
In The Name of God

Generalized epilepsy

Soroor Inaloo

Pediatric neurologist

Shiraz university of medical sciences

Diagnosis of generalized epilepsy

The patient would typically show generalized spikewave activity on EEG. Individuals with generalized epilepsies may have a range of seizure types including absence, myoclonic, atonic, tonic and tonic-clonic seizures.

The diagnosis of generalized epilepsy is made on clinical grounds, supported by the finding of typical interictal EEG discharges.

Caution needs to be exercised for a patient with generalized tonicclonic seizures and a normal EEG. In this case, supportive evidence would need to be present to make a diagnosis of generalized epilepsy, such as myoclonic jerks or a relevant family history

Idiopathic generalized epilepsy
Genetic generalized epilepsy

IGEs encompass four well-established epilepsy syndromes:

- Childhood Absence Epilepsy,
- Juvenile Absence Epilepsy,
- Juvenile Myoclonic Epilepsy
- Generalized Tonic-Clonic

Generalized seizure

- Primarily generalized seizures are those in which the first clinical changes indicate initial synchronous involvement of both hemispheres without clinical, electroencephalographic (EEG), or other evidence of focal onset
- Impairment of consciousness is usual during generalized seizures, although some seizures, such as myoclonic ones, may be so brief that the level of consciousness cannot be assessed
- primarily generalized seizures are reported to be less common than focal seizures
- Of the primarily generalized seizures, generalized tonic-clonic are the most common, followed by absence and myoclonic seizures

Generalized tonic clonic seizures

- Some children with GTC seizure, or their parents, are aware of the impending seizure hours or days before it occurs
- The child may have a headache, insomnia, irritability, or a change in appetite
- This prodrome is to be distinguished from an aura, which occurs before generalization of a seizure. Unlike the aura, the prodrome is not associated with any EEG epileptiform activity
- Generalized tonic-clonic seizures have two distinct phases: tonic and clonic
- Loss of consciousness usually occurs simultaneously or shortly after the onset of a generalized stiffening of flexor or extensor muscles
- The tonic phase typically lasts 10 to 30 seconds and is followed by the clonic phase, lasts 30 to 60 second
- Primary GTC can have version of the head and trunk or asymmetric myoclonus

Evaluation

- History
- Physical exam
- EEG
- Brain imaging :neuroimaging is recommended in all patients presenting with first unexplained GTC seizure
- Imaging of choice is brain MRI
- Comorbidity : depression .anxiety, cognitive impairment, learning disorder, ADHD and migraine
- Treatment : lamotrigine , sodium valproate. levetiracetam ,topiramate
- Second line :phenobarbital, lacosamide, zonisamide ,clobazam

Absence seizure (petitmal seizure)

- Characterized by an abrupt cessation of activity ,change in facial expression and impaired consciousness less than 30 seconds frequent attack
- Most absence seizures are accompanied by motor ,behavioral or autonomic phenomena automatism is common
- Clonic and myoclonic component are common but may be quite subtle (blinking, nystagmus head nod ,rapid jerking or trembling of the arm)
- Autonomic phenomena may be seen :
- Dilate pupils, pallor, flushing, sweating, salivation, even urinary incontinence
- Speech if it occurs during seizure usually preserve and may be slow and slurred
- Uncommon seizure less than 10 % of all type of seizure
- More common in age less than 10 years (4 – 10 y) with peak 6 – 7 years
- More common in girls than in boys
- Absence seizure can begin as early as the first year of life

Absence seizure

- Most children with absence seizure have normal or mildly low intelligence
- Mostly have lower general cognitive function ,with impaired visual –spatial skills and memory disturbances
- Have higher rates of ADHD ,behavioral problem , and psychological disorders
- 40 to 60 % of patients with absence seizure have GTC seizures mostly after onset of the absence seizures

