



How and Why to Identify Generalized Epilepsies

Greater specificity in diagnosis will improve the efficacy of treatment.

The term *epilepsy* refers to a syndrome of recurrent unprovoked seizures. However, there are many different kinds of epilepsy. As discussed in previous columns (see February 2008), simply diagnosing “epilepsy” is inadequate. To select the best treatment options, a more specific epilepsy syndrome diagnosis should be sought. In addition to aiding treatment selection, identification of the syndrome can help establish prognosis. For instance, some epilepsies will spontaneously remit, while others can be expected to be lifelong. Some epilepsies respond to low doses of medication while others may be difficult to treat almost from their onset. Some epilepsies are due to acquired injury, while others are genetic. In short, proper identification of the epilepsy syndrome can help to optimize treatment, establish prognosis, and refine patient education and counseling.

Broad Categories of the Epilepsies

It would be difficult to discuss all types of epilepsy in a brief column. Instead, it is helpful to break the epilepsy syndromes into different categories: partial or generalized. The term partial is used synonymously with localization related, and means the seizure started in a focal region of the brain. Simple partial and complex partial seizures are two examples. However, partial seizures can spread to adjoining or distant regions of the brain through interconnected populations of neurons. When the seizure starts in a focal region, but spreads to encompass the entire brain, it is called a secondarily generalized tonic-clonic seizure.

What sometimes is confusing is that a person can have more than one kind of partial seizure, and still have only one type

of localization-related epilepsy. An excellent example of this is temporal lobe epilepsy. In certain instances, a person may experience partial seizures that arise from scar tissue that forms in the hippocampus. This person may experience a déjà vu sensation without impairment of consciousness: a simple partial seizure. This kind of seizure is often called an “aura” or “warning” because it is the portion of the seizure that a person will remember. This same person may also have events that begin with déjà vu but progress to impaired or lost awareness, staring, and oral automatisms: a complex partial seizure. If the seizure then propagates to both hemispheres, it may become a secondarily generalized tonic-clonic seizure. In this instance, the person has three kinds of seizures, but only one epilepsy syndrome: mesial temporal sclerosis.

In contrast to focal seizures, generalized seizures involve the entire cerebral cortex (we think) from the moment they start. Absence, myoclonic and generalized (from onset) tonic-clonic seizures are three types of generalized seizures. A person with a generalized epilepsy may experience absence, myoclonic or generalized (from onset) tonic-clonic seizures in any combination. They would experience no warning or aura, because there is no portion of the seizure that is focal. In other words, during generalized seizures, the abnormal electrical activity occurs everywhere all-at-once, and consciousness is immediately lost. The best example of this is an absence seizure. They are brief, and the person typically resumes the activity that they were performing as the seizure started. Since the person cannot recall the event, and resumes their activity as if the seizure had not occurred, this type of seizure could easily go unnoticed.

The Generalized Epilepsies

There are many types of generalized epilepsy. The term applied to these is idiopathic. In most areas of medicine, the term idiopathic means that the cause of the illness is unknown. However, when applied to seizures, the term often means that there is a genetic cause. The reason for this is that the cause for these seizure types is better understood. Mutations of different ion channels (sodium, potassium and chloride) have been described in the idiopathic generalized epilepsies. In fact, as a group, they have been referred to as “channelopathies.” Evidence in support of the genetic cause is that 15-44 percent of the time, a person with an idiopathic generalized epilepsy will report an affected first degree relative. Up to 75 percent of monozygotic twins will have the same type of generalized epilepsy.

The Specific Syndromes

Childhood Absence Epilepsy (CAE).

Childhood absence epilepsy refers to an idiopathic generalized epilepsy that begins in childhood. As the name suggests, the main seizure type that occurs is absence. CAE affects 1.9-8 children per 100,000. Absence seizures start as young as four years old, and peak between the ages of 6-7. Up to 80 percent of children with CAE will stop having seizures by the time they reach adolescence. The earlier the age of onset, the more likely the syndrome is to spontaneously remit. If the absence seizures start later than age eight, the diagnosis of JAE (see below) should be considered. Children with CAE infrequently experience myoclonic and GTC seizures as well. If these seizure types occur frequently, a diagnosis other than CAE should be considered.

Table 1. Types of Generalized Seizures

Absence Seizures: Brief, usually 10-20 seconds, though they can last longer. The person will stop what they are doing, and complete loss of consciousness occurs. Occasionally, the person will have rhythmic eye blinking or demonstrate automatisms. This type of seizure is often easily induced with hyperventilation, which is sometimes used as a confirmatory “test” during a doctor’s visit. The EEG shows a 2.5 to 4 Hz generalized discharge during the absence seizure.

Myoclonic Seizures: These are very brief, often described as “split-second” by the patient. They consist of sudden shock-like muscular jerks, often involving both sides of the body at the same time. The EEG shows a complex generalized discharge often referred to as a polyspike when the myoclonic seizure occurs.

