

Hemiconvulsion Hemiplegia Syndrome in a young boy with developmental delay

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Abstract

Hemiconvulsion hemiplegia epilepsy (HHE) syndrome is a rare complication of prolonged focal seizures in children upto 4 years of age. It is usually idiopathic and seen in the setting of febrile seizures in otherwise normal children but less commonly is also associated with structural, infective, traumatic and degenerative diseases that predispose to seizures. It has 3 stages, the first of prolonged focal seizures, then the development of hemiplegia and then followed by final stage of development of epilepsy after a variable latent period. Early recognition and seizure control is important to prevent the development of hemiplegia and intractable epilepsy. We report a child with developmental delay and epilepsy who developed HH syndrome after prolonged unrecognized and difficult to control partial status epilepticus.

Keywords: Hemiplegia, Hemiconvulsion, Complicated febrile seizures.

Introduction

Hemiconvulsion-Hemiplegia Epilepsy syndrome (HHE) was first described by Gestaut and colleagues in 1961.¹ Its incidence is decreasing in the developed world. However it is an established but underdiagnosed and potentially preventable sequelae of prolonged status epilepticus in children younger than 4 years of age.² We present the case of a 3-year-old boy with developmental delay and epilepsy who developed hemiplegia after prolonged focal seizures.

Case Report

Our patient, a 3 year old boy, presented to the Emergency Department in April, 2016 with a five day history of seizures. He was found having continuous right sided focal clonic seizures one morning that persisted for two days followed by continuous left sided focal seizures for another three days. He remained unconscious during this period and also developed fever after two days of hospital stay. Prior to presenting to us he was admitted and had

received treatment for meningitis and status epilepticus in another hospital with workup showing a normal CSF exam and MRI findings as described in the images below. However his seizures were controlled only after intubation and continuous sedation.

He was born to consanguineous parents via an elective caesarean section with indication being maternal hypertension and IUGR. There was a history of neonatal sepsis with seizures and complex partial seizures at 2 years of age but he had never received antiepileptics. He also had meningomyelocele repair at 2 months of age.

His developmental milestones were delayed with walking achieved at two years of age and at 3 years of age he could speak a few words only.

There was a family history of epilepsy in the elder brother and maternal aunt but both were developmentally normal.

On presentation to the ER he was drowsy with a Glasgow Coma Scale (GCS) of 7/15, was initially intubated and sedated with midazolam infusion due to continuous left sided seizures, was withdrawing all his limbs to pain horizontally, had normal pupillary response, reflexes and downgoing plantar responses bilaterally. Workup is shown in Table.

He was admitted and treatment was started with broad spectrum antibiotics and intravenous (IV) acyclovir 250mg 8 hourly, IV levetiracetam 130mg twice daily, IV phenytoin 35mg 12hrly and a continuous infusion of midazolam. After a normal CSF exam and MRI findings suggestive of involvement of an entire hemisphere he was started on IV immunoglobulins with the suspicion of Rasmussen encephalitis and completed a five day course.

The status epilepticus was controlled after intubation on day 1 however he remained on mechanical ventilation due to pneumonia and persistent drowsiness. By the twelfth day of hospital stay, as his conscious level improved, he was noticed to have left hemiplegia with a normal tone and upgoing plantar response on the left side. An MRI was done and is shown in Figure with description of findings. A diagnosis of hemiconvulsion

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Table: Workup of the patient.

Test	Result
Cerebrospinal fluid(CSF) exam	CSF Routine analysis: Normal CSF gram stain and Culture: Negative HSV and MTB DNA PCR: Negative
ANA	Negative
Anti NMDA receptor antibody	Negative
Pan cultures	Negative
CMV	CMV IgM: negative CMV PCR: Detected with a viral load less than 31.0IU/ml
Chest Xray	Opacification with air bronchograms right lung suggesting infection
EEG	Day 1: Moderate diffuse encephalopathy worse on the right side, frequent epileptiform discharges from right temporal region Day 12: Persistent diffuse encephalopathy worse on the right with significantly reduced epileptiform discharges on the right Day 44: Moderate severe brain dysfunction in right hemisphere and mild dysfunction of the left, no epileptiform activity

ANA: Antinuclear antibody, NMDA: N-methyl-D-aspartate, CMV: Cytomegalovirus, EEG: electroencephalogram.

