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Hemimegalencephaly with intractable epilepsy: A case report

Prem Chand,¹ Muhammad Faraz Raghieb,² Muhammad Sohail Salat,³ Fazal Manzoor Arain⁴

Abstract

Isolated Hemimegalencephaly (iHME) is a rare form of congenital malformation of cortical development. It is characterized by enlargement of all or part of one cerebral hemisphere. It typically presents with intractable seizures, mental retardation, developmental delay, contralateral hemiparesis and hemianopia. The patient was a five and half month's old baby girl who presented first with focal seizures at 10th day of life. No other physical or behavioral abnormality was noted. However, Initial EEG showed excessive sharp EEG transients more over the right hemisphere, repeated EEG showed spikes, polyspikes, sharps and slow wave discharges predominately over right hemisphere. MRI brain showed asymmetric enlargement of the right cerebral hemisphere, suggestive of hemimegalencephaly. Initial treatment with anti-epileptics was successful in controlling the seizures but later on the seizures became intractable even on polytherapy. Identification of this and similar cases of iHME can help us better understand this disorder and its associated symptoms and eventually help us develop better treatment options for it.

Keywords: Hemimegalencephaly, Hemiparesis, Intractable epilepsy, Hemispherectomy.

Introduction

Hemimegalencephaly (HME) is a rare congenital malformation of cortical development characterized by enlargement of all or part of one cerebral hemisphere.¹ HME may occur as an isolated disease or as a part of Proteus syndrome, neurofibromatosis, linear sebaceous nevus syndrome, tuberous sclerosis complex, or Klippel-Weber-Trenaunay syndrome.² The typical characteristics of isolated hemimegalencephaly (iHME) include ipsilateral severe cortical dysplasia or dysgenesis, white matter hypertrophy and a dilated and dysmorphic lateral ventricle.³ This asymmetric and enlarged brain tissue is associated with intractable seizures, developmental delay, contralateral hemiparesis, and hemianopia.⁴ Because there is no cure for iHME, the principal aim of the

treatment of this disease is to control seizures, which is done by using a variety of anti-epileptic drugs.⁴ However, in majority of patients the seizures remain intractable and hemispherectomy is the treatment of choice.⁴ Even though this surgical procedure has been shown to be successful in reducing the frequency of seizures, the risks of morbidity, which includes hydrocephalus, intracranial haematomas and infections, remain high.³

Cases of iHME present as sporadic cases and do not show familial inheritance or sex preference.² This fact makes it very difficult to identify a particular genetic etiology for iHME. Nevertheless, different studies have shown association between iHME and mutations in AKT3, PIK3CA and MTOR genes. It has also been reported that Pitx2, lefty-1, lefty-2 and Zic3 genes play a role in asymmetric growth pattern of brain hemisphere.⁵ Therefore, it is important that more cases of iHME are identified and reported so that further research can be conducted to understand this disorder and develop better treatment strategy. There are only few cases of iHME has been reported from Pakistan.

Case Report

A five and half month's old baby girl presented to the Aga Khan University Hospital in January 2016 with history of focal seizures since 10th day of life. Her seizures consisted of jerky movement localized to the left side of the body with up-rolling of eyes and excessive crying. No other symptoms were noted. The child was born via spontaneous vaginal delivery after 40 weeks of normal gestation period. Upon examination at the time of birth the child had a visible right sided cephalhaematoma. The head circumference was 34 cm and body weight was 2.8 kg. She was the only child of non-consanguineous parents. There was no history of miscarriage or syndromic baby in either parent's family.

Initial workup included EEG, which showed excessive sharp EEG transients more over the right hemisphere and MRI brain, which showed asymmetric enlargement of the right cerebral hemisphere and diffuse thickening of cortical grey matter with increased myelination over right hemisphere, suggestive of right sided hemimegalencephaly (Figure-1). Initially her seizures were well controlled with phenobarbital.

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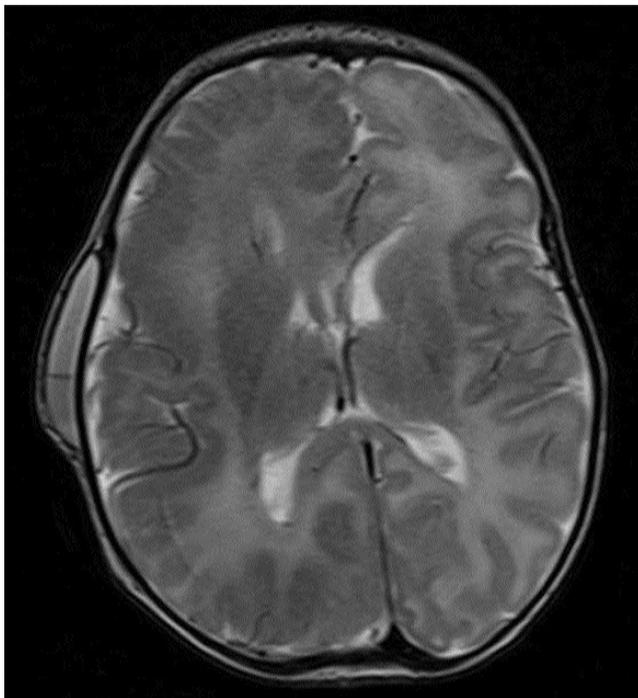


Figure-1: MRI showing transverse view of the brain. Hemimegalencephaly of the right side of brain can be easily identified. A cephalohematoma can also be seen on the right.

