Epilepsy
Epileptic Syndromes and Treatment

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KEYWORDS

• Epilepsy • Epilepsy syndrome • Infantile spasms • Lennox-Gastaut syndrome
• Childhood absence epilepsy • Juvenile myoclonic epilepsy
• Childhood epilepsy with centrotemporal spikes • Dravet syndrome

KEY POINTS

- An epilepsy syndrome is a specific set of seizure types and EEG and imaging features that tend to have age-dependent features, triggers, and often prognosis.
- Epilepsy syndromes may be classified based on age of presentation and outcomes.
- Characterization of epilepsy syndromes may help guide choice and duration of treatment and predict outcomes.
- Common pediatric epilepsy syndromes include West syndrome, Lennox-Gastaut syndrome, Dravet syndrome, Panayiotopoulos syndrome, childhood epilepsy with centrotemporal spikes, childhood absence epilepsy, juvenile myoclonic epilepsy.

BACKGROUND

Epilepsy has traditionally been defined as a disorder of the brain characterized by predisposition to have recurrent unprovoked seizures, widely accepted as 2 or more seizures at least 24 hours apart. In 2014, The International League Against Epilepsy (ILAE) proposed a practical definition of epilepsy[1] as a disease of the brain defined by any of the following conditions:

1. At least 2 unprovoked (or reflex) seizures occurring more than 24 hours apart.
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after 2 unprovoked seizures, occurring over the next 10 years.
3. Diagnosis of an epilepsy syndrome.

In 2017, ILAE updated the classification of seizures and epilepsy with an emphasis on etiologic classification[2,3]; this represents a significant change from the last classification in 1989. There are 3 levels of diagnosis in the new classification:

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1. Seizure type: focal onset, generalized onset, unknown onset (Fig. 1)
2. Epilepsy type: focal, generalized, combined focal and generalized, unknown (Fig. 2)
3. Epilepsy syndrome

ILAE recommends an attempt to determine the cause of patient's epilepsy at all 3 levels of diagnosis.

There are 6 etiologic groups identified: structural, genetic, infectious, metabolic, immune, and unknown. It is possible to have more than one cause in a patient.

CONCEPT OF EPILEPSY SYNDROME

An epilepsy syndrome is the third and final level of epilepsy diagnosis. An epilepsy syndrome is a specific set of seizure types and elecroencephalographic (EEG) and imaging features that tend to have age-dependent features, triggers, and often prognosis.[3]

NEED FOR A SYNDROMIC DIAGNOSIS (WHEN POSSIBLE)

1. Initiation of antiseizure medications (ASMs) and choice of ASM: Many age-dependent epilepsy syndromes have specific treatment implications. For example, many cases of benign epilepsy with centrotemporal spikes (BECTS) may not need treatment with ASMs. Childhood absence epilepsy (CAE) is typically treated with ethosuximide or valproic acid. Sodium channel blockers are contraindicated in Dravet syndrome (DS).

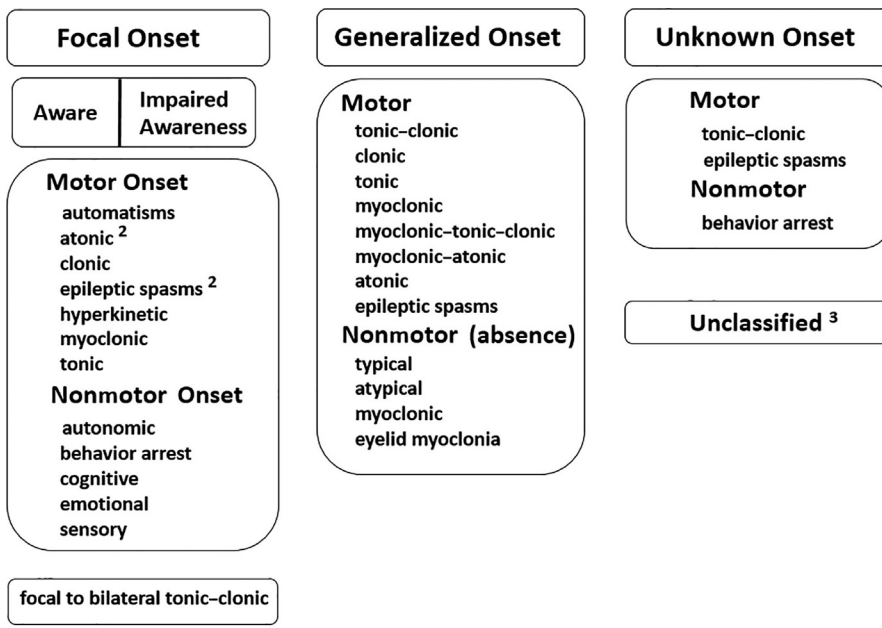

Fig. 1. ILAE classification of seizures (1).1- Definitions, other seizure types and descriptors are listed in the accompanying ILAE paper (2). 2- Degree of awareness usually is not specified. 3- Due to inadequate information or inability to place in other categories.

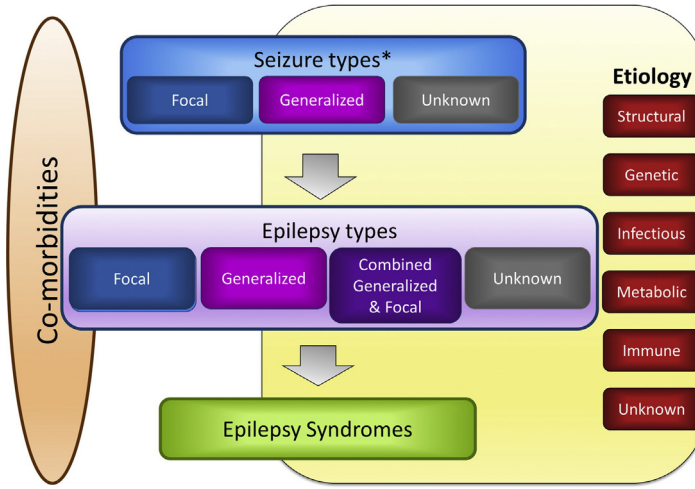

Fig. 2. ILAE classification of epilepsies.*Denotes onset of seizure.

