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Case Series

Hemiconvulsion Hemiplegia Syndrome with Iron Deficiency Anemia in Children: A Report of Two Cases with Review of Literature

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Abstract

Hemiconvulsion hemiplegia epilepsy (HHE) syndrome is a rare complication of prolonged focal seizures in children and usually idiopathic but may be associated with structural, infective, traumatic and degenerative diseases. We present two cases with initial presentation as left sided focal status epilepticus, later developing left sided hemiparesis with iron deficiency anemia. This is the first association of iron deficiency with hemiconvulsion-hemiplegia-syndrome illustrating the importance of testing for iron deficiency and neuroimaging in each case of status epilepticus. More importantly, these cases also raise the possibility that deficiency in iron could be a contributing factor in cases of HHE.

Keywords: Hemiconvulsion Hemiplegia Epilepsy (HHE); Febrile Seizure; Status Epilepticus; Iron Deficiency Anemia

Introduction

Hemiconvulsion-Hemiplegia-Epilepsy (HHE) or Hemiconvulsion-Hemiplegia-Syndrome (HHS) is a rare outcome of prolonged focal status epilepticus that usually occurs in children below 4 years of age [1]. This entity starts with a focal status epilepticus and concurrent febrile illness which subsequently evolves to ipsilateral hemiparesis of the convulsing side; on follow-up over months to years, two-third of the patients develop epilepsy. Magnetic resonance imaging (MRI) of the brain in the acute stages characteristically shows gross cerebral edema in the contralateral hemisphere, which later turns into atrophy [2]. At present, the underlying etiology of HHE remains poorly understood. Several etiologies for the initial seizures in HHE syndrome have been proposed and include viral infections, meningitis, subdural effusion, protein S deficiency, cyanocobalamin deficiency, L2 hydroxyglutaric aciduria and SCN1A and CACNA1A mutations [3-6]. Although there is an established association between iron deficiency anemia and febrile seizure and pediatric stroke, there is no such study stating correlation between iron deficiency anemia and HHE. Here we present 2 cases of hemiconvulsion hemiplegia syndrome with iron deficiency anemia.

Case Reports

Case 1

A- 3-yrs male child presented to the emergency with sudden onset left sided clonic convulsions involving both upper and lower limbs followed by loss of consciousness while playing with friends at his home. This episode was preceded by one day of fever.

The status epilepticus was managed with intravenous lorazepam, phenytoin, sodium valproate, levetiracetam and continuous midazolam infusion @ 6µg/kg/minute for 12 hours. The seizures got controlled and the child regained consciousness in 48hours but he was not able to move his left half of body.

On detailed examination, the child was conscious, irritable, lying supine in bed. His vitals were stable. Glasgow Coma Score was 11/15. There was left sided upper motor neuron type of 7th cranial

nerve palsy with left sided hemiplegia. He had neither loss of sensation nor signs of meningeal irritation.

CSF analysis, liver function test, renal function test and PT, aPTT, INR reports were normal. Urine for organic acid screening turned out to be normal. Mutational analysis of genes SCN1A and CACNA1A were also negative. MRI of brain (Figure 1) showed edematous right cerebral cortex, subcortical and deep white matter along with mass effect and dilatation of contralateral lateral ventricle. MR angiography of cerebral vessels was normal (Figure 2).

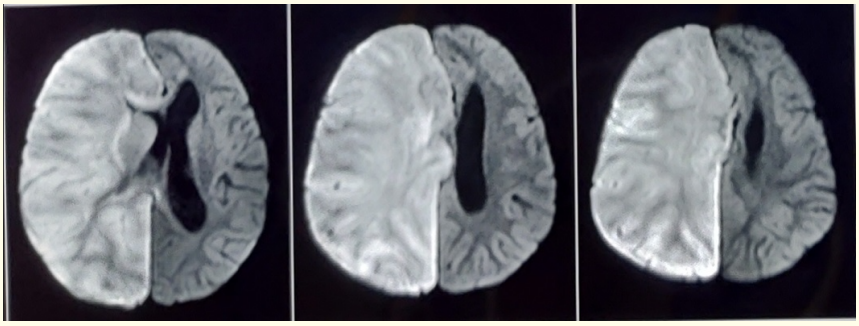

Figure 1: MRI Brain of Case no.1 showing edematous right cerebral cortex, subcortical and deep white matter along with mass effect and dilatation of contralateral lateral ventricle

