CASE TWO

Short case number: 3_12_02
Category: Children & Young People
Discipline: Paediatrics Medicine
Setting: Emergency Department
Topic: Afebrile Seizures_epilepsy

Case

You are the intern in ED, Justin Devers, a developmentally normal; previously well 8 year old is brought in by ambulance from the local primary school. The teacher accompanying him explains that he was in the playground, playing handball when he fell to the ground and started shaking. The episode lasted about a minute. There is no history of seizures that she is aware of and he does not have anything on his school medical records.
On assessment Justin is pale and still very sleepy, he knows his name and age, but he is not sure where he is. His vital signs are stable.

Questions

1. What are the key features of history and examination and how these help distinguish between the common differential diagnoses of epileptic seizures?
2. What clinical features distinguish between focal partial seizures and generalised seizures in children?
3. There are numerous seizure disorders in children, outline the key clinical features of the following seizure disorders; infantile spasms, benign focal epilepsies, primary generalised epilepsy with tonic clonic seizures, temporal and frontal lobe seizures.
4. Justin is stable, but you are concerned he has experienced his first tonic clonic seizure, what are the key steps in your assessment of Justin and why?
5. Justin's parents arrive while you are examining him. His father Erik explains that Justin used to have 'breath holding episodes' when he was toddler, he asks if this is something similar, what would you explain to Erik?
6. Justin is reviewed by the neurology registrar, what further investigations would be recommended and why?
7. Justin's EEG demonstrates features consistent with generalised epilepsy and he is commenced on Sodium Valproate, outline the principles of the pharmacological management of epilepsy and explain the common side effects of this medication and the monitoring that is required.
8. Outline the important non-pharmacological aspects of the management of epilepsy that need to be explained to Justin's parents and his school.

Suggested reading:

- South M, Isaacs D editors. Practical Paediatrics. 7th edition. Edinburgh: Churchill Livingstone; 2012.
- Sydney Health Pathways: https://sydney.healthpathways.org.au/index.htm?41276.htm
- The Royal Children's Hospital Melbourne https: //www.rch.org.au/clinicalguide/guideline_index/Afebrile_seizures/

ANSWERS

1. Prospective studies of new-onset epileptic seizures in childhood reveal that Approximately 50% of patients with a first seizure have a recurrence. Epilepsy as classically defined has a prevalence of about 5 in 1000 in childhood. Prospective studies of treated and untreated new-onset epilepsy reveal that about 80% of children go into remission, some with subsequent seizure relapses, and about 20% of children have treatment-resistant epilepsy.
   The first question to ask is whether the presenting event is really a seizure.
   Careful history taking from the patient and witnesses is paramount in confirming the diagnosis.
   The most common seizure presentation is the tonic-clonic type. Typically with this seizure type there is an ictal cry, followed by tonic extension of the body, with the arms either flexing or crossing the chest and later extending. The jaw is clamped, often with a bite to the side of the tongue. The tonic-clonic activity and cyanosis subside after a minute or a few minutes. The post-ictal state is characterized by tiredness, confusion and, later, muscle soreness and poor concentration.
   Syncopal episodes generally involves a person who may be in an upright position and may have been hot, dehydrated, in pain or experiencing high levels of emotional stress before the episode. Witnesses may describe early pallor, but not cyanosis, accompanied by sweating, and the person may complain of feeling nauseated. The eyes often roll back during the initial limp phase, the clonic phase is brief, and incontinence and tongue biting are rare. Recovery is usually rapid and not associated with confusion or muscle pain. There may be mild fatigue.
   In the absence of provocative factors a cardiac arrhythmia should be suspected.
   Toxicities usually produce states of altered awareness lasting longer than epileptic seizures which generally last seconds to minutes.

