

Epileptic Encephalopathies: A Short Review

Shubhankar Mishra*

Department of Neurology, S.C.B Medical College, Cuttack, India

***Corresponding Author:** Shubhankar Mishra, Department of Neurology, S.C.B Medical College, Cuttack, India.

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Abstract

Epileptic encephalopathies are conditions characterized by epileptiform abnormalities associated with progressive cerebral dysfunction. The precise mechanisms underlying epileptic encephalopathy are unknown, but they likely reflect widespread neuronal network dysfunction. The prognosis of these disorders is generally quite poor, but a significant minority of cases can be ameliorated and even cured by prompt diagnosis and successful treatment. These epileptic syndromes include early myoclonic encephalopathy (EME) and Ohtahara syndrome in the neonatal period, West syndrome and Dravet syndrome in infancy, myoclonic status in nonprogressive encephalopathies, and Lennox-Gastaut syndrome (LGS), Landau-Kleffner syndrome (LKS), and epilepsy with continuous spike waves during slow wave sleep in childhood and adolescences. This article tends to cover those diseases briefly with comparative analysis.

Keywords: *Epileptic Encephalopathies; West; EEG; Lennox-Gastaut Syndrome*

Introduction

The term epileptic encephalopathy refers to a 'heterogeneous group of epileptic disorders in which epileptic activity itself (ictal or interictal) impairs cognitive and behavioral function above and beyond what is expected from the underlying pathology alone' [1]. The report of the International League Against Epilepsy (ILAE) Task Force on classification and terminology includes 8 syndromes under epileptic encephalopathies: early myoclonic encephalopathy, Ohtahara syndrome, West syndrome, Dravet syndrome, myoclonic status in nonprogressive encephalopathies, Lennox-Gastaut syndrome (LGS), Landau-Kleffner syndrome (LKS), and epilepsy with continuous spike waves during slow-wave sleep [2]. But recently some authors have questioned the validity of the term epileptic encephalopathy (EE). The clubbing of severe epileptic syndromes along with intellectual disability in a spectrum questions the validity of the term [3]. However, the term is still in use along with its classification till new nomenclature. Most common feature is that these disorders are usually refractory to standard antiepileptic drugs (AEDs) along with decline in cognition. These diseases are generally classified according to age of presentation.

Syndromic features

Conclusion

Epileptic encephalopathies are severe epileptic syndromes of early age that manifest with (1) electrographic EEG paroxysmal activity that is often aggressive and refractory, (2) seizures that are usually multiform and intractable with high chance of recurrence, (3) cognitive, behavioural and neurological deficits with catastrophic consequences. It consists of disorders with diverse aetiology, highly variable

