Seizures and Epilepsy

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1 Overview

An epileptic seizure represents the uncontrolled, abnormal electrical activity of the brain that may cause changes in the level of consciousness, behavior, memory, or feelings. An epileptic seizure, informally known as a seizure, is a period of symptoms due to abnormally excessive or synchronous neuronal activity in the brain. Outward effects vary from uncontrolled shaking movements involving much of the body with loss of consciousness (tonic-clonic seizure), to shaking movements involving only part of the body with variable levels of consciousness (focal seizure), to a subtle momentary loss of awareness (absence seizure). These episodes usually last less than two minutes and it takes some time to return to normal. Loss of bladder control may occur.

2 Introduction

An epileptic seizure is the clinical manifestation of an abnormal, excessive, and synchronized electrical discharge in the brain cells (neurons). The occurrence of two or more unprovoked seizures defines epilepsy.

Terms

1. **Seizures** are only one manifestation of neurologic or metabolic diseases. They are paroxysmal phenomenons caused by electric hyper-excitability of a group of neurons.

Seizures have many causes, including a genetic predisposition, head trauma, stroke, brain tumors, alcohol or drug withdrawal, hypoglycemia, and other conditions.

2. **Epilepsy**, however, is a medical disorder marked by recurrent (more than two), unprovoked seizures, usually due to an underlying chronic condition.

3. **Status epilepticus** is defined as an enduring epileptic condition. There are many types of status epilepticus. Generalized convulsive status epilepticus is a medical emergency. Current definitions define status epileptics as a single generalized convulsion lasting greater than five minutes or a series of generalized seizures without full return of consciousness.

3 Etiology

Seizures may be either provoked or unprovoked. Provoked seizures, also known as acute symptomatic seizures, may result from electrolyte disorders, toxins, head injury, infectious processes, vascular anomalies, tumors or other mass lesions, and many other causes. A listing of **provoked causes of seizures** is lengthy and could include complications of almost any disease process. Some common causes are listed below:

- Electrolyte disturbances (hypoglycemia, hyponatremia, hypernatremia, hypocalcemia, others)
- Acute toxic effects (antidepressants, sympathomimetics, others)
- Withdrawal syndromes (ethanol, benzodiazepines, others)
- Brain infections
- Hypoxic brain injury
- Traumatic brain injury
- Stroke, both ischemic or hemorrhagic
- Neoplasm
- Inflammatory (lupus cerebritis, anti-NMDA receptor encephalitis, others)
- Fever
- Sleep deprivation

Epilepsy occurs because of a predisposition to seizures from genetic susceptibility or a chronic pathologic process. By definition, unprovoked seizures occur in the absence of provocative causes or more than seven days after an acute injury or insult such as stroke or brain hemorrhage. Recurrent unprovoked seizures define epilepsy.

4 Epidemiology

About 25% to 30% of new-onset seizures are thought to be provoked or secondary to another cause. About 70-75% are idiopathic (unknown origin).

Epilepsy incidence is highest in younger and older age groups and increases steadily after 50 years of age. The most common cause of seizures and epilepsy in older people is cerebrovascular disease.

5 Pathophysiology

Everyone has some propensity to have seizures. The concept of a **seizure threshold** means that each individual exists on a seizure susceptibility continuum with many factors influencing that susceptibility. Medications, genetic factors, electrolyte abnormalities, sleep state, infections, brain inflammation, or injury from many causes may lead to an individual crossing that threshold with a resulting seizure.

On a cellular level, seizures start with the **excitation of susceptible cerebral neurons**, which leads to **synchronous discharges** of progressively larger groups of connected neurons. Neurotransmitters are undoubtedly involved. Glutamate is the most common excitatory neurotransmitter, and gamma-aminobutyric acid (GABA) is an important inhibitory neurotransmitter. An imbalance of excess excitation and decreased inhibition initiates the abnormal electrical activity. These **electrical paroxysmal depolarization** shifts seem to **trigger** epileptiform activity. Increased activation or decreased inhibition of such discharges could result in seizures. The part of the brain affected often reflects in the clinical signs or symptoms of the seizure.

Generalized convulsive status epilepticus is accompanied by systemic changes of lactic acidosis, increased catecholamine levels, hyperthermia, respiratory compromise, and other systemic alterations. However, the ongoing excessive electrical activity that occurs with status epilepticus is damaging to the brain.

6 Type of seizures

All seizures are divided into 2 subtypes: motor onset and non-motor onset. Both focal motor and focal non-motor onset seizures can be further classified based on level of awareness: conscious, and unconscious. Seizures occur due to an epileptogenic lesion, and then they can propagate or not. Some focal onset seizures can be preceded by an "aura", which refers to symptoms and signs that occur before the onset of seizure activity. These symptoms may include vision changes, dyspepsia, déjà vu, paresthesias, hearing disturbances, and sensation of abnormal taste or smell.

Partial or focal seizure

A focal onset seizure refers to abnormal neural activity in only one brain area within one brain hemisphere with a fixed focal or localized onset. They can be divided in:

1. Simple Partial Seizures
2. Complex Partial Seizures

The term **complex** means that the patient **loses consciousness**. **Simple** means that the patient **remains aware** (i.e., conscious).