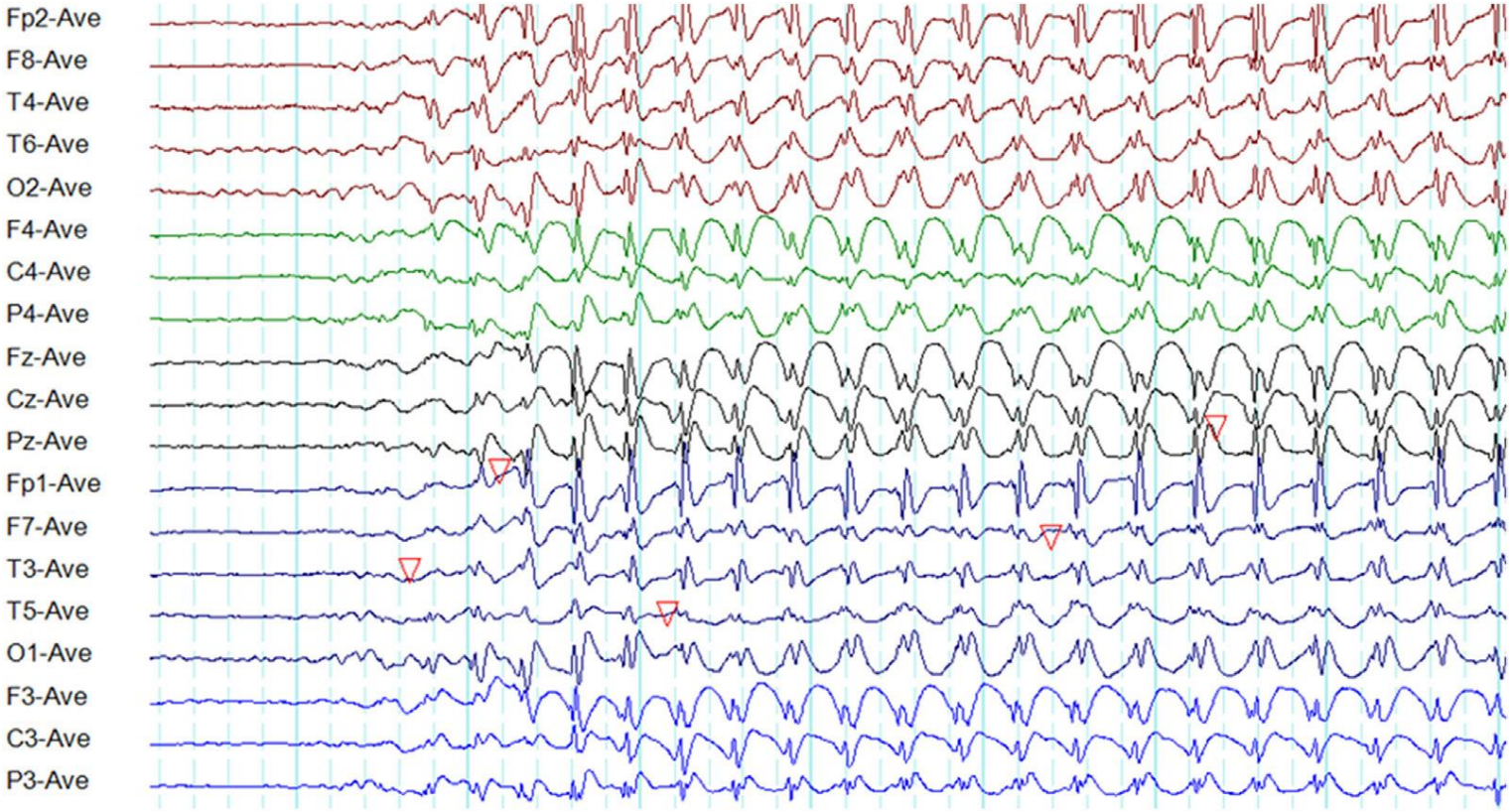
Evaluation in absence seizure

- History ,physical exam
- 3 minute hyperventilation
- EEG with hyperventilation and photic stimulation
- **Neuroimaging indicated in patients with** :
- Developmental delay
- Abnormal neurologic exam
- History suggestive of atypical absence
- EEG showing slow spike waves less than 2.5 HZ discharge
- Focal epileptiform discharge
- In patients with refractory absence : metabolic test ,LP(GTT 1 deficiency)

