(4).
The authors reported low density changes in the brain stem on CT of a 69 years old woman. She subsequently died from the disease and at postmortem her midbrain showed foci of microglia, astrocytic proliferation, and cuffing of vessels. Cases with abnormal CT and MR imaging within the brain stem have been reported \(^{(5,6,7)}\).

Bickerstaff's brainstem encephalitis (BBE) is a very rare disease of the central nervous system disease. Its exact cause remains unknown, but it is postulated that BBE has an autoimmunologic origin. Very often it follows preceding illness and an association with certain infections, including cytomegalovirus, campylobacter jejuni, typhoid fever and mycoplasma pneumoniae, has been documented \(^{(8,9,10)}\).

BBE is characterized by acute ophthalmoplegia, ataxia, pyramidal paresis and disturbance of consciousness. Lesions are located mainly in the brainstem and hence the presentation is related to brainstem dysfunction.

In this short communication we describe the clinical course and MRI changes in one patient presented to the National Center for Neurological Sciences, Khartoum, Sudan. To the best of our knowledge this is the first report with this kind of condition from Sudan.

**Case history**

A 26-year-old lady presented with one week history of progressive neurological disorder shortly following a febrile illness which was thought to be malaria. The blood film was positive for falciparum malaria; however this does not exclude co-infection with other bacteria, mycoplasma or viruses. The febrile illness was treated with artesunate injections and the fever subsided, but the neurological condition deteriorated. Follow-up blood film for malaria was negative. She became progressively fatigued, less ambulant and rather confused, so she was referred to the Neurology Department at Al-Shaab Teaching Hospital in Khartoum, the capital of Sudan.

On presentation, physical examination revealed the following: An ill looking lady with pulse rate of 86 beats per minute, blood pressure of 110/70 mm of Hg and normal body temperature. Chest, cardiovascular and abdominal examination was unremarkable. Neurological examination showed a Glasgow coma scale (GCS) of 8 out of 15. Cranial nerve examination showed weakness of left 5\(^{th}\) and 6\(^{th}\), bilateral 3\(^{rd}\), 4\(^{th}\), 7\(^{th}\), 9\(^{th}\), 10\(^{th}\), 11\(^{th}\) and 12\(^{th}\) nerve palsies. There was no evidence of meningeal irritation. Examination of the motor system showed quadriplegia with grade 0-1 power, deep tendon hyporeflexia and bilaterally extensor plantar responses. Sensory examination showed minimal impairment of pin prick on the whole left side of the body including the face. The right side sensation was normal except for minimal impairment of pin prick on the face. Posterior column sensations were intact on both sides of the body.

**Investigations**

Investigations showed haemoglobin of 13 grams/dl, WBC 46,000/ cu mm, ESR 15 mm in first hour, blood sugar 110 mg/dl, urea 40 mg/dl, Na 136 mEq/l, K 3.6 mEq/l, calcium 8.5 mEq/l. MRI of the brain (Fig 1) revealed expansion of the medulla oblongata and pons with hypointense signal abnormality on T1 and hyperintense on T2 and FLAIR sequences. These changes were confined to the brain stem and left cerebellar lobe. The lesions were minimally enhancing. Such abnormalities could be found in many diseases including multiple sclerosis, Behcet's disease, lyme disease, progressive multifocal leukoencephalopathy, sarcoidosis, Whipple's disease, listeria rhombencephalitis, vasculitis due to systemic lupus erythematosus (SLE), and acute disseminated encephalomyelitis \(^{(11)}\).

Various investigations for the above mentioned differential diagnoses were done and were unremarkable. They included ANA, Anti ds DNA, cANCA, pANCA, Rheumatoid factor and HIV tests.
CSF analysis showed a normal tension, a protein of 50 mg/dl and no cells on CSF smear. CSF gram staining, PCR for herpes simplex and tuberculosis were negative. CSF culture was not done.

Management and progress:
The diagnosis of BBE was made and the patient was started with high dose IV methyl prednisolone, one gram daily for 5 days followed by a taper of oral prednisolone. Within the first 2 weeks, she showed progressive improvement and she could manage to talk, swallow and walk within 3 months of treatment. By 5 months, she was back to work as a lawyer. Serial MRI scans were done and all showed progressive resolution of the lesion. MRI scan of the brain after 5 months of treatment was back to normal (Fig 2).
Discussion
The diagnosis of BBE is by exclusion and high index of clinical suspicion. One review of 62 patients found positive serum anti-GQ1b IgG antibody in 66%, and brain abnormality on MRI scan in 30% of patients(1). The presence of anti-GQ1b antibodies and an abnormal brain MRI can help to support its diagnosis but absence of anti-GQ1b antibodies and a normal MRI do not exclude the diagnosis, which remains based on clinical criteria and exclusion of other etiologies. The presence of a positive blood film for malaria in this patient may raise the possibility of malaria as an antecedent infection. However, this might be just an incidental association. Other bacterial infections were excluded by CSF examination, disappearance of fever following antimalarial treatment and the dramatic response to corticosteroids. To the best of our knowledge the possible association with malaria has not been reported before.

In our patient, the presence of extensor plantar response in spite of the hypotonia and hyporeflexia indicated that the weakness is caused by the brainstem lesion rather than polyradiculoneuropathy. The presence of cranial neuropathy, disturbed state of consciousness, and the dramatic MRI signal abnormalities in the brainstem indicated a diagnosis of BBE. Various treatment modalities have been used for treatment of BBE, including corticosteroids, intravenous immunoglobulin, and plasmapheresis. Our patient was treated with high dose methyl prednisolone for five days followed by a taper of oral prednisolone and she showed dramatic response without residual physical deficits or MRI abnormalities. Although the condition is very rare the favorable response to medical treatment warrant early diagnosis and prompt treatment.

References


