Pediatrics 19: 16-month-old male with first seizure

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Learning Objectives

Upon completion of the case, the student should be able to:

- List potential causes of altered mental status in a toddler.
- Categorize seizures (e.g. partial, generalized, simple, complex) according to typical clinical features.
- List key features to include in the history and exam in determining the etiology of a new-onset seizure.
- Outline normal developmental milestones for a 16-month-old child.
- Generate a differential diagnosis for a generalized seizure.
- Compare and contrast the clinical features of different causes of seizures.
- Distinguish simple from complex febrile seizures.
- Summarize national practice guidelines for the evaluation of simple febrile seizures.
- Discuss options for anticipatory guidance to families in the aftermath of a febrile seizure.
- Describe the typical history, presentation, and exam findings associated with roseola (exanthem subitum).

Knowledge

Differential Diagnosis of Altered Mental Status in a Child

Common causes	Less common causes
Toxic ingestion	• Most commonly seen in children between the ages of 9 months and 3 years of age. • Various medications can lead to a state of unresponsiveness. • Some of the more common medications would be opiates, benzodiazepines, and clonidine. • Other considerations would be medications that can cause a metabolic disturbance (e.g., oral diabetic agents causing hypoglycemia. • A careful history must be taken about all medications in the child's house and other homes where he or she spends time (grandmother's home, babysitter's home, etc.).
Seizure	• Seizures are common in children. • Best described as paroxysmal neurologic events and have variable forms of presentation, such as generalized or partial seizures. • Seizures can have many causes, from metabolic disturbances (hypoglycemia or hypocalemia) to head trauma resulting in cerebral contusion or intracranial hemorrhage. • Children with developmental abnormalities of the brain or genetic syndromes which involve the brain (e.g., tuberous sclerosis) may also have seizures. • In many children, seizures may be idiopathic. • Some children have only one seizure in their lifetime; others will have recurrent seizures and thus be given the diagnosis of epilepsy (typically classified as two or more unprovoked seizures). • Epilepsy (all forms) has a prevalence of approximately 1% throughout childhood. • Even in the absence of a seizure, other important neurologic causes should be considered in an unresponsive child.

Syncope	• Syncope due to breath-holding spells is common in children between the ages of 1 and 3 years. • Breath-holding spells are classified as either cyanotic or pallid type. • In the more common cyanotic type, the key historical feature is a precipitating event that upsets the child, resulting in vigorous crying and hyperventilation, followed by a prolonged expiratory apnea; transient hypoxia results in the child turning pale or cyanotic, followed by brief loss of consciousness and limpness. • The episodes quickly self-resolve and there is typically no associated post-ictal state. • Occasionally, a child with a breath holding spell may have a brief generalized seizure, most likely due to hypoxia. • For the most part, parents should be reassured that breath-holding spells are a benign and self-limited condition. • Very rarely, breath-holding spells have been reported to be associated with asystole. • Cardiac syncope is a bit more unusual in a child of infant or toddler age, but should be considered; it would most likely not be vasovagal type syncope. • However, cardiac causes such as supraventricular arrhythmias (supraventricular tachycardia) or ventricular arrhythmias (in the setting of prolonged QT syndrome) can decrease cerebral blood flow and cause syncope.
Closed head injury	• Closed head injury (with or without intracranial injury) may lead to loss of consciousness. • The family or caregiver may not have witnessed the traumatic event. • Should there be indications in the history; inflicted head trauma should also be considered as a possible diagnosis.
Infection	• Up to 30-40% of children with meningitis can present with seizure activity. • Fever and irritability may be the only signs seen on exam. • Children with encephalitis will frequently present with waxing and waning mental status, as well as fever and seizure. • After the seizure is over, children with meningitis or encephalitis typically do not return to baseline activity and remain impaired. • Enteroviral infections and herpes simplex virus should be considered as possible pathogens for encephalitis.
Less common causes	
Intracranial process	• Brain tumor can lead to both seizures or more global alterations in mental status. • The patient's medical history might include a preceding history of headache, behavior change, vomiting, or focal neurologic change. • Brain tumors are the most common solid tumors in childhood (approximately 1,200 cases per year) and usually occur in the posterior fossa.
Intussusception	• Intussusception is the telescoping or prolapsing of a portion of the intestine within another immediately adjacent portion of intestine-usually the terminal ileum into the colon. • Repeated episodes of colicky pain are the classic presentation of intussusception. • As the condition becomes more long-standing, lethargy with a near unresponsive state can be seen between the episodes of colicky pain. • In addition, children with intussusception commonly have intravascular volume depletion due to vomiting and third spacing of fluids; this may lead to mental status changes similar to a child who is very dehydrated.