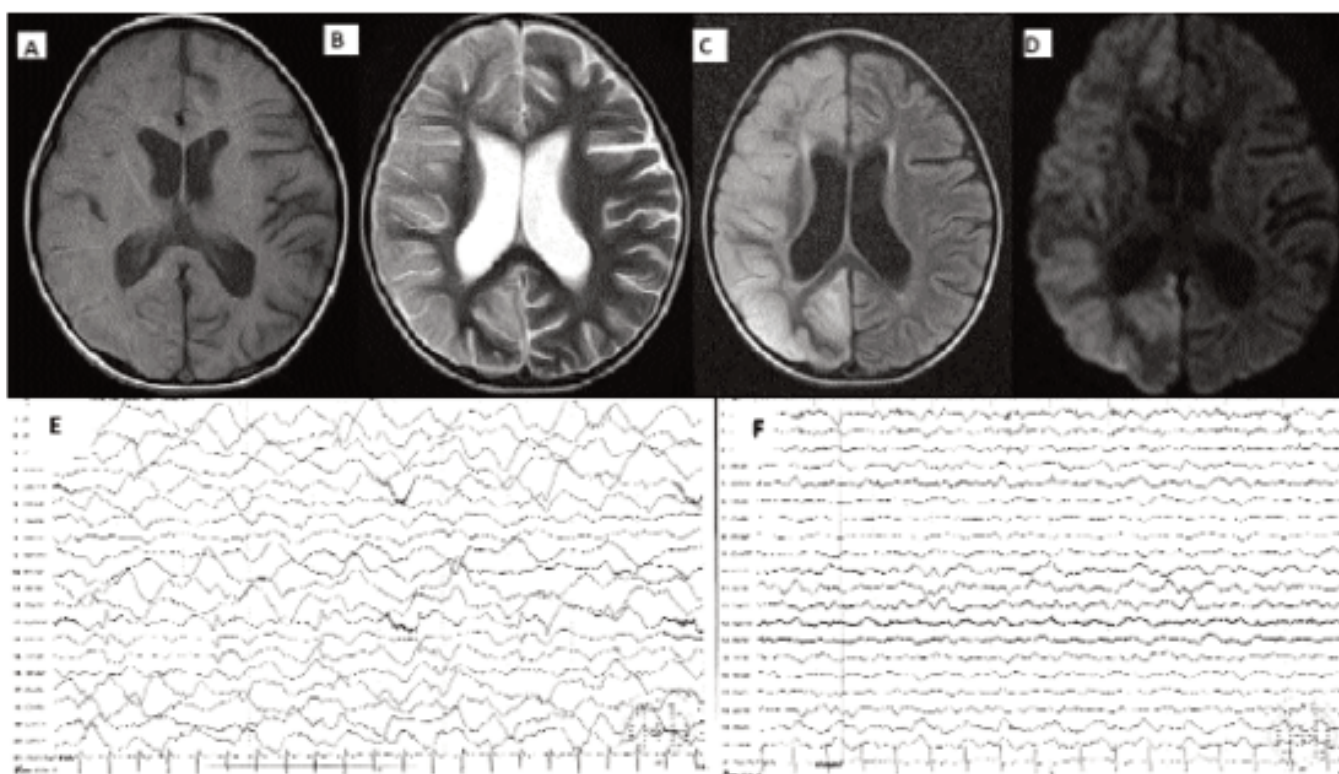


Figure: MRI brain shows right-sided panhemispheric sulcal effacement on T1 images (A) with diffuse cortical T2 and FLAIR hyperintense signal (B and C). Diffusion weighted image (D) shows corresponding hyperintensity which was low on ADC map (not shown), suggesting diffusion restriction due to cytotoxic edema. These abnormalities are not consistent with any vascular territories. Cerebellum was spared and there were no gross or petechial intracranial haemorrhages. EEG on day 1 shows moderate diffuse encephalopathy worse on the left with epileptiform discharges on the right (E). Subsequent EEG showed persistent encephalopathy with reduced epileptiform discharges (F).

hemiplegia syndrome was made.

He improved gradually as his systemic sepsis regressed and he was discharged on 32nd day of hospital stay. At the time of discharge he had persistent left hemiplegia, with tracheostomy tube and nasogastric tube in place. He

was alert and at times showed meaningful response to his parents gestures. He was discharged on 3 antiepileptics-phenytoin, levetiracetam and carbamazepine.

Till his last follow-up 3 months later, he had required readmission of right sided partial status that was

controlled after adjusting a sub-therapeutic blood level of phenytoin, addition of topiramate and treating pseudomonas tracheitis. There was some improvement in his left hemiplegia and he had almost achieved near to his pre-illness cognitive state.

Patient's father was contacted via telephone and consent for publication of the patient's case was taken and consent form shared via email.

Discussion

HHE usually affects children under 4 years of age.^{3,4} Presentation is with prolonged focal clonic seizures usually in the setting of a febrile illness, with or without impairment of consciousness. Focal seizures of one side followed by seizures of the other side as seen in our patient have been reported as well.^{3,4} Hemiplegia of the affected side then develops that may be permanent in upto 80% of cases. This is the hemiconvulsion-hemiplegia stage of the syndrome (HHS) which may be indistinguishable clinically from various other conditions having similar presentations. As seen in our patient at this stage he was treated for meningitis, Rasmussen encephalitis and the weakness considered as Todd's paresis or a complication of encephalitis. Intractable epilepsy then develops after a variable latent period - mostly within 3 years - in upto two thirds of children and the condition is then called HHE syndrome. Involvement of the dominant hemisphere may be associated with aphasia and patients may subsequently develop intellectual impairment.⁴

Neuroimaging in the acute phase characteristically shows unilateral panhemispheric sulcal effacement with slight grey-white de-differentiation on T1 images which may spare the deep nuclei.⁶ There is associated diffuse cortical hyperintensity on DWI with signal loss on ADC map and slightly increased signal on T2/FLAIR, indicating diffusion restriction consistent with cytotoxic oedema.^{6,7} The affected areas are independent of vascular territories.⁷ Our patient also had these typical findings on MRI (Figure-1). No vascular abnormalities are seen on TOF angiography.³ In late stages of HHE, imaging shows brain atrophy more pronounced on the hemisphere contralateral to the side of hemiplegia with dilation of the ventricular system.^{8,9} Imaging differentials include unihemispheric cerebral vasculitis and Rasmussen encephalitis.