2. Duration of treatment: Some epilepsy syndromes have age-dependent resolution, and hence its identification can guide duration of treatment. Most cases of CAE achieve seizure resolution by adolescence. Patients with juvenile myoclonic epilepsy (JME) typically need treatment for a long duration, many times lifelong.
3. Prognosis: Identification of an epilepsy syndrome may have prognostic implications. The outcomes of BECTS and PS are generally considered favorable, although neuropsychological comorbidities have been increasingly identified in typical patients. The outcomes for West syndrome and Lennox-Gastaut syndrome (LGS) are generally poor, with most patients experiencing developmental delay and refractory epilepsy.

CLASSIFICATION OF EPILEPSY SYNDROMES

There is no formal classification for epilepsy syndromes by ILAE. However, informal methods of classification have been suggested, mainly by age.

1. By age: ILAE educational Web site www.epilepsydiagnosis.org classifies epilepsy syndromes based on age[4] (**Table 1**)
2. By outcomes:
   - Self-limited, previously called benign, typically refers to epilepsy syndromes that often show spontaneous resolution. The term pharmacoresponsive is used for epilepsy syndromes that are well controlled on appropriately chosen ASMs. Examples include BECTS, CAE, and PS. The term benign is not recommended anymore given the concomitant cognitive abnormalities associated with these syndromes
   - Pharmacoresistant, previously called catastrophic or malignant. The term pharmacoresistant is not officially recognized by ILAE, but it is a logical opposite to the term pharmacoresponsive. These epilepsy syndromes typically do not show spontaneous resolution and often meet criteria for refractory epilepsy, with many associated with poor developmental outcomes (epileptic and developmental encephalopathy). Examples include West syndrome and LGS.

Table 1
Epilepsy syndrome classification based on age

Neonatal/Infantile Onset	Childhood Onset	Adolescent/Adult Onset	Any Age
Self-limited neonatal seizures and self-limited familial neonatal epilepsy	Epilepsy with myoclonic atonic seizures	Juvenile absence epilepsy	Familial focal epilepsy with variable foci
Self-limited familial and nonfamilial infantile epilepsy	Epilepsy with eyelid myoclonia	Juvenile myoclonic epilepsy	Reflex epilepsies
Early myoclonic encephalopathy	Lennox-Gastaut syndrome	Epilepsy with generalized tonic-clonic seizures alone	Progressive myoclonic epilepsies
Ohtahara syndrome	Childhood absence epilepsy	Autosomal dominant epilepsy with auditory features	
West syndrome	Epilepsy with myoclonic absences	Other familial temporal lobe epilepsies	
Dravet syndrome	Panayiotopoulos syndrome		
Myoclonic epilepsy in infancy	Childhood occipital epilepsy		
Epilepsy of infancy with migrating focal seizures	Photosensitive occipital lobe epilepsy		
Myoclonic encephalopathy in nonprogressive disorders	Childhood epilepsy with centrotemporal spikes		
Febrile seizures plus, genetic epilepsy with febrile seizures plus	Atypical childhood epilepsy with centrotemporal spikes		
	Epileptic encephalopathy with continuous spike and wave during sleep		
	Landau-Kleffner syndrome		
	Autosomal dominant nocturnal frontal lobe epilepsy		

KEY FEATURES OF EPILEPSY SYNDROMES COMMONLY SEEN IN GENERAL NEUROLOGY PRACTICE

In the following sections, we describe salient features of common pediatric epilepsy syndromes. Description of all epilepsy syndromes is beyond the scope of this article.

WEST SYNDROME

Introduction: West syndrome is described as a triad of epileptic spasms (ES), hypsarrhythmia on EEG, and psychomotor regression. The term ES is now interchangeably used with infantile spasms because whereas more than 85% of patients have onset in infancy, some have onsets after infancy. It is rare to have onset of ES beyond 2 years of age. West syndrome is not rare, and the incidence is 2 to 4 per 1000 live births.[5]

Clinical features: The main seizure type in West syndrome is ES. These seizures are clinically seen as brief, flexor, extensor, or mixed axial jerks typically occurring in clusters on awakening from sleep. The child may cry typically after the spasm but occasionally before. In early and/or treated cases, ES can be subtle and can just consist of a head nod or eye roll.

EEG features: The interictal EEG feature of West syndrome in most patients is hypsarrhythmia. There is no consensus definition for hypsarrhythmia, but cardinal features agreed upon by most neurophysiologists include a high-voltage background slowing (typically >200 μV), frequent or abundant multifocal spikes, and disorganization of the background (**Fig. 3**). The last parameter is highly subjective and leads to poor interrater reliability in diagnosis.[6] The ictal patterns with ES can be variable but classically seen as a slow wave of medium to high amplitude followed by diffuse flattening; an electrodecrement, considered the most important feature; and fast activity (**Fig. 4**). The "x" denotes when the mother reported the spasm.