Types of Seizure

Generalized tonic-clonic seizure

- This is the most common type seen in children.
- The event typically begins abruptly with tonic (rigid) stiffening of all extremities and upward deviation of the eyes.
- Clonic jerks of all extremities follow the tonic phase.
- Finally, the child becomes flaccid, and urinary incontinence may occur.

Simple partial seizure

- With this type, there are often motor signs in a single extremity or on one side of the body.
- However, focal onset seizure activity may spread to become generalized, making it difficult to distinguish from a generalized seizure.

Complex partial seizure

- This type of seizure can occur at any age.

- Altered level of consciousness is one of the hallmark features.
- Complex partial seizures may include blank stare, lip-smacking, drooling, gurgling, as well as nausea and vomiting.
- Automatisms are quasi-purposeful motor or verbal behaviors that are repeated inappropriately and commonly accompany complex partial seizures.
- Complex partial seizures often last 30 seconds to 2 minutes and are associated with a post-ictal phase of confusion, sleep, or headache.
- Secondary generalization can occur in up to one third of children, so it is important to question witnesses about initial features to help differentiate a complex partial seizure from a generalized seizure

Childhood absence epilepsy (petit mal seizures)

- This disorder typically starts around age 3 years.
- Absence seizures are characterized by loss of environmental awareness ("staring off into space") and automatisms (e.g., eye-fluttering or lip-smacking).
- While these are generalized seizures, children usually regain their consciousness more quickly than the post-ictal phase seen in a generalized tonic-clonic seizure.
- Absence seizures are not associated with loss of tone or urinary continence.
- Absence seizures can be precipitated by hyperventilation or photic stimulation.

Atonic (akinetic) seizure

- Involves loss of motor tone

Distinguishing Seizure from Seizure-Like Activity

True seizures result from sudden and abnormal electrical activity in the brain. Many other conditions (e.g., motor tics, myoclonus, gastroesophageal reflux (Sandifer's syndrome), and pseudoseizures - also known as psychogenic non-epileptic seizures" (PNES)), can result in movements or behaviors mimicking a seizure. Supportive evidence for a true seizure includes:

- A history of alteration of consciousness or loss of consciousness
- Incontinence
- Deviation of the eyes
- Often rhythmic motor movements that cannot be stopped by touching or holding the child
- A postictal state.

To address these issues, you may want to ask whether the child was distractible, and if the event could be interrupted. In addition, children who are old enough to verbalize may describe an aura or "premonition" prior to the onset of a seizure, or caregivers may be able to articulate unusual behavior just prior to the event.

Lethargy

It is important to remember that parents and physicians often use words differently to describe a child's behavior:

- To a physician, "lethargy" implies a serious alteration of mental status, suggesting diagnoses such as meningitis or toxic ingestion.
- To a parent, lethargy often means "more tired" or "less active than usual."

Be sure to clarify what this term means to the person using it.

How Accurate Is a Tactile Temperature?

Parents' subjective assessment of fever has been shown to agree with the presence of fever (temperature > 38 C or 100.4 F) as measured by rectal glass thermometer in 80% of cases.

Relationship Between Developmental Maturation and Seizures

Abnormalities in neurodevelopmental maturation could suggest serious underlying disease in a child with seizures.

Most children with febrile seizures are developmentally normal.

Pre-existing developmental abnormalities are a risk factor for subsequent epilepsy.

Heredity and Febrile Seizures

Family and twin studies provide evidence that febrile seizures are hereditary, but the exact mode of inheritance is still unclear.

- Many genetic loci have been linked to febrile seizures such as 8q13-21 (often called FEB1), 19p (FEB2), 2q 23-24 (FEB3) and others.
- Different studies have provided support for different modes of inheritance, including autosomal dominant, polygenic, and multifactorial.

