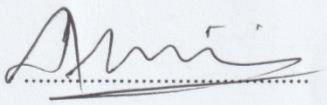
Case report 03

Title	: A young girl has gone to a deep sleep – A case of Bickerstaff Encephalitis due to EBV virus infection
Name of the patient	: Miss Emalsi Sandeepani
Age of the patient	: 15 year
BHT number	: 194070
Ward number	: ward 17
Name of the Hospital	: Teaching Hospital Karapitiya
Date of Admission	: 21 December 2019
Date of Discharge	: 28 January 2020

Supervising consultant



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A young girl has gone to a deep sleep – A case of *Bickerstaff Encephalitis due to EBV virus infection*

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Abstract

Bickerstaff encephalitis (BSE) is a rare neurological condition first described in middle of the 20th century. It is characterized by encephalopathy, hyperreflexia, ophthalmoplegia and ataxia. It is a disease in a spectrum of guillain – barre syndrome and miller fisher syndrome. Viral infections play a major role in its pathogenesis. In Sri Lanka, BSE is not reported frequently may be due to lack of resources to confirm the diagnosis. Here we are presenting a case of bickerstaff encephalitis presented with ataxia opthalmoplegia and drowsiness with evidence of past Epstein bar viral infection.

Introduction

Bickerstaff and Cloake reported three cases of Bickerstaff encephalitis for the first time. All three cases were characterized with drowsiness opthalmoplegia and ataxia. It is an extremely rare disease with the incidence of 0.000078% [1] .BSE is often associated with anti GQ1B IgG antibody in serum and CSF[2]. Pathogenesis is immunological act via molecular mimicry[3] with antecedent pathogens include HSV, EBV, CMV, VZV, measles virus and bacteria like Salmonella typhus, mycoplasma pneumonia and *Campylobacter jejuni*[4]. Majority of cases are spontaneously resolving while some needs intravenous immunoglobulin and total plasma exchange.