An initial 24-hour study capturing extended sleep is recommended in most patients suspected of having ES to capture ictal events and to look at extended sleep samples, as hypsarrhythmia may only be present in certain sleep segments.[5]

Diagnosis: The diagnostic approach to a patient with West syndrome starts with understanding the different etiologies. Broadly, patients can be subdivided into

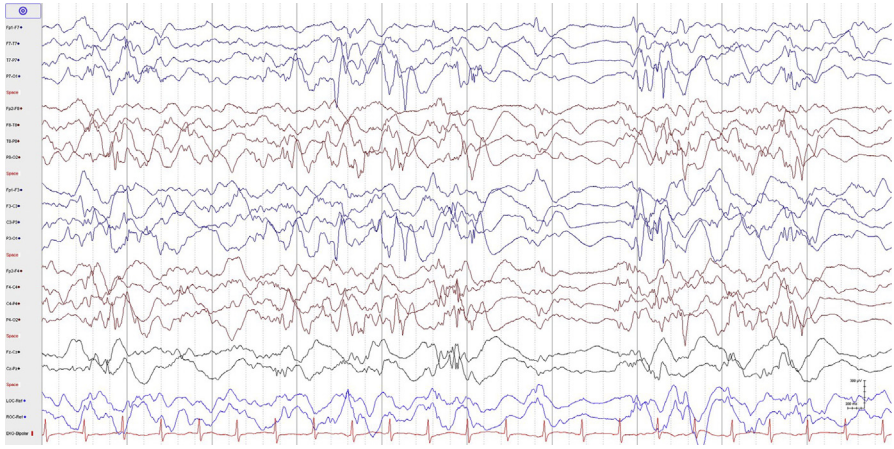

Fig. 3. Hypsarrhythmia EEG showing high-voltage, disorganized background with multifocal spikes.

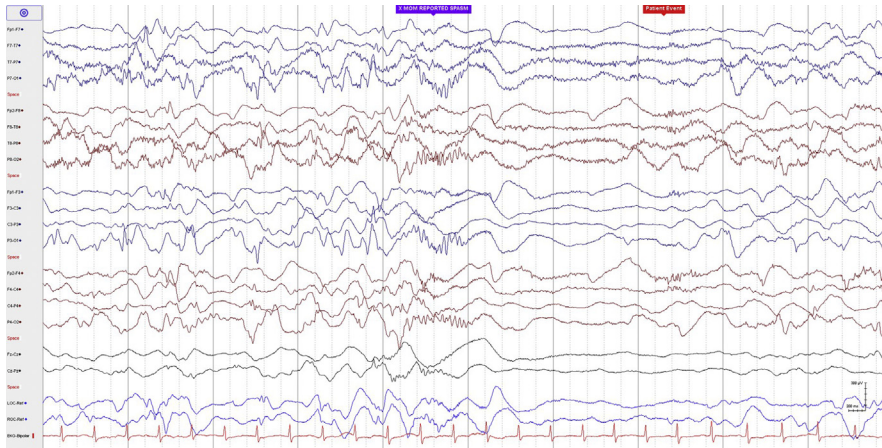

Fig. 4. Epileptic spasm ictal EEG with high-voltage slow wave, followed by flattening (electrodecrement). The "x" denotes when the mother reported the spasm.

symptomatic (with known etiology, 60%–70% of cases) or cryptogenic (without known etiology, 10%–40% of cases). In the symptomatic group, structural central nervous system abnormalities are the most common followed by genetic and metabolic.

After a thorough history and physical examination, an MRI of the brain is the highest yield study, followed by a genetic workup usually in the form of an epilepsy genetic panel with a chromosomal microarray. Depending on the clinical suspicion and outcome of initial workup, other studies, including spinal tap, metabolic studies, and further genetic work can be considered.

Management: Treatment of ES falls under 2 broad categories: hormonal (injectable or oral steroids) and vigabatrin. Vigabatrin is the preferred treatment in patients with tuberous sclerosis complex. For most other patients, hormonal therapy is the preferred initial method, especially in cryptogenic patients, in whom the outcomes have been shown to be better with hormonal treatment.[7] It should be noted that short-term outcomes (cessation of spasms at 2–6 weeks) is better with hormonal treatment[8] but long-term outcomes (at 2 years of age) are the same.[7]

For reference, the protocol used at Texas Children's Hospital is attached (**Fig. 5**A). A follow-up EEG (preferably an overnight study) is recommended at 2 weeks to assess response. Response is graded as an all-or-none phenomenon, with complete cessation of ES and resolution of hypsarrhythmia.[5]

Although adrenocorticotropic hormone has been the preferred hormonal treatment, studies have now shown comparable efficacy of high-dose oral steroids in treatment of ES[9]; this has been added as an option to our treatment protocol (**Fig. 5**B).

More recently, data have suggested combination therapy (hormonal treatment with vigabatrin) to be superior, at least to short-term to individual therapy alone, albeit with more risks for side effects.[10]

Early epilepsy surgery may be curative in patients who are good surgical candidates. Standard ASMs are generally not effective, although ketogenic diet may be of more benefit.

Prognosis: The prognosis of West syndrome is guarded and depends on the underlying cause. A significant majority (80% or more) of patients with West syndrome will have intellectual disability[5] and even more will have active epilepsy, although ES usually cease by 3 to 5 years and many evolve into LGS.