Fever Without a Source and Serious Bacterial Infection (SBI)

The term Fever Without a Source (FWS) is used when a child with acute fever has no localizing symptoms or signs on physical exam.

Guidelines for the management of Fever Without a Source in infants and toddlers focus on determining the risk serious bacterial illness (SBI).

Most experts include bacteremia, urinary tract infection, and meningitis in the definition of SBI.

Bacteremia	Bacteremia has become uncommon since the introduction of vaccines against Haemophilus influenzae type b and Streptococcus pneumoniae. Febrile, well-appearing children ages 3-36 months without a discernible focus of infection may have "occult" bacteremia (positive blood culture), but this is rare with current immunizations. Undiagnosed, the child with occult bacteremia is at risk for the development of a more serious bacterial infection such as meningitis or osteomyelitis, through bacterial seeding of distant sites.
Meningitis	Clinical signs and symptoms of meningitis can be subtle in young children. Very young infants (< 3-6 months) with bacterial meningitis may not show any signs of nuchal rigidity-even to an expert clinician. While not a specific finding, persistent irritability may be the only key to a child with a serious illness; in some cases this may be sufficient to warrant obtaining cerebrospinal fluid. CNS infection should be included in the differential diagnosis for a young, febrile child who has not returned to normal activity and behavior after a seizure.
Urinary Tract Infection	Urinary tract infection is the most common cause of SBI in children.UTI commonly presents as fever without a focus on physical examination and a relatively unremarkable review of systems.Fussiness and lack of appetite are common associated symptoms.Risk factors for males include: • Temperature > 39C (102.2F) • Absence of another source of infection • Fever > 24 hours Risk factors for females: • Age < 12 months • Temperature > 39C (102.2F) • Absence of another source of infection • Fever > 2 days Girls have a two- to four-fold higher prevalence of UTI than circumcised boys.

Pneumonia, bacterial gastroenteritis, osteomyelitis, and septic arthritis may also be considered SBIs.

Influenza

According to current CDC guidelines, the following patients are at high-risk for developing influenza complications and are candidates for treatment with a neuraminidase inhibitor (e.g., oseltamivir):

- Children aged younger than 2 years
- Children with the following types of chronic conditions:
- Pulmonary (including asthma)
- Cardiovascular (except hypertension alone)
- Renal
- Hepatic
- Hematological (including sickle cell disease),
- Metabolic disorders (including diabetes mellitus)
- Neurologic and neurodevelopmental conditions, children with immunosuppression (e.g. caused by medications or by HIV infection)
- Children who are receiving long-term aspirin therapy
- American Indians/Alaska Natives;
- Children who are residents of chronic care facilities.

Centers for Disease Control and Prevention. Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza. MMWR 2011;60(No. 1).

Febrile Seizures

	Simple	Complex
Incidence	More common	Less common
Duration	< 15 minutes	> 15 minutes
Frequency	Once in a 24-hour period	More than once in a 24-hour period
Type	Generalized	Focal

Risk of Recurrence

- If a child has his first febrile seizure before age 12 months, the recurrence risk for a second febrile seizure is about 50%.
- If a child has his first febrile seizure after age 12 months, the recurrence risk is about 30%.
- While seizure events are very scary for families, parents should be reassured that recurrent, simple febrile seizures have no long-term effects in terms of child development.

Risk of Epilepsy

- In a child who has a febrile seizure, the risk of developing epilepsy is slightly increased above the 0.5-1% baseline population risk.
- However, not all febrile seizure patients are alike.
- Epilepsy is more common among those children with early, recurrent febrile seizures, especially if there is a family history of epilepsy.
- This is to be compared to essentially the same risk as the normal population in a child with one or two simple febrile seizures and no other features.
- Children with complex febrile seizures, and those with abnormal development, are at increased risk of epilepsy.

Definition of Blanching

"Blanching" means that the rash disappears when the overlying skin is stretched taut, or pressed against.

This descriptor is often used to distinguish a superficial exanthem from a deeper process such as petechiae.

Roseola Infantum

Roseola infantum (also known as exanthem subitum, or sixth disease) is a common febrile rash illness of infants and young children under 2 years of age.