Characteristics of tonic-clonic seizure vs 'convulsive syncope'

Characteristic	Tonic-clonic seizure	Syncope
Ictal cry	Common	Rare
Clonic (jerking) activity	Vigorous	Mild
Duration	Usually >30 seconds	Usually <30 seconds
Tongue bite	Common	Rare
Incontinence	Common	Rare
Cyanosis	Common	Absent
Injury	Common	Rare
Recovery	Slow	Rapid
Post-ictal confusion	Common	Minimal/absent
Post-ictal myalgia, lassitude	Common	Minimal/absent

Characteristics of seizure vs pseudo-seizure

Characteristic	Epileptic seizure	Pseudo-seizure
Duration	Seconds to minutes	May be many minutes
Site of occurrence	Often random	Often situational
Seizure characteristics	Usually similar	Often variable
Recognisable seizure type	Common	Unusual features (eg, head rolling)
Injury	Occasional	Rare
Eyes	Usually open or rolled up	Often closed

Episodic altered awareness or behaviour – differential diagnosis

- Seizure
- Pseudo-seizure
- Metabolic abnormality
- Toxic states
- Presyncope in the elderly
- Behavioural inattention
- Migraine prodrome
- Breath-holding in infants
- Transient global amnesia
- Narcolepsy and sleep disturbances (parasomnias)

2. Epileptic seizure types can be based on clinical and EEG features.

<u>Focal (partial)</u>

• Simple partial - consciousness preserved
• Complex partial - consciousness impaired
• Partial seizures with secondary generalization

<u>Generalized</u>

•Tonic-clonic • Absence
• Myoclonic • Clonic
• Tonic (epileptic spasms are series of brief tonic seizures)
• Atonic

The benign or idiopathic focal (partial) epilepsies of childhood occur in otherwise normal preschool and primary-school-age children and typically manifest with infrequent sleep-related focal seizures. The aetiology and pathogenesis of the idiopathic focal epilepsies is unclear in that they are not due to underlying structural brain lesions.

Focal seizures may be simple partial with tingling or twitching of the mouth and preserved consciousness, often with associated drooling of saliva, choking noises and inability to speak. Seizures may progress to jerking of one side of the body, with or without impairment of consciousness. Some children have secondarily generalized seizures in which the focal onset is not recalled or witnessed. Attacks are most commonly from sleep.

Generalized tonic-clonic seizures typically begin with loss of consciousness, stiffening (tonic), temporary cessation of breathing and falling if standing, then progress to a phase with generalized, rhythmic jerking (clonic), which is initially rapid but gradually slows. Tonic-clonic seizures invariably cease spontaneously, usually within a few minutes, and are followed by a postictal period with depressed consciousness and

headache, during which the person usually sleeps. There are no warning symptoms (auras), no significant focal features to the seizure and no memory of the actual seizure. Generalized tonic-clonic seizures may begin at any age but onset around puberty is common.

3. Infantile spasms - usually between 3 and 8 months of age
   - males : females 2:1
   - flexor or salaam spasms are the most common with sudden drawing up of the legs, hunching forward of the neck and shoulders and flinging out of the arms
   - typically occur in series over a minute or more, usually many times a day
   - an age-dependent manifestation of a severe, localized or diffuse, acquired or developmental, disturbance in the immature central nervous system
   - an underlying cause is identified in about two-thirds of Infants
   - 70-80% develop some degree of intellectual disability and 30 – 50% develop chronic, focal or generalized epilepsy.

Benign focal epilepsies

- occur in otherwise normal preschool and primary-school-age children
- not due to underlying structural brain lesions
- onset usually 5 – 10 years of age, male predominance
- may be simple, partial with tingling or twitching of the mouth and preserved consciousness often with drooling, choking noises
- may lead to jerking of one side of the body, +/- impaired Consciousness
- attacks are most commonly from sleep
- in benign occipital epilepsy, onset usually before the age of six with female predominance, seizures are characteristically from sleep with staring, vomiting, head rotation, eye deviation and hemiclonic jerking.