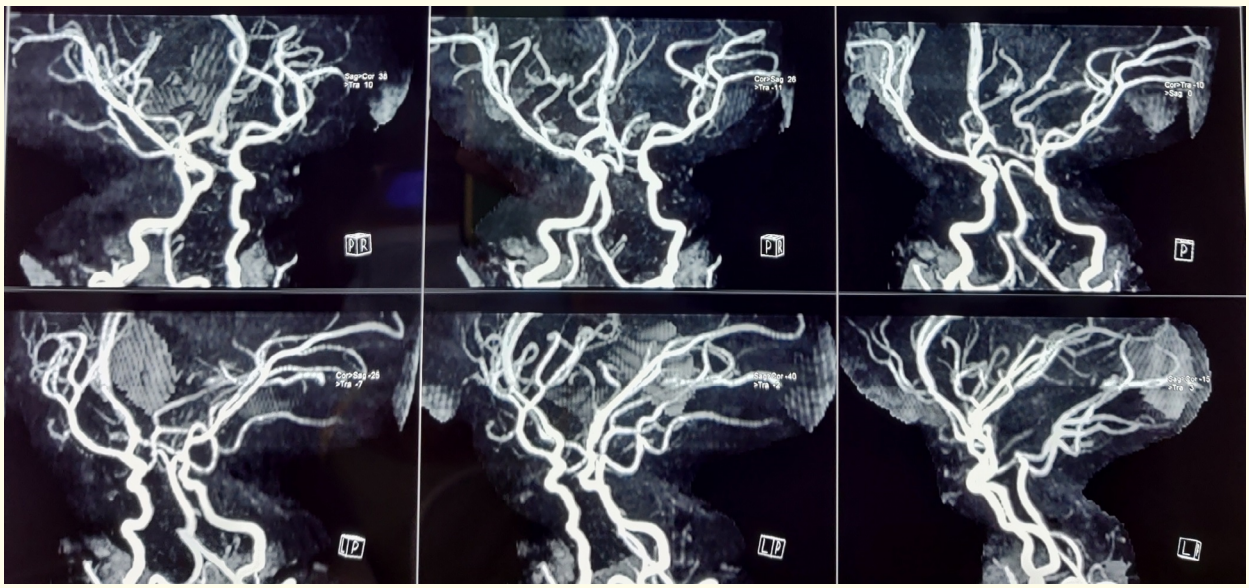

Figure 2: MR angiography no 1 showing no significant abnormality.

We treated the child with acetazolamide (50mg/kg/day), oxcarbazepine (10mg/kg/day) and low-dose aspirin (3-5mg/kg/day). Facial palsy improved gradually by the time of discharge but weakness of the left side of body persisted. The child was discharged after 7 days with a diagnosis of hemiplegia hemiconvulsion syndrome with iron deficiency anemia.

Case 2

A-3-years old male child who presented to us with chief complaints of fever and cough for 2 days and abnormal body movements of left half of body for 4hours. The left sided focal tonic clonic seizure could not be controlled with appropriate doses of lorazepam, phenytoin, levetiracetam and lacosamide. Then the child was intubated and midazolam infusion was started @ 4µg/kg/minute, gradually increasing to 16µg/kg/minute till the seizure subsided. The child regained consciousness after 24hours but developed left sided hemiparesis. There was no evidence of any infection on initial work up. After 3 days of admission, the child was extubated and MRI brain was done.

His MRI of brain (Figure 3) also showed edematous right cerebral cortex, subcortical and deep white matter along with mass effect and dilatation of contralateral lateral ventricle. The child was discharged on oral acetazolamide (50mg/kg/day), oxcarbazepine (10mg/kg/day) and low dose aspirin (3-5mg/kg/day).

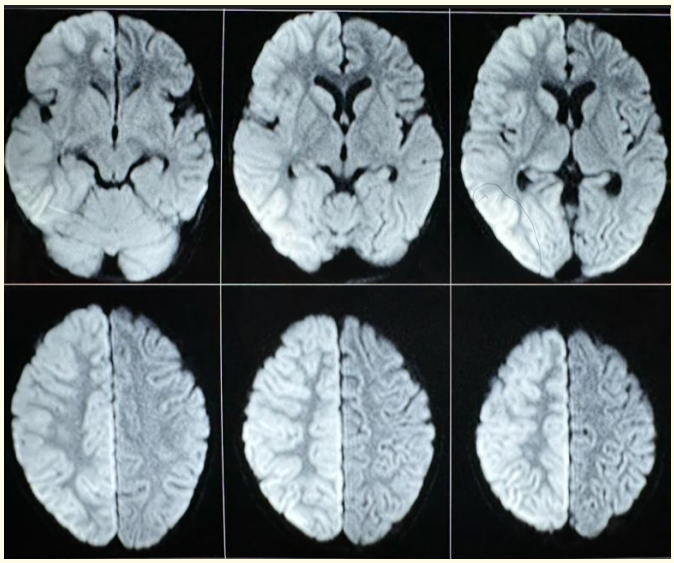

Figure 3: MRI Brain of case no.2 showing edematous right cerebral cortex, subcortical and deep white matter along with mass effect and dilatation of contralateral lateral ventricle.

Both the cases were follwed up for a period of 6 months. At 1 month oral iron @ 3mg/kg/day was added .At 3 and 6 months of follow up hemiparesis was persisting but no further episode of seizures occurred and iron deficiency anemia was corrected gradually.

Discussion

Hemiconvulsion-Hemiplegia/Hemiconvulsion-Hemiplegia-Epilepsy (HH/HHE) syndrome was first reported by Gastaut and colleagues in 1957. Pathophysiology of this syndrome still remains poorly understood and the long-term cognitive outcomes are still unclear [1].

Many literatures have confirmed that iron deficiency has a strong correlation with febrile seizures and pediatric stroke [7,8]. Iron deficiency anemia (IDA) holds a 10-fold increased risk of acute stroke in well toddlers [9]. Studies have reported frequency of iron deficiency in patients with febrile seizures to be around 63% in India [10]. Iron is required for hemoglobin synthesis as well as for enzymes participating in neurochemical reactions. Various hypotheses described about iron deficiency anemia in inducing seizures are decrease of GABA inhibitory neurotransmitter, change in neuron metabolism, reduction of enzymes such as monoamine and aldehyde oxidases and impairment in oxygenation and energy

metabolism of the brain [11]. Studies also revealed that low iron status as well as ferritin concentration may be a significant risk factor for the development of febrile seizures [12].

Although there is no such study stating correlation between iron deficiency anemia and HHE, we propose that along with neuroimaging, routine investigation for iron deficiency should be carried out in all patients presenting with focal status epilepticus.

Conclusion

As iron deficiency anemia (IDA) is already an established risk factor for febrile seizure and stroke in children, we would like to highlight that IDA may be a potential trigger to develop seizure and subsequently status epilepticus which may eventually lead to a catastrophic entity like Hemiconvulsion-Hemiplegia Syndrome. But whether IDA is a chance association or causation to HH/HHE syndrome will require further confirmation by more case reports or studies.

Conflict of Interest

None.

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