Etiology

Human herpesvirus-6 (HHV-6) is an important etiologic agent of roseola. About 30 percent of children with primary HHV-6 infection will develop roseola

Presentation

Hallmarks of roseola include:

- A high fever (38.5 to 40.5 C) for 3-5 days in a typically fairly well-appearing child, followed by abrupt resolution of fever and development of a maculopapular rash
- During the period of fever, some children have rhinorrhea.
- A bulging fontanelle. This is an unusual physical finding in roseola and may lead to evaluation for meningitis.

Relationship to Febrile Seizures

Primary HHV-6 infection is associated with approximately 20% to 30% of first febrile seizures in children.

Clinical Skills

Determining the Etiology of a Seizure

The following are all critical to know in determining the etiology of a seizure:

A detailed description of the event	In most cases you will not have the opportunity to observe the child having a seizure, so the event must be reconstructed by obtaining as accurate a history as possible: • Parents, or other observers, may be so upset by this scary event that they may have significant difficulty recalling details of the seizure. • Open ended questions work best. "Can you describe what happened?" • Ask the parents why they suspected something was wrong; what was the first thing they noticed? • They may mention that the child had a blank stare or that they observed lip smacking or facial twitching. • Then ask about atypical movements (e.g., "Did you notice any unusual movements in his arms or legs? How would you describe them?")
A detailed timeline of events	• A timeline of events leading up to and through the episode, including how the child recovered, can inform the differential diagnosis.
Any precipitating events, such as fever	Inquiring about precipitating events such as illness, especially with fever, is essential. • One of most common reasons for seizures in children is febrile seizures, and these are usually generalized seizures. • Febrile seizures occur in 2-4% of children between the ages of 6 months and 5 years. • Not all children who present with a seizure and fever have febrile seizures: The presence of fever may not help to make the distinction between the common, benign condition of febrile seizures and something much more serious such as meningitis or encephalitis. • In febrile seizures, a fever - typically caused by a benign illness like a viral infection - triggers a seizure in a susceptible host (young child, positive family history, etc.). • In a more serious central nervous system infection, such as meningitis or encephalitis, the infection itself causes both fever and seizure; this is because CNS infections directly involve the brain or the meninges surrounding the brain. Prolonged fever prior to the event, especially with irritability or inconsolability, is an indication of a more serious CNS condition causing the seizure. • Occasionally, one might consider whether the fever and the seizure are coincidental; this highlights that, at times, a febrile seizure can be difficult to differentiate from epilepsy. Every child with epilepsy has to have a first seizure at some point and the inciting event may be a mild infection with fever. • In practice, the characteristics of the child's seizure, the child's medical and developmental history, as well as whether the seizures recur over time, will help to more accurately classify the patient.
Possibility of toxic ingestion	• Especially worrisome in toddlers is the potential for toxic ingestion, usually from improperly stored medications.
Any history of injury	• The possibility of recent history of injury, particularly of the head, should be discussed, since head injuries, either recent or distant, can lead to post-traumatic seizures.
Pertinent medical and family history	• A past history of seizures • Developmental delay • Premature birth • Family history of seizure disorders or neurologic problems • Family members with certain medical conditions which require certain medications - which may have been ingested by the patient. For example, patient's grandparent with diabetes who is taking an oral hypoglycemic agent.

Management

Guidance About Febrile Seizures for Caregivers

Treatment for Fever

- Caregivers should feel free to give the child acetaminophen or ibuprofen if he is uncomfortable.
- Dosing recommendations should be carefully followed to prevent overuse and possible side effects.
- Experts agree-and studies have shown-that these medications are not helpful in preventing recurrence of febrile seizures.

In Case of Seizure

- Place the child on his side so that he won't choke on stomach contents or saliva.
- Be sure the child is in a safe setting so he won't hurt himself during the seizure activity.

- Contrary to what many people have heard, nothing should be placed in the child's mouth to keep him from biting his tongue.
- Do not restrain the child's movements during the seizure.
- The most important (and most difficult) thing to do is to remain as calm as possible.
- Most seizures stop on their own within a few minutes, so keep your eyes on a clock or watch.
- Call 911 if the seizure lasts more than five minutes.

