A case of SCN8A mutation

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The epileptic encephalopathies (EEs) are a group of severe epilepsies that predominantly begin in infancy and childhood. Application of next-generation sequencing led to the identification of multiple new genes for epileptic encephalopathies, one of them is the mutations in SCN8A. (1) Pathogenic variants in SCN8A have been associated with a wide spectrum of epilepsy phenotypes with variable severity but majority of the published SCN8A patients suffer from severe developmental and epileptic encephalopathy (DEE). (2)

Main features of SCN8A

*Seizure onset in the first 18 months of life (mean age 4 months)

*Focal clonic seizures evolving into bilateral convulsive seizures

*Development of multiple seizure types

*Motor abnormalities including hypotonia

* Movement disorders including dystonia, ataxia, choreoathetosis are the features of the disease. (3)

Treatment: Several reports have demonstrated that patients have respond preferentially to sodium channel blockers, especially to supratherapeutic doses of oxcarbazepine or phenytoin. (4)

CASE

A 4-month-old girl who was born from distantly related parents with no pre-post natal features, and neuromotor development appropriate for her age, applied with the complaint of frequent, repetitive focal clonic seizure. Phenytoin (PHT) and levetiracetam (LEV) loading was done after two doses of midazolam. Cranial imaging and electroencephalogram (EEG) was normal. PHT was stopped and discharged with LEV.

She presented the same clonic seizures on the face and arms then, repeated EEG was also normal. Phenobarbital (PB) loaded, LEV discontinued. Seizures continued at home but after PHT loading no seizure was seen in the service. Metabolic screening found normal. Clonazepam was added due to intermittent seizures continued. EEG showed epileptic activity and slowing of the background, topiramate (TOP) was added to the treatment. Cerebrospinal fluid examination was normal, epileptic encephalopathy genetic panel was sent. The result was reported as SCN8A heterozygous mutation c.3943G>A (p.Val1315Met). The patient's hypotonicity became evident, neuromotor development stalled. Physical therapy and rehabilitation program was started. Currently, 23 months old, hypotonic, holding her head but unable to sit without support equivalent the global development of six months age and has involuntary athetoid movements, no seizures with PHT, TOP and clonazepam treatment.

Clinical Synopsis- OMIM 614558(5)

DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY 13; DEE13

HEAD & NECK

Head

- Microcephaly, progressive (in some patients)

Eyes

- Poor eye contact

NEUROLOGIC

Central Nervous System

- Seizures, refractory
- Epileptic encephalopathy
- Epileptic spasms
- Delayed psychomotor development
- Psychomotor regression
- Intellectual disability
- Hypotonia
- Impaired coordination
- Impaired balance
- Inability to walk
- Speech and language regression
- Absent speech
- Generalized spike-wave activity seen on EEG
- Diffuse slowing
- Multifocal spikes
- Slow spike-wave discharges
- Cerebral atrophy (in some patients)

Behavioral Psychiatric Manifestations

- Autism

CONCLUSIONS

Evaluation of infantile epileptic encephalopathy is important.

Genetic analysis in terms of epileptic encephalopathy in the early period for patients with resistant epilepsy and growth retardation ensures clarification of the etiology and determination of the treatment plan.

REFERENCES

1.Larsen J, Carvill GL, Gardella E et al ; EuroEPINOMICS RES Consortium CRP. The phenotypic spectrum of SCN8A encephalopathy. Neurology. 2015 Feb 3;84(5):480-9

2.Johannesen KM, Gardella E, Encinas AC et al. The spectrum of intermediate SCN8A-related epilepsy. Epilepsia. 2019 May;60(5):830-844.

3. Hammer MF, Wagnon JL, Mefford HC, et al. SCN8ARelated Epilepsy with Encephalopathy. 2016 Aug 25. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022.

4. Gardella E, Møller RS. Phenotypic and genetic spectrum of SCN8A-related disorders, treatment options, and outcomes. Epilepsia. 2019 Dec;60 Suppl 3:S77-S85.

5.https://www.omim.org/search?index=entry&start=1&limit=10&sort=score+desc%2C+prefix_sort+desc&search=SCN8a+epilepsy