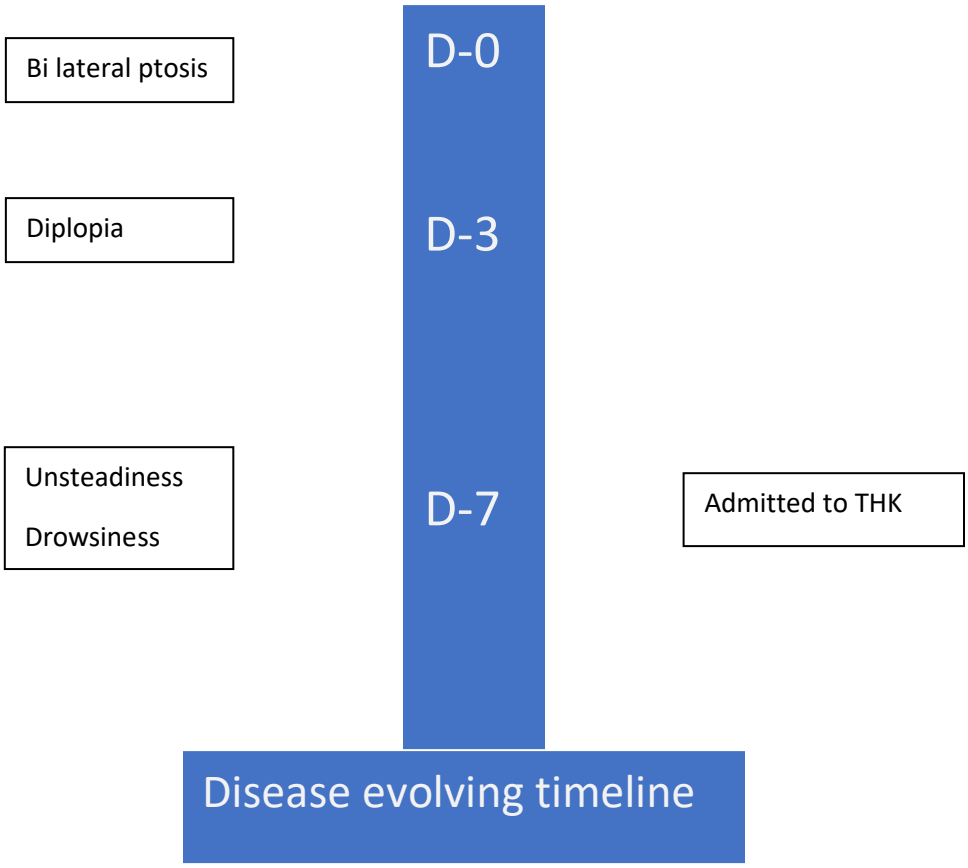
Case report

A fifteen-year-old schooling girl presented to us with drooping of eyelids, double vision and unsteadiness evolving over one-week duration. She was apparently well one week prior to this admission. Then she developed drooping of bilateral upper eyelids and which was progressive. However, there was no fatigability. She developed double vision towards left side since the 3rd day of illness. It was progressed to unsteadiness and excessive sleepiness on the seventh day .The symptoms were more pronounce in the evening. Her speech was nasal and complained of difficulty in swallowing as well.

She did not have fever, headache, photophobia or phonophobia. There was no bladder-bowel incontinence, retention, paresthesia or hyperesthesia. She did not have a recent history of diarrhea, urinary tract or respiratory tract illness. She did not give a history of difficulty in breathing or limbs weakness initially but later

she experienced inadequate respiratory effort. She did not have a consumption of fresh honey, honey based products or canned foods. She was not on any western or herbal medications. There was no history of snakebite, animal bites (stray dog or other potential rabies), and exposure to poisons, toxins or chemicals. There was no inflammatory type arthritis, oral ulcers, skin rashes, muco-cutaneous type of bleeding or photosensitivity rashes.

She has immunized according to EPI schedule and last vaccination given in 2017. She is the only child in her family and had good performances in academic and extra-curricular activities without recent deterioration.



Clinical findings

Her BMI was 20 Kg/m^2. On examination, she was oriented and not febrile, but she was drowsy. Rest of the general examination was unremarkable. Nervous system examination revealed normal fundi with intact direct and consensual light reflexes. Moreover, she had bilateral symmetrical partial ptosis with fatigability and bilateral adductor palsy, superior and inferior gaze palsy. Her palates showed bilateral reduce movements with normal upper and lower limb neurology with equivocal planter responses. There was no objective evidence of sensory impairment, cerebella signs except unsteady gait.

On air oxygen, saturation was 97% and single breath count was thirty-five per minute. Her cardiovascular and abdominal examination was normal.

Diagnostic assessment

Depending of the initial clinical findings, we considered several differentials. Generalized myasthenia gravis, Miller-fisher variant of GBS, brain stem encephalitis (viral, bacterial, autoimmune etc.), evolving demyelinating disease like multiple sclerosis were higher up in the list. In addition, we considered para-neoplastic Lambert eaten myasthenic syndrome, botulism, diphtheria, unrevealed krait bite in the bottom of the list.

Her arterial blood gas was normal. Serum electrolytes were normal including serum sodium, potassium, calcium and magnesium. Her Full blood count reveled WBC 5.64 x 10^9/L normal differential count. Hemoglobin concentration and platelets count were 12.6 g/dL and 247 x 10^9/dL respectively. Blood picture was normal. Her erythrocyte sedimentation was 110 mm in 1st hour while C reactive protein was normal. Her liver profile and renal profile were unremarkable. Her creatine phosphokinase 42 U/L (0 – 145) and acetylcholine receptor antibody level was 0.34 nmol/L (Ref; < 0.45). “Anti GQ1b antibody” assay was not performed due to financial constraints. Peripheral nerve conduction study(NCS) (both sensory and motor) were normal except F-wave abnormality noted in peroneal, R/S median and R/S ulnar, that could be due to early GBS. However, there were no definite evidences of Guillain Bare Syndrome (GBS). Furthermore, peripheral nerve-conduction-study findings could be normal in Millar Fissure variant of GBS (MF-GBS). Repetitive nerve conduction study was normal. ANA was negative. Cerebro-spinal fluid (CSF) Protein was 93 mg/dL while normal glucose and cell count fourth day of illness. CSF culture for TB PCR, HSV-1, HSV-2, and VZV and enterovirus infection did not show evidences of particular infection. CSF for NMDA receptor antibody was negative. CSF analysis for oligoclonal band was negative. CMV IgM was negative. EBV IgM was positive. EEG showed epileptiform as well as non-epileptiform abnormalities (more prominent in Right), Burst of sharp wave discharges, Sharp contoured slowing, intermittent delta and theta range slowing. In conclusion, The EEG features could be due to focal encephalitis R>L or structural pathology. Seizure could have origin secondary to encephalopathic process or independent seizure foci. MRI brain showed mild swelling of mid brain and pons with T2 and FLAIR hyper intensities. There are two tiny hyper intense foci in relation to L/S internal capsule in T2/FLAIR images. Features are in favor of brain stem encephalitis involving mid brain and pons. Even though, Anti GQ1b antibody assay was not available, clinical and investigational evidences led to more favored diagnosis of bickerstaff encephalitis.