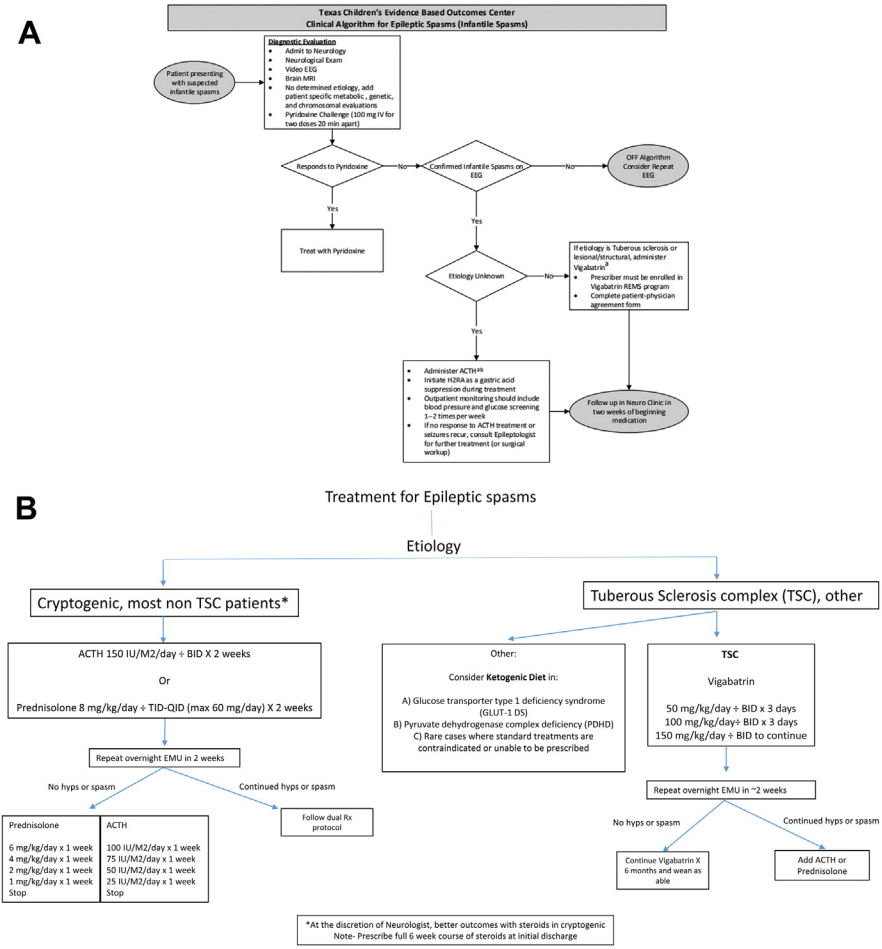

Fig. 5. (*A*) Clinical algorithm for epileptic spasms at Texas Children's Hospital. (*B*) Treatment algorithm for epileptic spasms at Texas Children's Hospital.[a] Dose per table 5b, [b] can also consider prednisolone.

LENNOX-GASTAUT SYNDROME

Introduction: LGS is also classified as an epileptic and developmental encephalopathy. The classic triad of LGS is multiple seizure types, including tonic, atonic, myoclonic, atypical absence seizures; interictal findings of slow spike wave complexes; and associated intellectual disability. Age of onset is typically between 3 and 5 years, and many cases evolve from a prior diagnosis of West syndrome.

Clinical features: Tonic seizures are the most common and characteristic seizure type of LGS. These seizures are seen as sustained axial or appendicular muscle contractions that may last for a few seconds to a few minutes. These seizures are often subtle and frequent in sleep. Atonic seizures (drop attacks) can be seen in up to 50% of patients. Atypical absence seizures, usually seen as alteration of awareness that has a gradual onset and termination (thereby distinguishing from typical absence seizures), are also frequent and may result in nonconvulsive status epilepticus (NCSE).[11] Myoclonic seizures, generalized tonic-clonic seizures (GTCSs), and focal seizures are also seen.

EEG features: The hallmark interictal finding in LGS are slow spike wave complexes, seen typically as bilaterally synchronous 1- to 2-Hz diffuse spike wave complexes, often occurring in prolonged runs and may be associated with atypical absence seizures and NCSE (Fig. 6). Bursts of paroxysmal fast rhythms in the 10 to 20 Hz range (typically generalized, hence called generalized paroxysmal fast activity) are seen in sleep and are also the ictal signature of tonic seizures (Fig. 7). The notation indicates that the eyes are open wide and deviated. Most experts believe the presence of paroxysmal fast activity during sleep, which may or may not be associated with tonic seizures, to be present to establish a diagnosis of LGS.

Diagnosis: Diagnosis typically requires overnight video-EEG monitoring to characterize ictal and interictal patterns. MRI of the brain and genetic testing will result in diagnostic yield in most patients.

Management: A 2013 Cochrane review for treatment of LGS concluded that the optimal treatment of LGS is uncertain and no study to date has shown any one drug to be highly efficacious; lamotrigine, rufinamide, topiramate, and felbamate may be helpful as add-on therapy.[12] Expert opinions identify valproic acid as one of the most commonly used agent for LGS, although it is not specifically licensed for its use. Clobazam is considered highly effective for atonic seizures. Felbamate is considered to be one of the most effective medications for treatment of seizures in LGS, but use is reserved for refractory patients owing to increased risk for aplastic anemia and liver failure.[13] More recently, cannabidiol has been approved for the treatment of seizures in LGS and is an increasingly popular choice. Ketogenic diet remains an effective nonpharmacologic option. Vagus nerve stimulator and corpus callosotomy (for atonic seizures) are effective surgical options in refractory cases. Focal resective surgery, especially in the presence of a single or unilateral lesion, should be considered, at times on a palliative basis, even if no convincing lateralizing ictal or interictal features are found.[14]

Prognosis: Most patients with LGS continue to have refractory seizures and intellectual disability into adulthood, although many evolve from a generalized to a focal epilepsy syndrome.

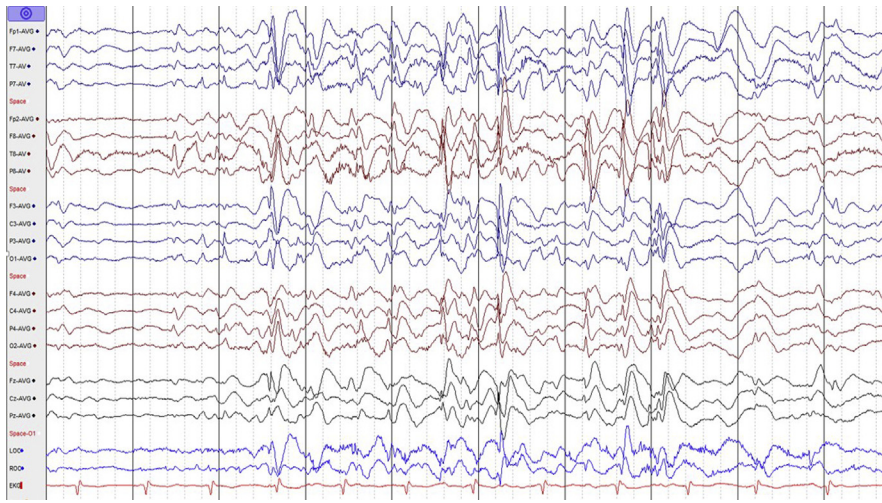

Fig. 6. Lennox-Gastaut syndrome, interictal EEG with "slow spike-wave".