Motor manifestations of focal motor onset seizures include abnormal movements, like the following:

- Tonic movements.
- Clonic movements are characterized by repeated, short contractions.
- Atonic movements are characterized by loss of tone in a limb.
- Myoclonic movements are characterized by irregular, nonrhythmic jerking of the limbs.

The clinical manifestations of **focal non-motor seizure** include autonomic, behavioral arrest, cognitive, emotional, or sensory symptoms:

- Changes in blood pressure, heart rate, sweating, skin color, or gastrointestinal upset.
- Behavioral arrest seizures are characterized by cessation of movement.
- Cognitive seizures are characterized by abnormal language or thinking, eg, jamais vu, déjà vu, hallucinations, and visualization of illusions.
- Emotional seizures are characterized by emotional changes such as fear, dread, anxiety, or pleasure.
- Sensory seizures are characterized by changes in sensation, such as abnormal sensations of vision, paresthesias, hearing, smell, or pain.

A focal seizure **can rapidly spread** and evolve into a bilateral tonic-clonic seizure, that is, **becomes a secondary generalized seizure**.

Generalized seizures

They result from diffuse cortical activation at seizure onset (**primarily generalized**) or generalization of partial seizure activity (**secondary generalized)**.

A generalized tonic-clonic seizure, also known as grand mal seizure, is defined as a seizure that has a tonic phase followed by clonic muscle contractions. Among patients, families, and observers, they are most feared of seizure types. They are usually associated with impaired awareness or complete loss of consciousness.

Absence seizures consists of generalized, non-convulsive seizures characterized by impairment of awareness and intermittently has other manifestations such as automatisms or subtle myoclonic, tonic, atonic, or autonomic phenomena.

Special types of seizures

1. **Absence seizures** are brief seizures characterized by a behavioral arrest. A genetic component exists. Absence seizures (also known as petit mal) are brief seizures during which the patient is unresponsive. They are generally seen in children between 4 and 12 years of age. Childhood absence epilepsy is a common pediatric epilepsy syndrome. Good prognosis, seizure freedom is reported up to 74
2. **Febrile seizures** are generalized seizures, typically in children between the ages of 6 months and 5 years, that occur with a fever greater than 38 °C not associated with a central nervous system infection, a known seizure-provoking etiology (eg, electrolyte imbalance, hypoglycemia, or substance abuse). There is a complex genetic predisposition, immaturity and vulnerability of the central nervous system, and various environmental factors. As a result of these various risk factors, the immature brain, with fever-enhanced neuronal excitation, is more susceptible to seizures.
3. **Juvenile Myoclonic Epilepsy**. Its characteristics are the presence of absence, myoclonic, and generalized tonic-clonic seizures. Seizures are usually well controlled with medications and generally improve after the fourth decade of life. But it requires lifelong treatment.
4. **Lennox-Gastaut Syndrome**. It is a rare but severe form of childhood epilepsy. It is characterized by a multiple seizure types, characteristic electroencephalogram findings, and intellectual impairment.

7 Evaluation

Further clinical evaluations are guided by history and physical examination. If the clinician believes that the event is a seizure, the first question is whether it is provoked or unprovoked. Typically laboratory work, including electrolytes, is obtained, and determining serum glucose and sodium is recommended. Lumbar puncture should merit consideration in patients with fever, a history of immunosuppression, or other factors suggesting possible central nervous system infection.

Neuroimaging is often obtained and is of higher yield based on historical factors or focal findings on the neurologic examination. Imaging is a recommendation whenever there is suspicion of an acute intracranial process in patients with a history of acute head trauma, history of malignancy, immunocompromise, fever, persistent headache, anticoagulation use, age older than 40 years, or focal seizure onset.

Electroencephalography (EEG) is a biomarker for epilepsy. Focal or generalized epileptiform discharges constitute the EEG hallmark of seizure activity. Frequently EEG is obtained as a risk-stratification tool for a patient with a seizure of possibility of seizures. Should the EEG show epileptiform or other abnormalities, management might change.

EEG is needed to accurately diagnose seizures and aid in the localization of seizure focus. If an EEG contains focal epileptiform discharges, it is imperative to obtain brain imaging with magnetic resonance imaging (MRI) to determine the presence and location of structural abnormalities.

8 Treatment

Patients with reversible causes of seizures, such as hypoglycemia, may be discharged after appropriate correction of the abnormalities. Testing for medication levels may be appropriate if available for the particular antiepileptic drug. If the patient has been noncompliant with an antiepileptic drug regimen, medications should be resumed.

Patients with alcohol withdrawal seizures represent another group of patients who may be discharged after appropriate treatment and a period of observation.

A first unprovoked seizure in an adult who has returned to a normal neurological baseline often does not require initiation of medical treatment.

If deciding to start drug therapy, many medications are options to treat a chronic seizure disorder or epilepsy as first-line medication. Drugs can be grouped based on their mechanism of action and include:

- carbamazepine, oxcarbazepine, lamotrigine, lacosamide
- benzodiazepines and fenobarbital
- topiramate
- levetiracetam
- valproic acid
- phenytoin

For the patient with generalized convulsive status epilepticus, immediate treatment of the seizures should begin while stabilization and other diagnostic procedures commence. Supportive care with attention to airway, breathing, and circulation issues are vital. Benzodiazepines such as diazepam are acceptable as the first-line medications for continuing seizures. The second-line medications include **anti-epileptic drugs** (AED).