Primary generalized epilepsy with tonic clonic seizures

- may begin at any age but onset around puberty is common
- typically begin with loss of consciousness, stiffening (tonic) temporary cessation of breathing and falling if standing then progress to generalized, rhythmic jerking (clonic) movement initially rapid
- invariably cease spontaneously, usually within a few minutes followed by a postictal period with depressed consciousness and headache
- no warning symptoms, no focal features, no memory of the actual seizure

- *juvenile myoclonic epilepsy* typically begins in the teens with generalized tonic-clonic seizures, early morning myoclonic jerks and sometimes brief absence seizures, the episodes are often precipitated by sleep deprivation

Temporal (TLE) and frontal lobe (FLE) epilepsies

- generally considered symptomatic focal epilepsies in which an underlying scar, tumour, cyst or malformation is either known or suspected to be the basis of the recurring focal seizure
- seizures may commence at any age but often not until later childhood or adolescence

- may be simple partial with preserved consciousness, complex partial with impaired consciousness, or secondarily generalized in TLE seizures are usually complex partial,

- characteristically manifest by motionless staring, fearful or bewildered facial expression, unresponsiveness, fidgeting hand movements (automatisms) and postictal amnesia and confusion, in some head turning or jerking of the limbs on one side. Autonomic disturbances are common e.g. facial flushing or pallor, lip smacking, salivation, chewing, swallowing and sometimes vomiting are common.
- In a young or developmentally delayed child an aura may manifest as fear, unusual smells or tastes, abdominal discomfort and dizzy or dreamy states.
- in FLE seizures often occur from sleep, are brief in duration and commonly manifest with prominent motor features such as unilateral or bilateral stiffening or jerking, asymmetric tonic posturing with head deviation to one side, loud vocalization and hyperkinetic behaviours (automatisms) such as tapping, cycling or running. Seizures may occur on a multiple nightly basis. Secondary generalization is common.

4. More history is required - specific questions for the teacher, if they witnessed the apparent seizure was there any evidence to suggest focal epilepsy, secondarily generalized vs primary generalized and was there associated incontinence
   - the family needs to be contacted and specific questions asked with regard to previous episodes that may indicate an epilepsy syndrome, important clues would include risk factors such as
     - family history
     - a record of birth trauma or perinatal complications
     - prolonged or repeated febrile convulsions during infancy
     - recent or past head injury

   A thorough physical examination is required especially a full neurological examination to exclude the presence of focal signs, a cardiac examination to exclude congenital heart disease, BGL if not already performed and evidence of injury associated with the episode in the playground e.g. tongue biting . Children with suspected epilepsy should be examined for dysmorphic features, neurocutaneous stigmata, signs of raised intracranial pressure and markers of systemic disease.

5. Breath-holding attacks are frequently misdiagnosed as seizures in infancy, they usually commence in the first or second year of life and are reported in up to 4% of children. Crucial to the diagnosis is recognition that attacks are precipitated by either physical trauma, e.g. knock or fall, or emotional trauma e.g. fright, anger or frustration. Attacks commence with crying then apnoea and bradycardia with cyanosis or pallor following but may progress with the child becoming unconscious, limp and sometimes briefly stiffening or jerking in response to the cerebral ischaemia. Recovery is usually rapid although some may remain drowsy and lethargic.

   The cause is not well understood but affected children probably have an age-related dysfunction in the autonomic nervous system.

   Iron deficiency has been shown to be more prevalent in children with breath-holding spells compared with controls and appears to contribute to the occurrence of breath-holding spells and the underlying dysautonomia.

Breath-holding attacks are not a cause of death, epilepsy, intellectual disability or cerebral damage and therefore the family can be reassured of their benign nature.

6 Routine blood tests for electrolytes, BGL (hypoglycaemia) and serum calcium (hypocalcaemia) and magnesium to exclude contributory causes such as a metabolic disorder.