The pathogenesis is not known. Most patients reported with HHE have idiopathic HHE - i.e. - with no underlying intracranial pathology, with very few cases with underlying intracranial infection or brain pathology that would predispose to the development of seizures.⁴ HHE

may be a severe form of complicated febrile seizures that develops in a small percentage of children^{3,4} who may have additional genetic predispositions like a mutation in CACNA1A gene which is also seen in familial hemiplegic migraine.⁵ This may implicate similar pathogenic mechanisms like cerebral vasospasm and spreading cortical depression as a cause of hemiconvulsion and hemiplegia as in migraine. The unilaterality of the syndrome is hypothesized to be due to the relative lack of maturation of the corpus callosum in children.³ It is usually idiopathic and seen in the setting of febrile seizures in otherwise normal children but less commonly is also associated with structural, infective, traumatic and degenerative diseases that predispose to seizures. Our patient had a history of developmental delay as well as seizures prior to the development of HHS. He had no fever at the onset of the illness and developed it only after 2 days of seizures and within hospital. We suspect that he probably has secondary HHS with underlying predisposition for seizures.

Treatment for HHE syndrome during the acute phase of the illness is mainly supportive. No guidelines exist as to whether children with HHS should be on chronic anticonvulsant medication to prevent the remote seizures. There is evidence that surgical treatment of delayed intractable epilepsy in HHE syndrome is beneficial.⁴

The importance of early effective seizure control is well known. However it is also important to have an understanding of this syndrome so that it can be suspected and the complications of oedema with fatal herniation can be anticipated and managed appropriately. Early seizure control is also of paramount importance for the prevention of hemiplegia. The etiology and pathogenesis of the condition also needs to be studied further so that at risk population can be identified, preventive strategies developed and new modalities of treatment be explored.

Conclusion

HH syndrome as well as HHE is a potentially reversible complication of prolonged focal seizures, so prolonged focal seizures and focal status should be managed urgently and appropriately to prevent long term sequelae.

Disclaimer: None to declare.

Conflict of Interest: The chairman of our IRB who has signed our IRB statement is also a co-author of our article.

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References

1. Gastaut H, Poirier F, Payan H, et al. H.H.E. syndrome: hemiconvulsions, hemiplegia, epilepsy. *Epilepsia* 1960; 1: 418-47.
 2. Auvin S, Devisme L, Maurage C, et al. Neuropathological and MRI findings in an acute presentation of hemiconvulsion-hemiplegia: a report with pathophysiological implications. *Seizure* 2007; 16: 371-6.
 3. Tenny J, Schapiro M. Child Neurology: Hemiconvulsion-hemiplegia-epilepsy syndrome. *Neurology* 2012; 79: e1-e4.
 4. Auvin S, Bellavoine V, Merdarius D, Delanoë C, Elmaleh-Bergés M, Gressens P, et al. Hemiconvulsion-hemiplegia-epilepsy syndrome: current understandings. *Eur J Paediatr Neurol* 2012; 16: 413-21.
 5. Yamazaki S, Ikeno K, Abe T, Tohyama J, Adachi Y. Hemiconvulsion-hemiplegia-epilepsy syndrome associated with CACNA1A S218L mutation. *Pediatr Neurol* 2011; 45: 193-6.
 6. Freeman JL, Coleman LT, Smith LJ, Shield LK. Hemiconvulsion-hemiplegia-epilepsy syndrome: characteristic early magnetic resonance imaging findings. *J Child Neurol*. 2002; 17: 10-6.
 7. Auvin S, Devisme L, Maurage CA, Soto-Ares G, Cuisset JM, Leclerc F et al. Neuropathological and MRI findings in an acute presentation of hemiconvulsion-hemiplegia: a report with pathophysiological implications. *Seizure*. 2007; 16: 371-6.
 8. Toldo I, Calderone M, Boniver C, Dravet CH, Guerrini R, Laverda AM. Hemiconvulsion-hemiplegia-epilepsy syndrome: early magnetic resonance imaging findings and neuroradiological follow-up. *Brain and Development*. 2007; 29: 109-11.
 9. Salih MA, Kabiraj M, Al-Jarallah AS et-al. Hemiconvulsion-hemiplegia-epilepsy syndrome. A clinical, electroencephalographic and neuroradiological study. *Childs Nerv Syst*. 1997; 13: 257-63.
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