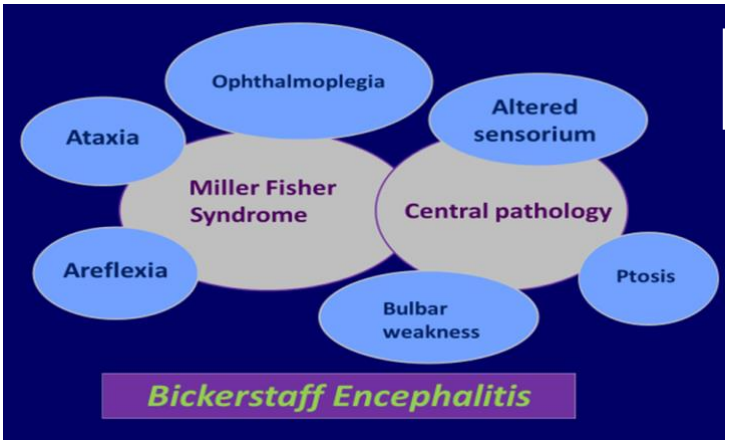


Fig 1
Evaluation of clinical symptoms

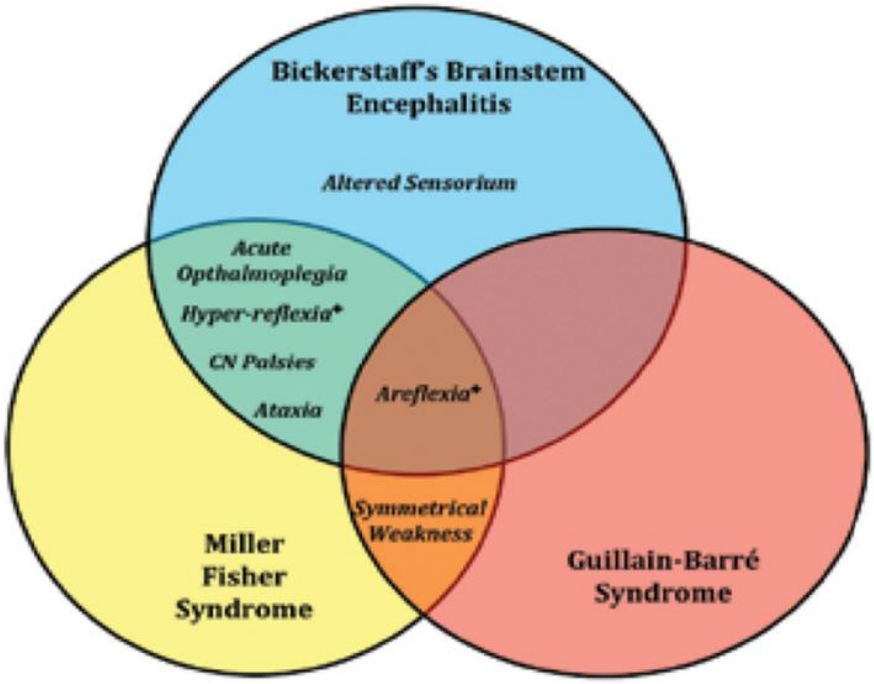


Fig 2 Comparison between Guillain- barre syndrome, Miller Fisher syndrome and Bickerstaff's brainstem encephalitis

Management

Initial supportive care started with close monitoring of vitals and vital capacity. She was not improved and ICU care with ventilator support commenced on 3rd day. IVIG (0.4mg/Kg/day) commenced and continued for 5 days but there was no expected recovery. We came to diagnosis of Bickerstaff Encephalitis with MRI findings. Intravenous methylprednisolone 1g daily for 3 days started and she had a dramatic improvement. After five days methylprednisolone switched to oral prednisolone 1mg/kg and tailed off gradually. At the same time

other supportive measures were planned such as DVT prophylaxis, physiotherapy, prevention of aspiration, nutrition etc.