EEG is helpful in characterizing seizures and epilepsies but should not be done to clarify the nature of undiagnosed events. (video-EEG monitoring may be needed for undiagnosed episodic phenomena)

Imaging is performed when the seizures, EEG, history or examination suggest an underlying cerebral abnormality, such as focal abnormalities on the EEG. A CT scan is useful to exclude any gross cerebral pathology such as a tumour. MRI, when available, is the imaging of choice, because subtle lesions in a variety of conditions may escape CT.

7 Seizures can usually be controlled with one medication at an optimal dose, especially in idiopathic epilepsies. Children vary greatly in their dosage requirements and tolerance of antiepileptic drugs, patient age and associated disabilities being the main determinants. Although children often require higher medication doses for weight than adults, initial dosing should be calculated using their weight, bearing in mind that doses will probably need to be increased as they grow. Factors influencing the choice of drug include the syndrome and the age and sex of the patient. Idiopathic and secondary generalized epilepsies respond to sodium valproate whereas focal epilepsies respond to any of the antiepileptic drugs.

Antiepileptic medications are usually commenced singly and in low dosage and then increased gradually to a dose where seizure control is obtained, side effects appear or maximum dosage and serum levels are achieved. The duration of therapy depends on the type of epilepsy and its natural history, the degree of seizure control and the patient's lifestyle. Several years of freedom from seizures are desirable before antiepileptic drugs are ceased, and this is best done slowly over a period of months. Antiepileptic drug interactions are common, both pharmacokinetic and pharmacodynamic, some being advantageous (e.g. sodium valproate and lamotrigine) and others leading to side effects.

Almost all antiepileptic drugs produce side effects such as drowsiness and unsteasdiness if given in excess. They often wear off after the maintenance dose is reached. Some antiepileptic medications have side effects of an idiosyncratic type, such as rash or behavioural disturbance.

Use of serum levels for monitoring some antiepileptic medications is particularly useful if seizure control is inadequate, side effects attributable to toxicity are suspected or compliance is uncertain. Blood level monitoring is of particular value in young infants, in children with intellectual disability and in patients with impaired consciousness.

In addition to regular prescription of antiepileptic medication to prevent seizures, some parents and carers are instructed in the use of buccal midazolam or intranasal midazolam to treat prolonged or recurring seizures

Side effects of antiepileptic medications

Medication	Side effects
Toxicity	
Common to most Antiepileptic medications	Drowsiness, ataxia, tremor, nystagmus, dysarthria, confusion , nausea, vomiting, sleepiness , insomnia
Idiosyncratic	
Carbamazepine	Rash, leucopoenia, hyponatraemia, irritability,

Clonazepam	Behaviour disturbance, increased secretions
Lamotrigine	Rash, severe hypersensitivity syndrome
Phenytoin	Rash, serum-sickness-type illness
Phenobarbitone	Rash, behaviour disturbance
Sodium valproate	**Weight gain, alopecia, moodiness, behaviour changes, pancreatitis, hepatic failure (rare).**
Topiramate	Kidney stones, weight loss, speech disturbance
Vigabatrin	Peripheral vision impairment, weight gain

8. Explanation and reassurance, provision of information about the child's specific seizure disorder, first aid advice about how to manage future seizures, discussion of potential seizure precipitants (sleep deprivation, gastroenteritis leading to malabsorption of medications) , consideration of lifestyle modification and safety advice regarding bathing, swimming and heights are all important aspects of seizure management.

   Above all, it is best to 'normalise' life as much as possible, highlighting all the activities in life that can be done without interruption, such as sport, most types of recreation, TV and cinema.

   When treating epilepsy it is necessary to consider the whole child and family in their environment, and not only the seizures. Problems pertaining to education (the stigma of epilepsy may become an issue with peers at school) and vocation , problems related to adjustment to the diagnosis, and associated psychological and behavioural problems may be more difficult to manage than the actual seizures.