EEG in absence seizures

- Typical EEG :sudden onset of 3 HZ generalized symmetric spike and waves or multiple spike –waves complex
- Maximal voltage in the frontal –central region
- Frequency faster (4HZ)in onset and may slow (2HZ) toward the end of discharge lasting longer than 10 second
- Hyperventilation is a potent activator of typical absence
- Photic stimulation precipitate seizures
- Failure of response to HV (3-5 min) in untreated child with absence would make the DX of absence unlikely
- EEG in atypical absence : ictal 1.5 - 2.5 HZ slow spike and waves or multiple spike and waves discharge may be irregular or asymmetric and interictal background abnormal slowing with multifocal epileptiform discharges

EEG of typical absence seizure

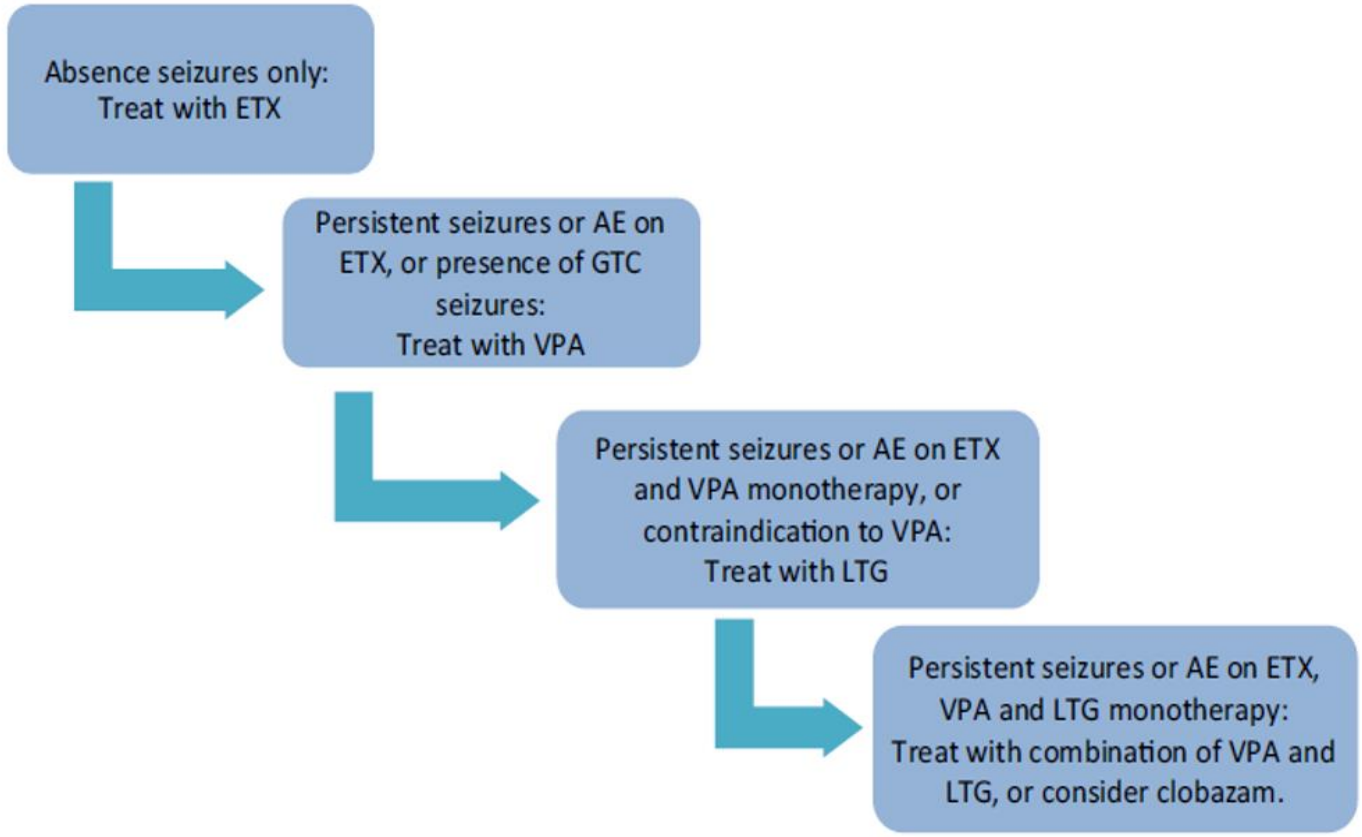


Treatment

- Drug of choice in absence seizure : Ethosuximide, valproate, lamotrigine, levetiracetm? , clobazam, topiramate, zonisamide
- ETX syrup (250 mg/mL) or a capsule (250 mg). The initial target dosage of ETX is 20–30 mg/kg/day, usually divided into two doses, initial dosage 10 mg/kg/day with upward titration to the target every week to 50 mg/kg
- The capsules can be frozen and then cut in half
- VPA is the drug of choice as initial monotherapy in CAE when a generalized tonic– clonic seizure has occurred, or when ETX failed
- Gabapentine, oxcarbazepine, carbamazepine, phenytoin, phenobarbital, tiagabine, and vigabatrin may worsen absence seizures or cause absence status epilepticus and should be avoided

Proposed treatment algorithm for CAE

Fig. 2 Proposed treatment algorithm for childhood absence epilepsy. *AE* adverse effects, *ETX* ethosuximide, *GTC* generalized tonic–clonic, *LTG* lamotrigine, *VPA* valproic acid



Treatment Cont

- There is some evidence that suggests initial treatment with ETX is more often associated with remission than initial treatment with VPA
- The current widespread practice in CAE is to maintain patients on antiepileptic medication for 2 years after achieving seizures