Follow-up visits were arranged

Discussion

Bickerstaff Encephalitis is a rare encephalitis .it is common in Japan mainly in summer months[11]. Bickerstaff and Cloake first reported BSE in mid of twentieth century. They described it with spectrum of clinical sings, preceded infection and protein-cytological dissociation in cerebral spinal fluid[6].

BSE is an anti GQ1b associated syndrome. Half of anti GQ1b associated syndrome preceded by infection. Most common is upper respiratory tract infection[7] including H.Influenza[8]. AntiGQ1b antibodies interact with gangliosides of peripheral nerves[9] and damage integrity of blood brain barrier[10].

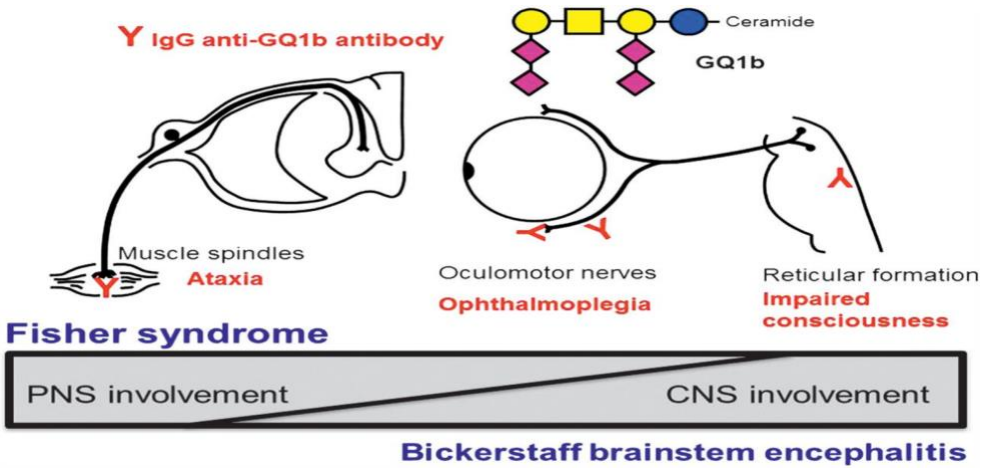


Fig. 3: Action of anti-GQ1b antibody on target sites in MFS and BSE

BSE presents with ataxia, opthalmoplegia, and clouded sensorium[5].however, absence of one does not exclude the BSE. BSE can be differentiated from other Anti GQ1b associated syndrome by presence of clouded sensorium. It can be associated with either exaggerated or diminished reflexes.

BSE should diagnose on clinical suspicion and presence of anti GQ1b antibodies (BSE-70 %. MFS-83–100 %, GBS- 8%).However, a one third of BSE does not associate with anti GQ1b antibodies[10].EEG shows slow wave activities. MRI showed mild swelling of mid brain and pons and two tiny hyper intense foci in relation to L/S internal capsule in T2/FLAIR studies which were in favour of brain stem encephalitis involving mid brain and pons.

Some clinicians believe BSE as a disease of one clinical spectrum of Guillain-barre syndrome (GBS) and Miller Fisher Syndrome (MFS). However, GBS and MFS are main differentials for BSE. Wernicke's encephalopathy, multiple sclerosis, brain stem tumors or vascular pathologies and botulism toxicity can be considered as differential diagnoses[12].

Spontaneous recovery is a frequently seen. Most of the patients achieve normal function in six months[5]. Due to low prevalence and spontaneous recovery, treatment consensuses are not adequately evaluated. However, steroids, plasmapheresis and intravenous immunoglobulin consider as effective treatment options[5]. Resistance cases can be treated with Rituximab[13].

Conclusion

BSE is a rare disease, which can treat successfully. It is a clinical diagnosis. More understanding about disease, diagnostic criteria and treatment option evaluation are essential for management.

Consent

Informed consent was obtained from the patient for publication of the case report

Acknowledgement

The authors sincerely thank all health care workers who contributed to manage him. Especially thanks for consultant neurologist who gave us very valuable help to manage the patient.

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