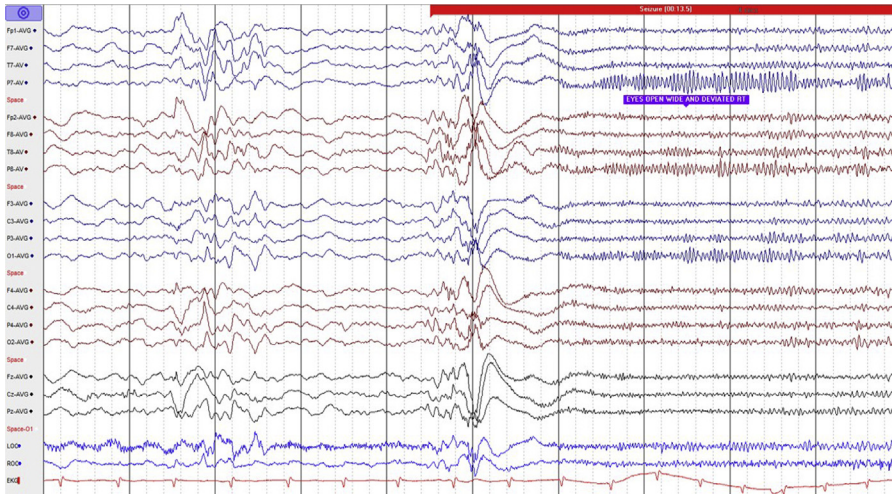

Fig. 7. Lennox-Gastaut syndrome, ictal EEG, with electrodecrement and fast activity. Notation of eyes open wide and deviated to right.

DRAVET SYNDROME

Introduction: DS (previously known as severe myoclonic epilepsy of infancy) is an early-onset medically intractable epilepsy syndrome that typically presents during the first year of life and causes an epileptic encephalopathy. The incidence of DS is estimated at 1 per 22,000 to 40,000, and it affects males twice as often as females.[15] The clinical diagnosis is supported by the presence of abnormalities in the sodium channel gene SCN1A (found in 70%–80% of cases).[16]

Clinical features: This syndrome is characterized by onset of seizures typically around 6 months of age. The seizure type consists of prolonged, febrile, and afebrile hemiclonic or generalized clonic seizures in a previously healthy child, often resulting in status epilepticus. Seizures are often provoked by fever or immunizations. Over the subsequent months, affected individuals experience recurrent febrile and afebrile seizures that often affect alternate sides of the body. Between 1 and 4 years of age, other seizure types develop, including myoclonic and atypical absences, focal seizures, and GTCS. In some individuals, myoclonic seizures do not develop and other seizure types, particularly focal or multifocal seizures, are the predominant seizure types.

Seizures tend to become less frequent and less severe in adolescence and adulthood. The most common seizure type in adulthood is generalized tonic-clonic, which may be focal in onset and occurs mainly during sleep.[17]

Head size and neurologic examination are usually normal initially; over time ataxia (60%), pyramidal signs (20%), uncoordinated movements, and interictal myoclonus may develop.[18] Neurodevelopment is typically normal in the first year of life followed by decline later on.

EEG features: EEG is typically normal during the first year of life. Subsequently, the EEG background may be slow. Generalized spike and polyspike wave and multifocal spikes usually develop by the second to fifth years of life. A photoparoxysmal response may be seen.

Diagnosis: DS is a clinical diagnosis that should be suspected in an infant younger than 1 year with repeated and prolonged febrile and afebrile seizures.[18] The presence

of SCN1A mutation provides a strong argument, as well as other genetic abnormalities (PCDH19, GABRG2, SCN1B, and SCN2A) that may cause a similar phenotype as DS.

Neuroimaging is usually normal at onset.

Management: Goal of treatment is to significantly reduce seizure frequency, particularly of prolonged seizures, because a greater degree of cognitive and behavioral impairment has been linked to a higher frequency of both convulsive and nonconvulsive seizures.

With regard to emergency rescue, a benzodiazepine would be first line for home including intranasal midazolam or intranasal or rectal diazepam. In patients with DS, it is reasonable to indicate use of emergency medication immediately rather than wait a customary period of time. Subsequent second-line medication may depend on previous response of an individual to such medication, as well as local protocols.

For chronic treatment, first-line ASMs are valproic acid and clobazam. However, most children will require addition of a second-line agent. At present, most epileptologists consider stiripentol, topiramate, or the ketogenic diet as the best second-line options for patients who continue to experience poor seizure control despite valproic acid and clobazam.[19] Cannabidiol and fenfluramine are recently approved and are being increasingly used as second-line agents.[6] Third-line agents include addition of an antiepileptic drug, such as clonazepam, levetiracetam, zonisamide, ethosuximide (for atypical absence seizures), and phenobarbital, or consideration of vagus nerve stimulator.[20] Sodium channel blockers such as lamotrigine, carbamazepine, oxcarbazepine, and phenytoin may worsen seizures.

Prognosis: Children with DS have high mortality, and death may be due to status epilepticus, sudden unexpected death in epilepsy (up to approximately 15-fold higher than in those with other childhood epilepsies), or accidental death, and it may also be related to seizures associated with drowning or injury.[15] Most patients with DS will have moderate to severe delay into adulthood.