- At the end of these 2 years, an EEG can help determine risk of relapse with medication withdrawal

Prognosis

- Two third of child with absence seizure can be expected to enter long term remission
- approximately 2/3 to 3/4 of children with CAE responded to the first or second treatment
- **Favorable prognostic signs** :
- Negative family HX of epilepsy
- Normal EEG background activity
- Normal intelligence
- Onset of GTC seizure before absence seizure is a poor prognostic factor
- 15 % of children with CAE will develop to JME

Juvenile absence

- Occurs in children 10–15 years old and is characterized by less frequent absence seizures (sometimes occurring a few times dailyor less than daily) as well as the occurrence of generalized
- tonic–clonic seizures in 80% or more of children with the juvenile absence
- EEG :The spike-wave discharge frequency in juvenile absence epilepsy (JAE) (mean 3.25 Hz) is faster than childhood absence epilepsy (CAE) and slower than JME

Juvenile myoclonic epilepsy

- Juvenile myoclonic epilepsy (JME) is the most common epilepsy type that affects adolescents (5% of all epilepsies)
- It has been linked to mutations in many genes including CACNB4, CLNC2, EJM2,3,4,5,6,7,9, …..
- It is characterized by myoclonic jerks, predominantly after awakening, and may be aggravated by sleep deprivation alcohol stress and photic stimulation.
- The majority of patients experience occasional generalized tonic–clonic seizures (GTCS), and about one-third have absence
- Characterized by sudden onset ,brief(less than 350 microsecond) shock like contractions, may be generalized or confined to the face and trunk or extrimites

Inter ictal EEG in JME

- The classic EEG abnormalities in JME are generalized polyspike and polyspike-wave discharges
- The interictal EEG is characterized by 3–6 Hz spike and polyspike-wave discharges in an irregular mix
- Focal EEG abnormalities are common (45). PPR is seen in the majority