The child again presented at the age of five and half months in the emergency room with multiple left sided focal seizures. This time a paucity of movement over left sided body was also noted. The head circumference was 37.5 cm, weight 5.5 kg and height was 58 cm. She had partial neck holding, could reach out objects and coos. No dysmorphic features or skin manifestation were noted and she did not present with any syndromic features.

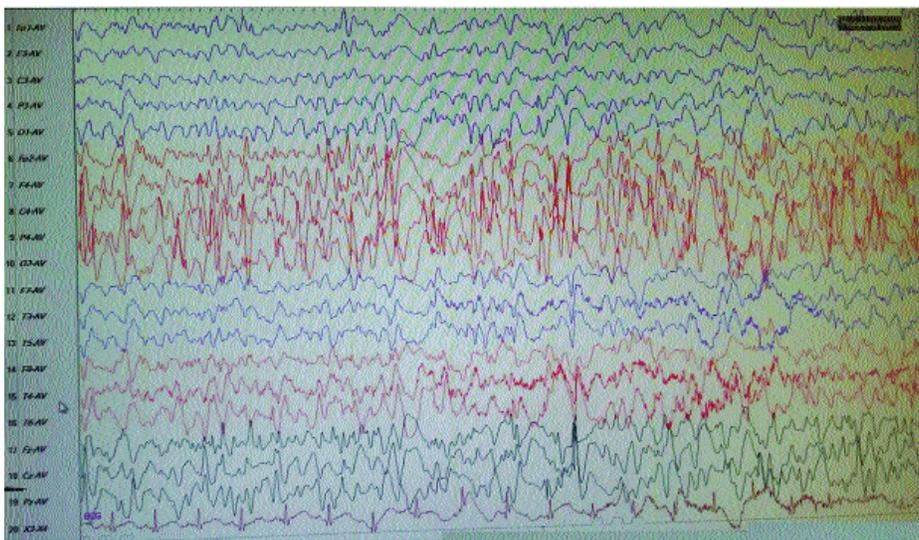


Figure-2: EEG recording shows predominantly right sided spike, polyspikes and wave discharges.

Another EEG was done which showed right sided dominant spikes, polyspikes, sharps and slow wave discharges (Figure-2). Her seizures were difficult to control with first line of antiepileptics, so Levetiracetam and Topiramate were added to the management. Treatment option of surgical intervention was also discussed with the parents.

Discussion

Malformations of cortical development arise due to disruption in the proliferation, migration or post-migration stages during the development of cortex.⁶ Disruption in any of these processes can cause seizures and neurodevelopmental delay in children.⁶ Hemimegalencephaly, characterized by hamartomatous growth of a cerebral hemisphere, has been categorized under the term of "cortical dysgenesis" owing to disorders of proliferation.⁷

Hemimegalencephaly is categorized into three types: Isolated, syndromic and total.⁸ Isolated hemimegalencephaly has no associated hemispheric hypertrophy or cutaneous or systemic involvement. Syndromic hemimegalencephaly (for example, epidermal nevus syndrome and Proteus Syndrome) is associated with other features which include hemispheric hypertrophy of the ipsilateral part of the body. Total hemimegalencephaly, which is the least common form, also involves enlargement of the brainstem and cerebellum. Cases of syndromic hemimegalencephaly have been reported from Pakistan previously, however, here we are reporting the first case of isolated hemimegalencephaly from our institute after receiving consent from the parents.

Previous studies have shown that mutations in AKT3, PIK3CA and mTOR genes are associated with iHME.² In particular, the association of the modulation of mTOR signaling cascade and iHME has been the focus of many studies.⁹ Some studies suggest that mTOR activation itself can produce nerve cell excitability and this can be helpful in explaining why patients with iHME have seizures.⁹ These findings show that further research needs to be conducted on iHME, not only to better understand this disorder but also to develop better treatment

options for these patients.

Conclusion

Here we have presented a rare case report of iHME with intractable epilepsy. Identification of this and other similar cases can allow us to conduct further research on this rare disease. Findings of these studies will not only improve the treatment options for iHME but they can also help us understand the mechanism of its symptoms. Hence, these findings can improve our understanding of other disorders which share similar symptoms.

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