Idiopathic Hemiconvulsion Hemiplegia Epilepsy in an eight year old boy! Is it time to revisit HHE definition?

| Dr. Mahesh Kamate* | Dr. Bhavana Koppad* | Dr Virupaxi Hattiholi**

*Dept of Pediatric Neurology **Dept of Radiology

ID-303

J. N. Medical College and KLES Dr. Prabhakar Kore Hospital & MRC, KLE Academy of Higher Education & Research, BELAGAVI, KARNATAKA STATE, INDIA

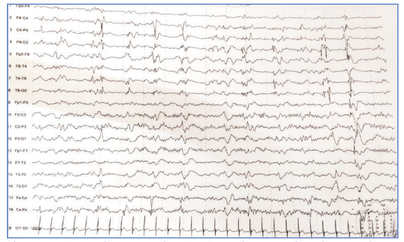
HEMICONVULSION HEMIPLEGIA EPILEPSY (HHE) SYNDROME

- HHE is unique clinic-radiological entity that has been reported mainly in young children up to 4 years.
- ILAE defines Infantile hemiconvulsion-hemiplegia and epilepsy syndrome as a specific syndrome in a patient <2 years old, presenting as New onset refractory status epilepticus (NORSE) with unilateral motor seizures
- It has been reported in children with prior epilepsy and in children with underlying structural lesion.
- The reason for the unique age predilection is not clear
- If HHE be an unilateral presentation of AESD (acute encephalopathy with biphasic seizures and restricted diffusion)/ ALERD (acute leukoencephalopathy with restricted diffusion) is not clear from literature but likely.
- There are reports of AESD with unilateral presentation that has resemblance with HHE (Takahashi et al, Kamate et al).
- Whether the uncontrolled seizures result in the hemispheric oedema or is it the inflammation in the brain that results in the status epilepticus needs further studies
- If HHE resembles AESD, then can it be a form of autoinflammatory disease and can the same strategies used for AESD be adopted in HHE also
- Similarly there are reports of HHE occurring in older children (> 5 yr) and in adults. (Athwal et al)
- We here report an eight year old child who was previously normal. He presented with hemiclonic status epilepticus and had HHE on neuroimaging.
- Thus, there is a need to broaden the definition of HHE

CASE REPORT

- Eight year old boy, previously normal, born to non-consanguineously married couple
- Presented with fever, cough and cold for 4-5 days
- On the 3rd day of illness, he had recurrent seizures (clonic type) occurring for few minutes up to few hours in the left upper and lower limb. The seizures persisted despite use of i.v phenytoin, valproate, levetiracetam, lacosamide and oral topiramate with perampanel. Seizure continued for 2 weeks
- Child had right hemiparesis in between seizures and there were no meningeal signs. Child was in altered sensorium
- MRI showed cerebral oedema in the entire left cerebral hemisphere and there was restricted white matter in the left cerebral hemisphere suggestive of hemiconvulsion hemiplegia epilepsy syndrome
- LP CSF examination was within normal limits. Serum MOG antibody was negative
- EEG showed short interval generalized periodic epileptiform discharges
- A clinical diagnosis of HHE was made and child started on pulse methylprednisolone along with midazolam drip. The seizures subsided after one week and child was discharged after 3 weeks of hospital stay

EEG



EEG in bipolar montage showing short interval generalized periodic epileptiform discharges through out the record

MRI Brain (2 weeks after onset)

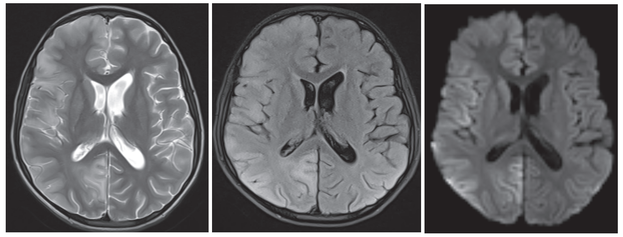
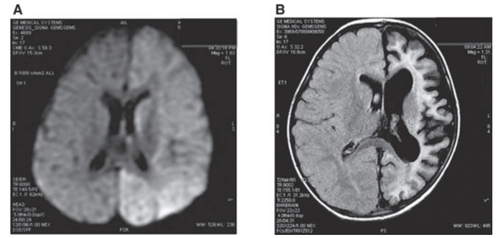


Figure-1 : MRI shows left hemispheric oedema with signal hyperintensities and diffusion restriction in the same areas (more in white matter). Changes are more pronounced in the cortex than the white matter

DISCUSSION

- Hemiconvulsion-hemiplegia epilepsy syndrome (HHE) is characterized by the combination of unilateral convulsive status epilepticus (SE), mainly clonic, followed by transient or permanent ipsilateral hemiplegia.
- In order to differentiate this condition from the more common unilateral deficit (Todd's paralysis) after a "complex" febrile seizure, a minimum duration of hemiplegia of 1 week is required.
- Several months following the status pharmacoresistant partial epileptic seizures recur. This sequence is stereotyped and is known as HHS with or without epilepsy (HHS +/-E)
- Three fourths of patients remain with epilepsy
- Seizures start with rhythmic unilateral. They predominate on one side and last several hours, up to 24 h.
- Electroencephalography (EEG): Ictal EEG shows high amplitude 2–3 Hz rhythmic slow-wave activity with low-amplitude fast activity and rhythmic spikes contralateral to the predominating jerks
- Magnetic resonance imaging (MRI) shows increased diffusion on one side, mainly in the perisylvian and parietooccipital areas (Fig. 2A), followed by atrophy (2B)
- Early MRI demonstrates diffuse signal anomalies confined to one hemisphere hypersignal on T2 sequence and diffusion imaging (DWI) involving the whole pathologic hemisphere, within some cases, mass effect on contralateral hemisphere.
- Hypersignal on diffusion imaging (DWI) is also noted on early MRI reflecting a restricted diffusion due to cytotoxic edema; consequently, ADC (apparent diffusion coefficient) is decreased, resulting in hypointensity on ADC map. This reduced ADC involved the entire affected hemisphere with predominance in the subcortical white matter. All these anomalies affect only one hemisphere. MR angiography is normal
- On day 8-15, cytotoxic edema decrease, with pseudonormalization of the ADC maps, but hypersignal due at this stage, to gliosis, with ongoing loss of volume is visible on T2 images.

Figure 2



- HHE occurs in infants during the course of a nonspecific febrile illness, mainly in the first 2 years of life and in any case before 4 yrs.
- Most definitions of HHE mentions this age predilection. However there are reports of HHE in adults (Athwal et al) and as our case illustrates HHE can occur in children beyond 2-4 yr of age. Hence, there is a need to revisit the definition of HHE
- Occurrence of HHE in both otherwise healthy children and in those with an underlying brain abnormality suggests the underlying epilepsy or seizure per se does not result in the hemispheric edema or restriction of white matter
- Similarly in cases of febrile illness related refractory epilepsy syndrome who also have status going on for days together we do not get the MRI changes like those seen in HHE
- These facts suggest that the uncontrolled seizures per se do not cause the MRI changes
- HHE is possibly due to cytokine storm or a manifestation of autoinflammatory condition that affects on hemisphere. In other words HHE is probably hemispheric AESD or hemispheric ALERD.
- Thus to minimize the sequelae in children with HHE, we should adopt measures used in ALERD like methylprednisolone, dextromethorphan, cyclosporine, adaravone and IL-6 inhibitors like tocilumab.

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