CASE REPORT

A Case of Bickerstaff Brainstem Encephalitis and Acute Lymphoblastic Leukaemia

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SUMMARY

Bickerstaff Brainstem Encephalitis (BBE) is a post-infectious immune disorder. It is rare, yet the most severe variant of Guillain-Barre Syndrome (GBS) in terms of initial presentation. Moreover, the coexistence of BBE and Acute Lymphoblastic Leukaemia (ALL) is distinctly uncommon. We report a case of a patient with a background history of Precursor B cell Acute Lymphoblastic Leukaemia (pre B ALL) presented with a mixture of peripheral and central nervous system involvement with cortical, subcortical and cerebellar lesions on brain magnetic resonance imaging (MRI), and was eventually diagnosed with BBE. In this case, we illustrate the complexity in diagnosing BBE, a rare variant of GBS due to atypical presentation.

Keywords: Bickerstaff Brainstem Encephalitis, Guillain-Barre Syndrome, Lymphoblastic Leukaemia

INTRODUCTION

Guillain-Barre Syndrome (GBS) is an acute inflammatory demyelinating polyneuropathy (AIDP), a disorder predominantly affecting the peripheral nervous system. It is also heterogeneous syndrome with several variant forms with distinguishing clinical, pathophysiologic and pathologic features. Bickerstaff brainstem encephalitis (BBE) is one of the variants of GBS. In this case, we highlight the complexity of diagnosing BBE in view of atypical presentation.

CASE REPORT

A 24-year-old man with background history of Precursor B cell Acute Lymphoblastic Leukemia (pre B ALL) achieved remission after completing induction and consolidation chemotherapy one month prior to admission. On the first admission (about five weeks after initiation of consolidation phase chemotherapy), he presented with one-week history of generalised weakness and numbness of the extremities. Clinically, he had power of grade 4/5 for both upper and lower limbs, with generalised areflexia and down-going plantar response bilaterally.

Full blood picture (FBP), bone marrow aspiration and trephine biopsy (BMAT) showed no residual blasts present to suggest a relapse of leukaemia. Nerve conduction study (NCS) revealed mild abnormality with prolonged latencies for left tibial nerve and left common peroneal nerve and marked reduction in amplitude in both common peroneal distal motor nerves.

The first MRI revealed foci of high signal intensities on the T2/FLAIR sequence in the cortex and subcortical white matter of the right frontal and left parietal lobe (Fig. 1). In view of the MRI findings, he was treated as cerebral vasculitis with intravenous methylprednisolone and followed by oral prednisolone. There was significant improvement as he could ambulate. He was discharged well after two weeks of hospitalization.

However, three days after discharge, he was readmitted with a one-day history of progressive weakness of both lower limbs ascending to his upper limbs. This was associated with dysphagia and diplopia. On examination, he was drowsy and his eyes showed conjugate deviation to the right with nystagmus.

Second brain MRI revealed multiple punctate, hyperintense lesions seen on the T2/FLAIR, in the cortical, subcortical and white matter, predominantly over both cerebellum and these cerebellar lesions were not seen in the previous MRI (Figure 2). Electroencephalogram (EEG) showed low amplitude and absent alpha wave, with no epileptic phenomenon seen.

Four days later, his Glasgow Coma Scale (GCS) was deteriorated to 4/15. Nystagmus was present in the left eye with convergent squint on primary gaze. He had generalised hypotonia with power of 2/5 on the left upper limbs and 0/5 on the right upper limb and both lower limbs. He was generally areflexic with absent plantar responses.

Based on his history and clinical findings (progressive symmetrical ascending weakness,

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opthalmoparesis, bulbar involvement, dysautonomia and impaired conscious level he was diagnosed as GBS with BBE. He was immediately intubated and transferred to the intensive care unit. He was started on immunoglobulin and methylprednisolone followed by oral prednisolone. Oral fludrocortisone was commenced for autonomic neuropathy.

Second FBP and BMAT did not demonstrate any excess blast cells to suggest relapse of leukaemia, and BCR ABL fusion gene was undetectable. Lumbar puncture was done and revealed very high protein in the cerebrospinal fluid (CSF); 713 mg/L with no white blood cell count detected (albuminocytologic dissociation). CSF glucose was normal (3.0 mmol/L, random blood glucose 6.9 mmol/L). Other CSF investigations, including culture and sensitivity, Indian ink, cryptococcal and cytology were negative. Second NCS showed generalised sensory and motor axonal with demyelinating component polyneuropathy, in keeping with GBS with AMSAN variant (Acute Motor Sensory Axonal Neuropathy).

Despite treatment, his general condition deteriorated further where he succumbed to his illness on ten days after second hospitalization.

DISCUSSION

The presence of CSF albuminocytological dissociation in our patient (elevated protein content with no white cell count detected in cerebrospinal fluid) which is present in about 75% GBS patients in third week of illness, further support the diagnosis of GBS with BBE[1]. Given the persistent negative results of FBP and BMAT post chemotherapy, leukaemic infiltration was unlikely.

NCS and EEG are valuable not only for confirming the diagnosis of GBS but also for providing some information regarding prognosis. It has been shown that the limb weakness in the BBE cases was considered the result of overlap with the axonal subtypes of GBS[2]. In our patient, the NCS revealed acute motor and sensory axonal neuropathy (AMSAN). EEG recordings in 57% of BBE patients, who were fully conscious, showed diffuse slow activities[2]. Our patient had low amplitude EEG with absent alpha.

A comprehensive review of 62 patients with BBE reported by Odaka et al revealed up to 30% of the patients had brain MRI abnormalities[3]. Hyperintense lesions located mainly in the brainstem, especially in the pons, midbrains and medulla oblongata, as well as cerebellums are described in the literature. This is supported by the findings of definite inflammatory changes in the midbrain in postmortem examinations of BBE patients[3]. The brain MRI of our patient showed multiple hyperintense lesions in cortical and subcortical grey white matter, predominantly in the cerebellum.

Despite the fact of most GBS cases (approximately two-thirds) are reported following an infectious trigger, it also has been shown to have an association with non-infectious trigger such as haematological malignancies[4,5,6]. The occurrence of GBS in patients with ALL is very rare with only a handful of cases reported in literature so far[7,8,9]. The correlation of GBS with hematological malignancies implies the link in between disruption of the immune system by long term chemotherapy and the development of GBS in these patients[4].

The relationship of GBS and paraneoplasm has been demonstrated in the literature. It has been shown that paraneoplastic brainstem encephalitis is correlated with anti-Hu (ANNA-1), anti-Ri (ANNA-2) or anti-Ma antibodies. When associated with anti-Hu antibodies, brainstem encephalitis is often part of encephalomyeloneuritis and usually antedates the diagnosis of the underlying tumour, almost always small cell lung carcinoma[10]. The clinical syndrome of brainstem encephalitis represents the predominant syndrome in 11% of patients with anti-Hu antibodies[10].

CONCLUSION

The clinical presentation of progressive symmetric ascending weakness with areflexia, bulbar involvement, ophthalmoparesis, dysautonomia and impaired conscious level in our patient, supported by the CSF, NCS, EEG and brain MRI findings led to the diagnosis of coexisting AMSAN and BBE. This case also demonstrates the association of GBS and ALL.

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ADDENDUM

The order of authors in an original article title *"**Efficacy of Intra-Articular Steroid Injection in the Management of Primary Frozen Shoulder**" published in Pakistan Journal of Medical & Health Sciences, Lahore on Page No. 717, Issue 3, July-September 2014 issue is as under:*

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The name of M. Saeed Akhtar (2nd author) has been wrongly typed in this article. This typographical error is regretted.