Disease	Features
Early Infantile Epileptic Encephalopathy (Ohtahara Syndrome)	<ul style="list-style-type: none"> - Symptoms appear within the first 3 months of birth and usually within the first 10 days. Onset is acute in previously normal children. - Main seizure pattern is tonic spasms; other patterns include tonic/clonic, clonic, myoclonic, atonic, absences, partial, complex partial (with or without secondary generalization), gelastics, and Jacksonians. Seizures can appear in clusters or singly and patterns are likely to change with time. It is not uncommon for patterns to reappear at a later stage [4,5] - EEG burst suppression during both waking and sleeping states - Vigabatrin, phenytoin, Zonisamide, Phenobarbitone, steroid therapies using ACTH and Prednisone
Early Myoclonic Encephalopathy	<ul style="list-style-type: none"> - Onset either in the neonatal period or the first months of life, is characterized by erratic, fragmentary, or massive myoclonus, partial seizures, and late tonic spasms. Myoclonus usually involves the face or extremities and may be restricted to an eyebrow, a single limb, or a finger [6] - EEG burst suppression pattern with bursts of spikes, sharp waves, and slow waves, which are irregularly intermingled and separated by periods of electrical silence - Multiple AED, No effective therapy Inborn error of metabolism to be evaluated
Infantile Spasms (West Syndrome)	<ul style="list-style-type: none"> - Usually occurs in the first year of life and consists of the triad of infantile spasms, developmental deterioration, and a hypsarrhythmia pattern on EEG [7] - ACTH and vigabatrin Corticosteroids may be less efficacious than ACTH, Others include valproate, levetiracetam, topiramate, zonisamide, lamotrigine, and benzodiazepines [8]
Malignant Epilepsy with Migrating Partial Seizures in Infancy	<ul style="list-style-type: none"> - Onset of this rare syndrome occurs in the first year of life and may occur in the neonatal period. Frequent partial seizures of multifocal onset, with autonomic or motor involvement. Semiology of the seizures include lateral head and eyes deviation, focal clonic seizures of the eyes, face or limbs, unilateral or bilateral focal tonic seizures, automatic movements such as chewing, mastication, autonomic features such as apnea, salivation or facial flushing and secondary generalized tonic clonic seizures [9]. - Interictal EEG reveals multifocal epileptiform activity and slowing, diffuse slowing of the background activity - Seizures are often difficult to control with standard AEDs. Bromides, stiripentol, and clonazepam may be helpful in some cases
Myoclonic Status in Nonprogressive Encephalopathies	<ul style="list-style-type: none"> - Seizures typically begin with partial motor seizures. Myoclonic status may occur at onset. Myoclonic absences, massive myoclonias, and rarely generalized or hemiclonic seizures may occur. Myoclonias may be multifocal and occur with startles [10]. - Interictal EEG consists of multifocal epileptiform discharges and background slowing - Episodes of myoclonic status may respond to benzodiazepines. AEDs that may be efficacious include valproate with ethosuximide or clobazam
Severe Myoclonic Epilepsy in Infancy (SMEI) Dravet Syndrome.	<ul style="list-style-type: none"> - Starts with seizures which may not initially differ from those associated with feverish illnesses. This syndrome tends to develop during the second year of life. In addition to the partial seizures are the myoclonic jerks. Often the children are photosensitive and associated with cognitive decline. "SCN1A" mutation seen in many patients [11,12]. - EEG by the 2nd year epileptic activity with spike and wave or polyspike discharges, which occur either as single event or in bursts - Phenobarbital, sodium valproate are usually tried first. Other options include stiripentol, topiramate, clonazepam, and clobazam. - A combination of sodium valproate with either topiramate or stiripentol may be the most helpful.

Table 1: Epileptic encephalopathy syndromes in infancy.

Disease	Features
Lennox-Gastaut Syndrome LGS.	<ul style="list-style-type: none"> - Multiple seizure types; mental retardation or regression; abnormal findings on electroencephalogram (EEG), with paroxysms of fast activity and generalized slow spike and wave discharges (1.5 - 2 Hz). - The most common seizure types are tonic-axial, atonic, and absence seizures, but myoclonic, generalized tonic-clonic, and partial seizures can be observed [13,14] - EEG, with paroxysms of fast activity and generalized slow spike and wave discharges (1.5 - 2 Hz) - Valproic acid and benzodiazepines such as clonazepam, nitrazepam and clobazam, vigabatrin, zonisamide, lamotrigine, topiramate and rufinamide proven effective
Electrical Status Epilepticus during Slow Sleep (ESES)	<ul style="list-style-type: none"> - A status heterogeneous epileptic disorder, deterioration of neuropsychological functions associated with or independent from the epileptic disorder, and deterioration of motor functions [15] - EEG pattern characterized by “subclinical” spikes and waves occurring almost continuously during slow sleep and appearing every night for a variable length of time in children - The typical EEG changes appear 1 year to 2 years after the first seizure and are associated with behavioural deterioration. - Combined use of benzodiazepines and valproate is considered the treatment of choice in this condition
Acquired Epileptic Aphasia Landau-Kleffner Syndrome (LKS)	<ul style="list-style-type: none"> - Progressively lose receptive and expressive language ability coincident with the appearance of paroxysmal electroencephalographic (EEG) changes. Aphasia usually appears at age 4 - 7 years, and there is a slight male predominance [16]. Mild, focal/multifocal Seizures, Acquired auditory agnosia. - Paroxysmal electroencephalographic (EEG) changes - Valproic acid, ethosuximide, and benzodiazepines alone or in combination have been partially or transiently effective in some cases. In a recent study, clobazam and levetiracetam to be the most efficacious antiepileptic drugs in the treatment of ESES [17].

Table 2: Epileptic encephalopathy syndromes in childhood.

age of onset, and heterogeneous response to therapy. Although prognosis is generally poor, even dismal, for children with the earliest onset of epileptic encephalopathy, important exceptions occur. Improvement, with respect to both seizures and neurocognitive outcomes, depends upon prompt electro clinical diagnosis followed by expeditious and appropriate therapy. Epileptic encephalopathy remains a challenging focal point of ongoing clinical, translational, and basic research. Early diagnosis and proper AED can provide better outcome.

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