EEG in juvenile myoclonic epilepsy

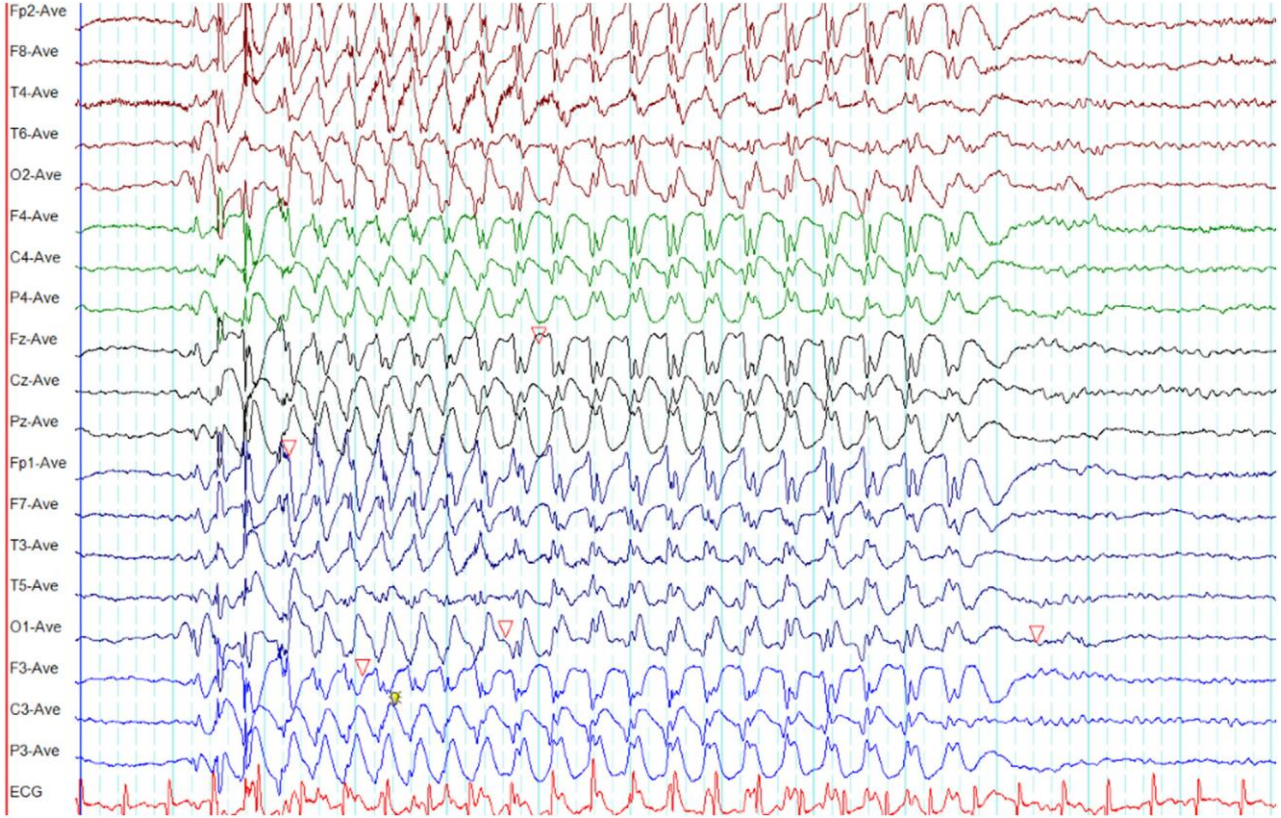
- Generalized spike-wave (GSW) activity is seen more often in non-rapid eye movement (NREM) sleep
- sleep deprivation significantly increases the density of spike-wave discharges in both sleep and wakefulness
- In JME, routine EEGs (without sleep deprivation) done in the morning are more often abnormal than those done in the afternoon
- In JME, sleep EEG always shows epileptiform discharges
- When quantified, 67% of epileptiform discharges are detected in NREM sleep whereas
- 33% occurs in wakefulness.
- The best time for the optimal yield of EEG abnormalities is from 11 p.m. to 7 a.m
- In untreated children, hyperventilation induces in 33% of JME

- The use of provoking stimuli such as sleep deprivation, intermittent photic stimulation, hyperventilation and reflex triggers during EEG recording can help increase the diagnostic yield
- Some EEG features help differentiation among electroclinical syndromes
- However, it should be emphasized that such differences are also influenced by several confounding variables including sex, age, state of alertness, activation methods, technical factors, and antiepileptic drug therapy

