A Case of Carbamazepine Responsive Neonatal Epilepsy Secondary to *PACS2* Gene mutation

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Introduction

Mutations in PACS2 gene are responsible for an early-onset developmental and epileptic encephalopathy, presenting with seizures starting within the first weeks of life. The phenotype of this new syndrome is also characterized by hypotonia, global developmental delay, intellectual disability with or without autistic features, mild facial dysmorphism and cerebellar dysgenesis with folia abnormalities. We present a case of *PACS2* mutation associated neonatal epilepsy, which clinically and electrographically behaved like BNFE(Benign neonatal familial epilepsy) with complete response to Carbamazepine, suggesting an important therapeutic option.

Case Report

To describe a unique clinical presentation of the *PACS2* gene mutation related neonatal epilepsy.

Methods

A 2 weeks old Emirati male neonate, second born of non consanguinous couple, with an uneventful birth and negative family history, presented with unprovoked seizures since day 18 of life.

The presentation was brief isolated myoclonic jerks in wakefulness. The initial EEG was normal.

On day 30 of life, the infant presented with increased frequency of seizures in wakefulness and sleep. The semiology included high-pitched cry followed by unilateral eye deviation and a stary look with or without asymmetric tonic posturing of the upper limbs with dusky skin discoloration followed by hiccups. Each episode self-aborted in less than 2 minutes, followed by sleep.

Examination was unremarkable with intact neurological examination.

Levetiracetam at maximal dose failed to control the seizures.

Investigations done included metabolic work-up and MRI Brain which were normal. Comprehensive epilepsy gene panel had been sent. A 24hr EEG showed a normal background with occasional sharp transients. One recorded seizure showed epileptic activity beginning from left and spreading toward right temporal region, reminiscent of migrating focal seizures of infancy or benign neonatal familial epilepsy (BNFE).

Results

The patient was started on Carbamazepine at 10 mg /kg/day in two divided doses. His seizures completely responded within 24 hours.

Epilepsy gene panel showed a heterozygous mutation in the *PACS2* gene c.625G>A p.(Glu209Lys), which has been reported as de novo in several individuals with neurodevelopmental disorder characterized by epileptic encephalopathy.

At 3 months age, the patient remains seizure free with normal developmental milestones for age and normal EEG.

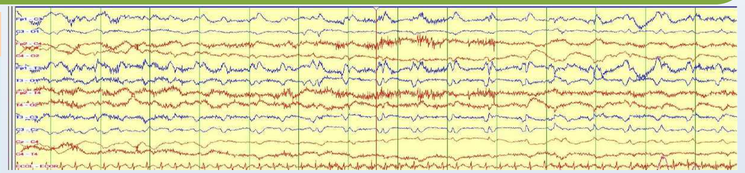

Figure1

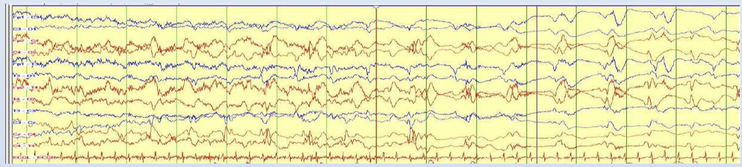

Figure2

Figure 1: Top: EEG showing rhythmic electrographic seizure activity in the left hemisphere in the temporal chain.

Figure 1: Bottom: Migration of same seizure to the right hemisphere which shows high amplitude rhythmic epileptic discharges with relative attenuation of the seizure activity on the left side.

Conclusion

1. Screening for PACS2 gene should be part of gene panel for early onset neonatal epilepsies.

2.Carbamazepine should be considered in cases with neonatal onset seizures refractory to other routine antiseizure medications.

References

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