PANAYIOTOPOULOS SYNDROME

Introduction: Panayiotopoulos syndrome (PS) is an early childhood epilepsy with focal autonomic seizures that are often prolonged with EEG that shows shifting and/or multiple foci, often with occipital predominance.[21,22] Onset is between 3 and 6 years of age.[23] The prevalence of PS is 13% among early-onset epilepsies and 6% in children between 1 and 15 years.[23]

Clinical features: Autonomic seizures and autonomic status epilepticus are hallmark of the disease, in a normally developing child. These usually present with a full triad of nausea, retching, and vomiting that occurs in 80% of patients.[24] Other autonomic features include pupillary (especially mydriasis), circulatory (pallor, cyanosis), thermoregulatory, and cardiorespiratory changes. Most seizures start in sleep. Seizures are often prolonged (minutes to hours), constituting NCSE (lasting more than 30 minutes). However, the child recovers without residual neurologic or cognitive deficit. As the seizure evolves, other more conventional epilepsy manifestations appear, such as loss of responsiveness and head and eye deviation, and hemiclonic activity may develop.

Seizures are infrequent in most patients, with 25% having a single seizure and 50% having 6 seizures or less. Seizures usually resolve by age 11 to 13 years.

EEG features: The background EEG is normal. The interictal EEG is characterized by sleep-potentiated multifocal high-voltage, repetitive spikes and sharp waves in 90% of patients, with occipital spikes seen in 60% of patients (**Fig. 8**).

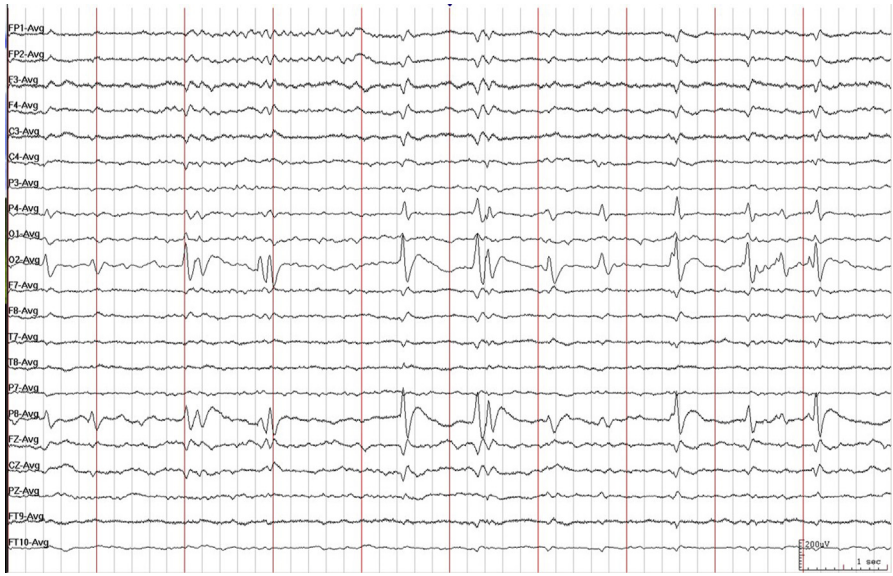

Fig. 8. Panayiotopoulos syndrome EEG with high-amplitude, occipital spikes.

Diagnosis: PS is a clinical diagnosis, supported by EEG findings. Neuroimaging is typically normal.

Management: Prophylactic treatment with ASM may not be needed for most patients because of infrequent seizures. Most neurologists treat recurrent seizures with ASMs such as carbamazepine, oxcarbazepine or levetiracetam.

Prognosis: PS has a good prognosis. Remission often occurs within 1 to 2 years of onset.

CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

Introduction: Childhood epilepsy with centrotemporal spikes, also referred to as BECTS or Rolandic epilepsy is the most common childhood epilepsy syndrome accounting for 15% to 20% of all epilepsies in children. Mean age of onset is between 6 and 9 years.

Clinical features: Presentation is with nocturnal focal aware seizures corresponding to the origin in the Rolandic (centrotemporal) cortex, manifesting as hemifacial sensorimotor seizures with associated gurgling and hypersalivation and speech arrest. Focal to bilateral tonic-clonic seizures may occur in up to 50% of patients.[25] The term benign is not preferred now because of association with cognitive dysfunction in most patients, including attention and memory impairment and learning difficulties,[26] and is not necessarily related to seizure control.

Atypical evolutions may be seen in a significant minority of patients (9%–50%, depending on the criteria used). These evolutions may vary from status epilepticus, Landau-Kleffner syndrome, electrical status epilepticus in sleep (ESES), epileptic encephalopathy with continuous spike and wave during sleep, and atypical benign childhood focal epilepsy.[27] The classic atypical variant was first described in 1982[28] and evolves from a typical focal epilepsy presentation into a generalized epilepsy syndrome, with atypical absence and atonic and negative myoclonic seizures.

EEG features: The classic interictal epileptiform abnormality is a biphasic discharge characterized by a prominent, negative sharp wave with a relatively rounded peak, at times preceded by a short-duration positive prespike and followed by a prominent positive sharp wave (amplitude up to 50% of the preceding negative sharp wave).[29] The later negative slow wave is often subtle and lower in amplitude than the preceding negative sharp wave. Location is in the centrotemporal region with a positivity in the frontal region, commonly referred to as a tangential dipole. Discharges can be unilateral or bilateral, independent or bilateral synchronous, and sleep potentiated as a rule (**Fig. 9**).

Diagnosis: A careful history and classic EEG findings are sufficient for diagnosis in most patients. Neuroimaging is generally not indicated, unless there are atypical features on history and examination or on EEG, such as focal slowing.

Management: Many patients do not need ASMs, which are indicated if seizures are frequent or have multiple convulsive seizures. Carbamazepine, levetiracetam, and oxcarbazepine are the most commonly used ASMs. However, in patients with atypical evolution, carbamazepine and phenobarbital may precipitate ESES and/or generalized seizures[30] and hence broad-spectrum ASMs such as valproic acid and benzodiazepines are preferred.

Prognosis: This is considered a self-limited epilepsy with most patients experiencing remission within 2 to 4 years of onset, almost always after puberty.

CHILDHOOD ABSENCE EPILEPSY

Introduction: CAE is the second most common pediatric epilepsy syndrome after BECTS. CAE is an idiopathic/genetic generalized epilepsy syndrome characterized mainly by typical absence seizures. Age of onset is between 4 and 10 years, and children usually have normal development. However, cognitive abnormalities are commonly found in these patients.