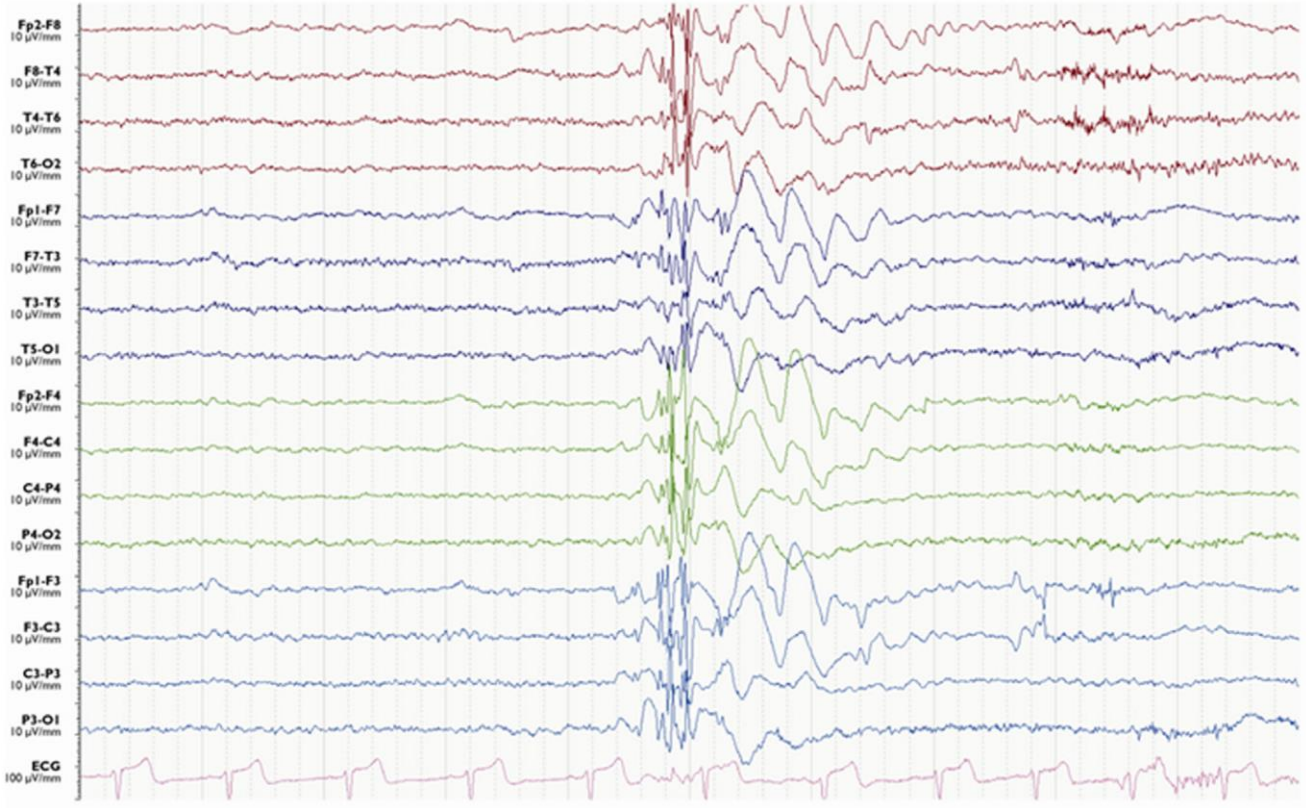
Treatment of JME

- According to clinical studies and evidence-based guidelines from the UK, initially valproate, then lamotrigine, levetiracetam, or topiramate are the main AEDs of choice in JME, even if the evidence is limited
- valproate and levetiracetam had significantly better efficacy against GTCS than lamotrigine
- Lamotrigine may be worsen myoclonic jerk
- The present study demonstrates that in a regular clinical setting, a large proportion of people with JME continue to experience occasional myoclonic jerks

EEG of myoclonic absence



EEG of myoclonic seizure



Thanks for your Attention