Generalized Tonic-Clonic Seizures: These usually last 2-3 minutes (though the postictal confusion can last longer, and is often confused with the seizure itself). The tonic or stiffening phase of the seizure is first, lasting 10-30 seconds. This is followed by clonic movements, rhythmic symmetric contractions of muscle groups. The EEG shows characteristic generalized discharges that evolve simultaneous to the clinical manifestations.

Table 2. Common Idiopathic Generalized Epilepsy Syndromes

Childhood Absence Epilepsy (CAE): This accounts for 2-10 percent of the epilepsies. It starts between ages 4-8, and peaks between 6-7 years of age. Some studies have suggested that girls are affected twice as often as boys; other studies have reported no difference between boys and girls. Hyperventilation will precipitate absence seizures. Fifteen to 44 percent will have a family history of epilepsy. Up to 80 percent of people with CAE will experience spontaneous remission. Although generalized tonic-clonic (GTC) and myoclonic seizures also occur, these are rare in CAE.

Juvenile Absence Epilepsy (JAE): In this syndrome, the absence seizures start later in age. The seizures begin between ages 7-16, with a peak at 10-12 years of age. Most (80-93 percent) will also experience GTCs. Fifteen to 25 percent will experience myoclonic seizures. Unlike CAE, which often remits, JAE is thought to be lifelong: discontinuation of meds often result in relapse.

Juvenile Myoclonic Epilepsy (JME): The seizures begin in adolescence, peaking at about age 13. In this syndrome, the primary seizure type is myoclonic. Less often a person with JME will have GTCs. Infrequently, they may also have absence seizures. Seventeen to 49 percent of those with JME will report a positive family history of seizures. Some studies suggest that women are more likely to be affected than men. As with JAE, the condition is lifelong, and discontinuation of medication results in relapse.

In CAE, the absence seizures are caused by abnormal electrical discharges in the thalamocortical loop. The seizures are 10-15 seconds in duration: the average duration in one study was 12.4 seconds. If a person was talking as the seizure started, they will stop talking within three seconds of its onset.¹ Simultaneous EEG shows a 2.5 to 4 Hz generalized rhythmic discharge. The electrical discharge is frequently in the middle of this range, at about 3 Hz, giving rise to the “pathognomonic” finding of 3 cycles per second during “typical” absence seizures. In between seizures, the presence of generalized 3 Hz discharges would support the diagnosis of CAE.

Juvenile Absence Epilepsy (JAE). As the name suggests, JAE starts in late childhood or adolescence, typically after age 10 and peaking at about age 13. Unlike CAE,

people with JAE are more likely to experience GTCs and myoclonic seizures. More specifically, 80-93 percent of people with JAE have GTCs and 15-25 percent have myoclonic seizures. On EEG, the “characteristic” 3 Hz discharge is found. As in CAE, 3 Hz discharges also occur in between seizures, and are a reliable marker of this syndrome. Unlike CAE, which is likely to remit, JAE is considered a lifelong illness. Although it tends to respond to low doses of medication, when the AED is stopped, seizures return.

Juvenile Myoclonic Epilepsy (JME). JME starts in adolescence, often at about the same time that secondary sexual characteristics develop. Though to be activated by the presence of sex steroid hormones, the main seizure type in this epilepsy syndrome, as expected, is myoclonic. The

myoclonic seizures are very brief, and patients typically call them “split-second.” They usually occur in the AM, shortly after awakening, and are exacerbated by stress, sleep deprivation, and alcohol intake. A person with JME often experiences GTC seizures as well, and less often absence seizures. The EEG may show characteristic generalized polyspike-and-wave discharges as well as rhythmic 2.5 to 4 Hz generalized discharges. Up to half of people with JME will describe a family history of epilepsy. Like JAE, JME is considered lifelong. In small case series, when medications were withdrawn, seizures returned in nearly 100 percent of affected individuals.

A less common generalized epilepsy is the syndrome of GTCs on awakening. It often starts in adolescence, and like JAE and JME is considered lifelong. Individuals with this syndrome may also experience absence seizures; however, in these cases the absence seizures are generally “mild.”

Conclusions

Idiopathic generalized epilepsies often begin in childhood or adolescence. The age of onset and the description of seizure types, along with supportive medical testing, will help to make the epilepsy syndrome diagnosis. Proper epilepsy syndrome diagnosis is important for several reasons. First, optimal medication(s) can be selected while avoiding ones that may exacerbate seizures. Second, the prognosis for these epilepsies is good: they usually respond to low dose medications, and some may spontaneously remit. Finally, the proper diagnosis leads to improved patient education and counseling. Next month, we’ll discuss treatment strategies for generalized seizures. **PN**

1. Panayiotopoulos CP. Absence Epilepsies. In *Epilepsy: A Comprehensive Textbook* edited by J Engel, Jr., and TA Pedley. Lippincott-Raven Publishers, Philadelphia 1997. Pp 2327-2346.

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