Clinical features: The prototypical seizure in CAE is a typical absence seizure, characterized by a brief (usually 5–10 seconds), sudden impairment of awareness, often

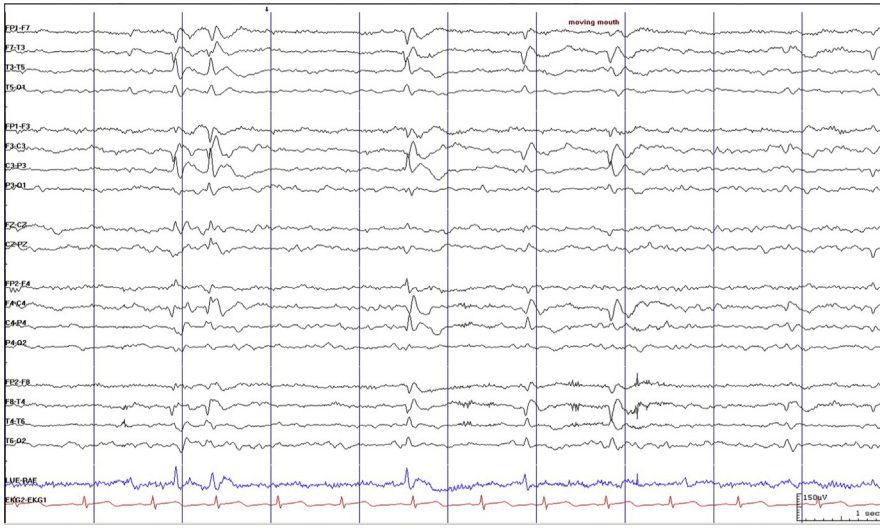

Fig. 9. Childhood epilepsy with centrotemporal spikes EEG, showing the tangential dipole.

noticed by caregivers as a staring episode from which the child is not distractible. Oral automatisms and eye movements are common. Seizures happen multiple times a day. Seizures can be easily provoked by hyperventilation, leading to a provisional diagnosis in many patients at the office visit.

Presence of other seizure types during the active stages of absence seizures is considered exclusionary for CAE. However, a significant minority (12%) of patients with CAE may develop generalized tonic-clonic seizures later during the course,[31] often after remission from absence seizures. Diagnostic criteria for CAE have been proposed by Panayiotopoulos[23] and are widely accepted.

Children with CAE commonly have significant attention issues,[32] anxiety, behavioral dyscontrol, and cognitive, emotional, and language problems. These deficits can persist despite adequate seizure control by ASMs.

EEG features: Classic ictal EEG findings with absence seizures are 3-Hz generalized spike waves, although they may vary in frequency from 2.5 to 3.5 Hz (usually faster at onset and slower at termination) (**Fig. 10**). The figure indicates that the eyelids are fluttering. Interictal background is normal, and occipital intermittent rhythmic delta activity may be seen (**Fig. 11**). NCS refers to no clinical signs.

Diagnosis: History and EEG are usually sufficient for diagnosis. Neuroimaging is not needed in typical cases. Testing for glucose transporter-1 (GLUT-1) should be considered in early-onset absence seizures, even in the absence of other typical clinical features of GLUT-1.

Management: The drug of choice for CAE is ethosuximide followed by valproic acid and lamotrigine.[33] Ethosuximide and valproic acid have comparable efficacy, but ethosuximide has a better side effect profile and a lower risk for attention issues. Other medications such as levetiracitam, topiramate, acetazolamide have been studied but are generally considered less effective. Ketogenic diet therapies have good efficacy

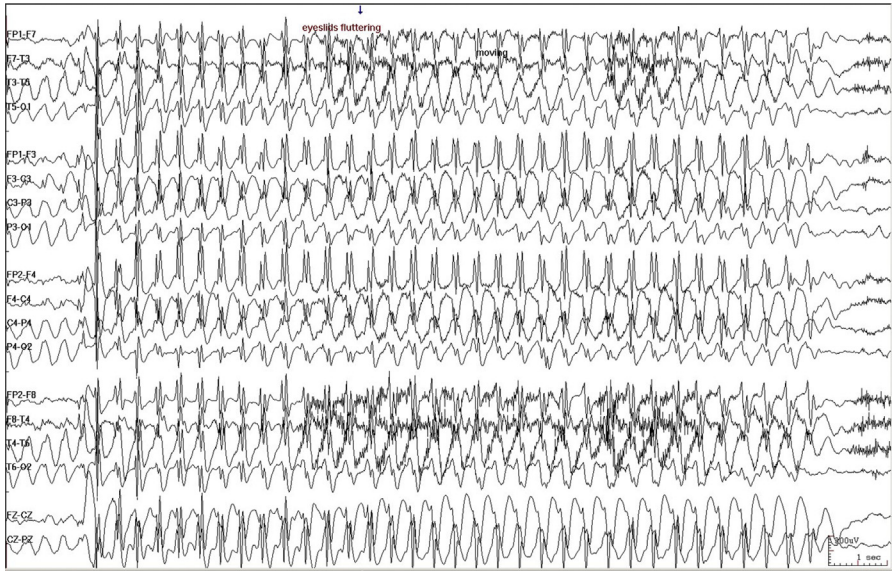

Fig. 10. Childhood absence epilepsy ictal EEG showing 3-Hz spike-and-wave seizure, with notation of eyelids fluttering.

