CASE REPORT

Early Myoclonic Encephalopathy

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Early myoclonic encephalopathy (EME) is a rare malignant epileptic syndrome. The erratic myoclonus with or without focal motor seizures, onset before 3 months of age, and persistent suppression-burst pattern in electroencephalograph (EEG) are accepted as the diagnostic criteria for EME. We report an 11 month-old infant with EME which was secondary to non-ketotic hyperglycinemia.

Keywords: Early myoclonic encephalopathy, Epilepsy, Infant, Non-ketotic hyperglycinemia, Suppression-burst patttern.

Early myoclonic encephalopathy (EME) is one of the two recognized epileptic encephalopathies which are seen in early infancy, the other being early infantile epileptic encephalopathy (EIEE or Ohtahara syndrome). EME is characterized by characteristic suppression burst (SB) on electroencephalogram (EEG). It is a malignant epilepsy syndrome(1).

According to the International Classification of Epilepsies and Epileptic Syndromes (ILAE, 1989), EME is categorized as age-related, generalized symptomatic epilepsy of non-specific etiology(2). EME is clinically characterized by the onset of erratic or fragmentary myoclonus (usually involving the face or extremities), massive myoclonus, other refractory partial seizures and marked neurologic abnormalities(2,3). We report an 11 month-old infant presenting with EME, who on metabolic work was found to have non-ketotic hyperglycinemia (NKH).

CASE REPORT

An 11 month-old infant, born to second-degree consanguineously married couple, presented to us with recurrent seizures, developmental delay and recurrent respiratory tract infections. He was born normally after an uncomplicated term pregnancy. After birth, baby was hypotonic and had difficulty in sucking and swallowing. He developed myoclonic and focal tonic seizures in the first week of life and was started on phenobarbitone. Biochemical tests (including calcium, magnesium and glucose) done at that time and MRI brain were normal. EEG done at 3 months showed SB pattern with multifocal spikes and sharp waves and by then, child had developed erratic fragmentary myoclonia. Child was receiving adequate doses of valproate and clobazam but the child continued to have myoclonic seizures and frequent tonic seizures appeared by 4-5 months. Child did not attain any milestones expected for his age and remained floppy.

He presented to us at 11 months with an episode of bronchopneumonia which was managed with antibiotics. His weight, length, and head circumference were within normal limits. He was lethargic and had hypotonia with hyperreflexia. EEG was repeated and it showed SB pattern (***Fig.*1**). In

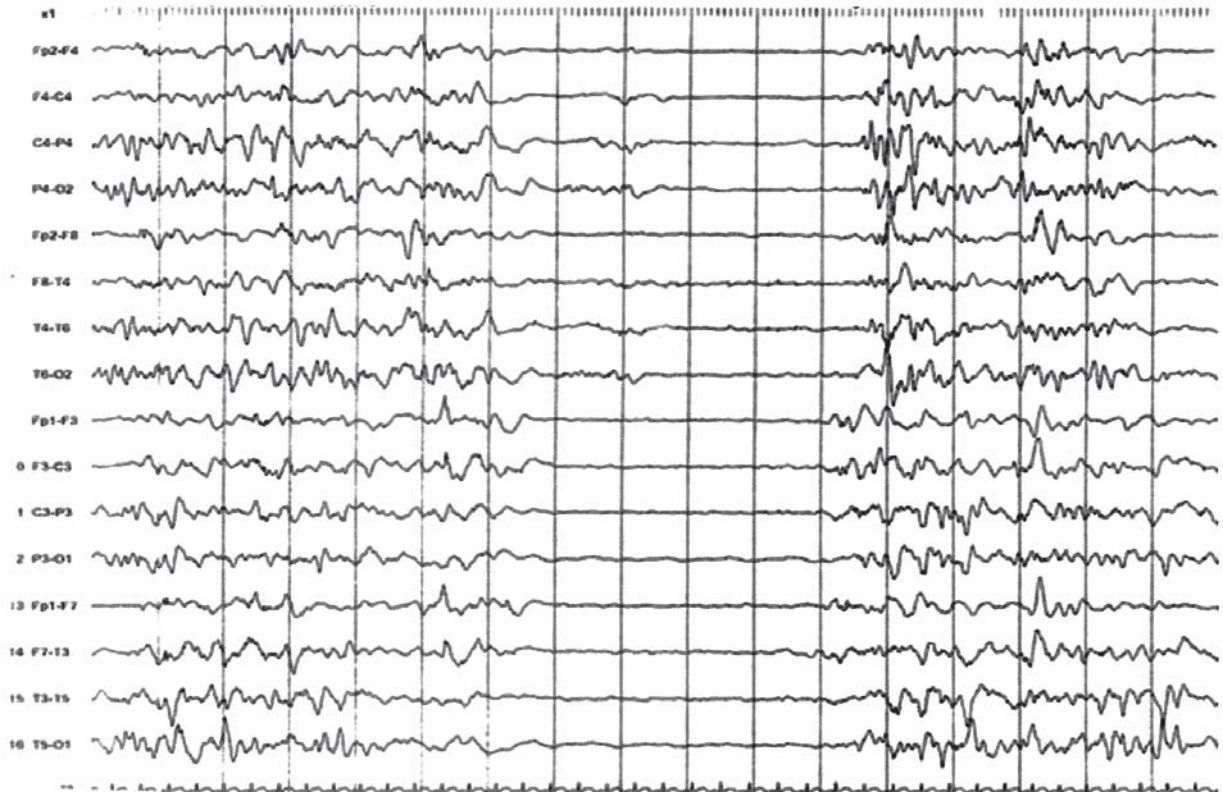

FIG.1 *Sleep EEG showing suppression burst pattern and poorly organized background. Bursts lasts for 1-5 seconds alternating 3-10 seconds suppression.*