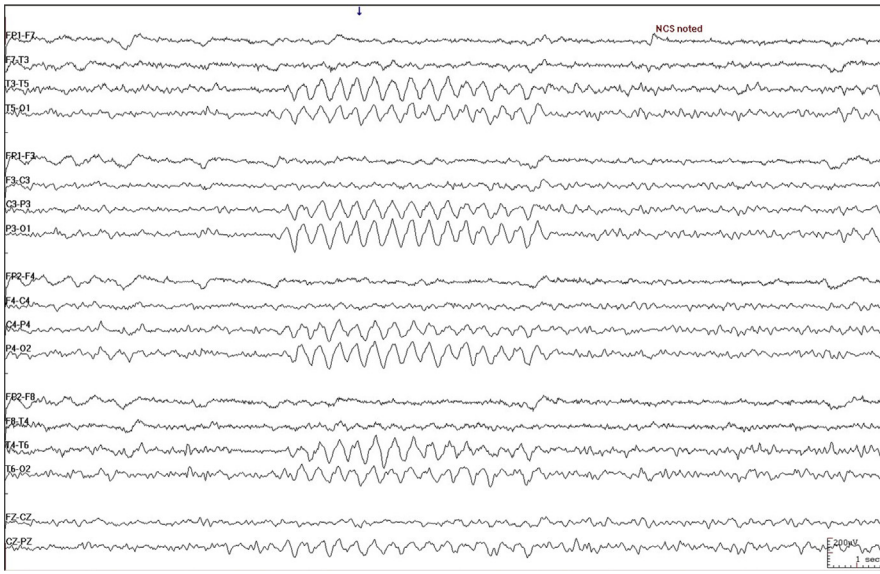

Fig. 11. Childhood absence epilepsy interictal EEG showing occipital intermittent rhythmic delta activity. The notation NCS refers to no clinical signs.

and should be considered in refractory cases after combination therapy with first-line agents has failed.

Prognosis: Seizure remission often occurs by puberty, but some patients may develop GTCS in adolescence. Behavioral problems may persist despite remission of absence seizures.

JUVENILE MYOCLONIC EPILEPSY

Introduction: JME is one of the most common genetic/idiopathic generalized epilepsies (IGEs).[3] JME is characterized by myoclonic seizures (97% of patients), GTCSs (58%), absence seizures (9%), or all 3 seizure types (21%).[34] Onset is typically around puberty. Prevalence is 8% to 10% among adult and adolescent patients with epilepsies.[23]

Clinical features: Presentation is with myoclonic seizures and GTCSs shortly after awakening from sleep in a normally developing adolescent. Myoclonic seizures can be subtle or severe, and the patient may drop objects or fall. These usually occur in clusters and often with an accelerating frequency and severity may precede a GTCS, as the so-called myoclonic-tonic-clonic generalized seizure.[35] Sleep deprivation and fatigue, particularly after excessive alcohol intake, are precipitants of myoclonic jerks and GTCSs.

EEG features: The background is normal. The interictal EEG is characterized by sleep-potentiated fast generalized spike and polyspike wave discharge, usually at 3.5 to 6 Hz (**Fig. 12**). The figure shows a fast spike and wave and polyspikes. The typical EEG discharge of myoclonic jerk is a single generalized burst of polyspike and wave discharges. Absence seizures are associated with regular fast (3.5–6 Hz) generalized spike and polyspike wave discharges. In one-third of cases, a photoparoxysmal response to intermittent photic stimulation is seen. Hyperventilation may

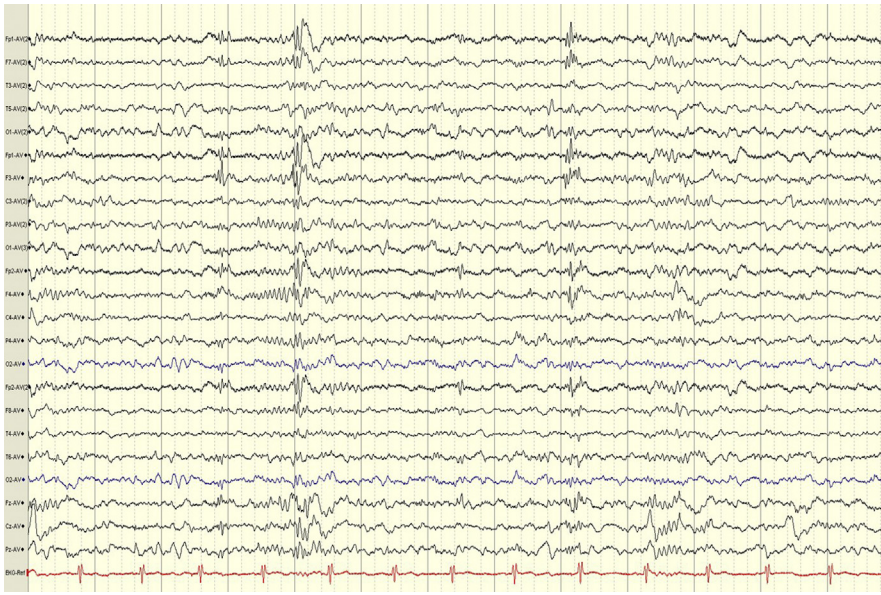

Fig. 12. Juvenile myoclonic epilepsy interictal EEG showing a fast spike and wave and polyspikes.

augment epileptiform discharges, although less reliably than in CAE or juvenile absence epilepsy.

Diagnosis: JME is a clinical diagnosis, supported by EEG findings. Neuroimaging is typically normal.

Management: Valproic acid is still considered the first-choice treatment, which is effective in 80% of the cases.[36] Levetiracetam and lamotrigine are alternative first choices in women of child-bearing age. Lamotrigine may exacerbate myoclonus, which may be prevented by the addition of clonazepam. Other add-on treatments if the first-line treatment fail are topiramate, zonisamide, clobazam, and acetazolamide. Vagal nerve stimulation may be considered as a last resort in pharmacoresistant cases.[36]

Several ASMs are contraindicated in JME including phenytoin, carbamazepine, oxcarbazepine, gabapentin, pregabalin, tiagabine, and vigabatrin because they can exacerbate myoclonic jerks in JME.

Prognosis: Most patients can achieve complete seizure control through a combination of ASM and adequate sleep. JME is considered a lifelong condition in which taper of ASMs should not be considered.

DISCLOSURE

The authors have nothing to disclose.

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