view of erratic myoclonia, tonic seizures, severe developmental delay, hypotonia and persistent SB pattern on EEG, a diagnosis of EME was considered. Repeat MRI brain was normal. Tandem mass spectrometry of blood, revealed high glycine levels (1068.48 µmol/L; normal 2-745 µmol/L) suggesting NKH. Enzymatic analysis or mutational studies could not be done and a diagnosis of EME secondary to NKH was made. We tried to control the seizures with high-dose valproate, lamotrigine and pyridoxal phosphate. Dextromethorphan (25 mg/kg/day) in combination with benzoate (500-750 mg/kg/day) was prescribed for NKH. However, seizures continued to persist and there was no much improvement. Parents were counseled regarding the outcome and recurrence risk.

DISCUSSION

Early myoclonic encephalopathy is a rare epileptic syndrome with onset nearly always in the first three months of life, mostly within the neonatal period. The main ictal manifestations are partial or fragmentary erratic myoclonus, massive myoclonus, partial motor seizures and tonic infantile spasms(5). The usual and earliest seizure type is fragmentary myoclonus and is regarded as an essential symptom in EME. The closest differential diagnosis for EME is Ohtahara syndrome (OS) which has an early onset, within a few months of birth, and frequent tonic spasms with or without clustering, as the main seizure type. Unlike EME, more than two third cases of OS evolve to West syndrome at 4-5 months of age(5).

EEG shows SB pattern in which complex bursts of spikes, sharp waves and slow waves are separated by episodes of flattening of the tracing and localized discharges that resemble those of neonatal seizures. The bursts last for 1-5 seconds and alternate with 3-10 seconds of suppression. This SB pattern is more distinct during sleep, especially deep sleep(4,5). EEG later evolves towards atypical hypsarrhythmia or multifocal paroxysms at 3-5 months of age. However, in most cases, this phase is transient, and a return to the SB pattern is observed. The SB pattern

primarily reflects a diffuse structural or junctional disturbance of gray matter connectivity. In OS, the most characteristic EEG feature is also SB pattern, but this is consistently seen during both awake and sleep states and later evolves to hypsarrhythmia in many cases in first six months of life. A persistent SB pattern beyond 6-8months of age on EEG is pointer towards EME(1,3,4).

There are no clear guidelines for treatment of seizures in EME. Conventional antiepileptic drugs, ACTH, corticosteroids and pyridoxine are ineffective in controlling the seizures(3). Even the alternative strategies for epilepsy like ACTH, ketogenic diet and zonisamide were found to be more beneficial in OS than EME(6). The prognosis is poor as more than 50% patients die before one year of age and the remaining enter a vegetative state. In patients with NKH, oral administration of ketamine (8 mg/kg/day, in four divided doses), tryptophan (100-150 mg/kg/day) and dextromethorphan (5-35 mg/kg/day) in combination with benzoate (500-750 mg/kg/day) have brought about only partial improvement of neurological symptoms and EEG findings(7).

Non ketotic hyperglycinemia, being an autosomal recessive condition, there is 25% chance of recurrence in the next pregnancy. This is important for genetic counseling and prenatal diagnosis.

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REFERENCES

1. Chen PT, Young C, Lee WT, Wang PJ, Peng SS, Shen YZ. Early epileptic encephalopathy with suppression burst electroencephalographic pattern-an analysis of eight Taiwanase patients. Brain Dev 2001; 23: 715-720.
2. Commission on Classification and Terminology of International League Against Epilepsy: Proposal for revised Classification of Epilepsies and Epileptic syndromes. Epilepsia 1989; 30: 389-399.
3. Ohtahara S, Ohtsuka Y, Oka E. Epileptic encephalopathies in early infancy. Indian J Pediatr 1997; 64: 603-612.
4. Ozyurek H, Turanli G, Aliefendioglu D, Coskun T. Repetitive EEG recordings are necessary for the diagnosis of early myoclonic encephalopathy. Neurol India 2005; 53: 235-237.
5. Ohtahara S, Ohtsuka Y, Erba G. Early pileptic encephalopathy with suppression burst. *In:* Engel J Jr, Pedley TA, Eds. Epilepsy - A comprehensive Textbook. Vol III. Philadelphia: Lippincott-Raven Publishers; 1997.
6. Ohno M, Shimotsuji Y, Abe J, Shimada M, Tamiya H. Zonisamide treatment of early infantile epileptic encephalopathy. Pediatr Neurol 2000; 23: 341-344.
7. Sehgal V, Ramji S. Nonketotic hyperglycinemia in a neonate. Indian Pediatr 1998; 35: 278-281.