Medications

- While there are some medications that may prevent future seizures, the child would have to take them either all the time or intermittently (when he is sick).
- When the risks and benefits are weighed, experts agree that such these medicines as phenobarbital, diazepam, or valproic acid should not be used in children with simple febrile seizures because of the potential for serious side effects. Antiepileptic drugs are not recommended when one considers their side effects versus the fact that a febrile seizure recurrence is likely to be of little harm to the child.

Studies

Meningitis and Febrile Seizures: When to Obtain a Lumbar Puncture (LP)

Data show that the overall risk of meningitis is low in children who present with a simple febrile seizure. In fact, a retrospective analysis of over 700 children ages 6-18 months who had a first simple febrile seizure demonstrated no cases of bacterial meningitis in the 260 CSF samples obtained.

However, obtaining a lumbar puncture may be recommended nevertheless for a number of reasons:

- The younger the child, the more subtle the signs of meningitis may be on examination. Very young infants (< 3-6 months) with bacterial meningitis may not show any signs of nuchal rigidity-even to an expert clinician.
- While not a specific finding, persistent irritability may be the only key to a child with a serious illness; in some cases this may be sufficient to warrant obtaining cerebrospinal fluid.

A lumbar puncture can be considered for a child age 6-12 months with incomplete or unknown immunizations against Haemophilus influenzae type b or Streptococcus pneumoniae, particularly if the child's neurologic status is worrisome, or difficult to assess - for example, if the child is not exhibiting complete recovery after the seizure

Clinical Reasoning

Differential Diagnosis of Seizure

Diagnosis	Comments
CNS infection (meningitis/encephalitis)	• The presence of fever suggests a viral or bacterial infection; at this point it's important to determine if the infection might be causing the seizure directly, such as in a serious infection like meningitis or encephalitis. • Irritability, together with seizure, might suggest a serious underlying neurologic infection. • Approximately 30% of infants with meningitis present with a seizures. However, they typically also have other signs of illness such as vomiting, lethargy or behavior change.
Febrile seizure	Alternatively, the fever may be a sign of an infection of little consequence (such as a viral upper respiratory infection) which led to a febrile seizure: • Febrile seizures occur in children ages 6-60 months at a frequency of 2-5% in this age group. • Seizures usually occur on the first day of the febrile illness, often as the first sign to the parents that the child is ill. • Fever > 38 C is typically present. • Children with febrile seizures tend to be developmentally normal and often have a positive family history for other first-degree relatives with febrile seizures as children. • Most febrile seizures are generalized.
Head injury/post-traumatic seizure	• A seizure related to head injury generally occurs 1-2 hours after the incident. • Even if parents report no history of trauma, it is important to keep non-accidental injury in mind.

Ingestion/poisoning	• Even though an insulin overdose has been ruled out, one should always consider an accidental ingestion in a child this age. • Many other poisonings can lead to generalized seizures: Acute alcohol poisoning and more longstanding lead poisoning are two examples. • Fever would be unusual in most ingestions and argues against this diagnosis for Ian.
Idiopathic seizure/epilepsy	• A fever often triggers the first seizure in children with epilepsy. • Although some children with epilepsy also have developmental delay due to genetic, congenital, or acquired disorders (symptomatic epilepsy), many other children with epilepsy are developmentally normal (idiopathic epilepsy). • In patients with very prolonged seizures, fever may be due to sustained motor activity and possibly the release of inflammatory mediators.
Hypoglycemia	• Low blood sugar can be a cause of seizure. • A blood glucose level is a quick and simple way to immediately check if this is a factor.
Brain tumor	• Seizure resulting from a brain tumor or other intracranial mass lesion would most likely begin as a partial seizure.
Breath-holding spell	• Breath-holding spells can be complicated by hypoxic seizures. • These are generally very brief.

Evaluation of First Seizure

Evaluation of first febrile seizure

- The implicit relationship between fever and seizure activation makes the distinction between febrile seizures and new-onset epilepsy challenging.
- Does this child have a simple febrile seizure or is this his first epileptic seizure triggered by a fever?
- In general, if the child's clinical history is consistent with the classic pattern of a simple febrile seizure and if his past medical history and physical examination are normal, then he likely has a febrile seizure and no further workup is necessary.

Evaluation of first non-febrile seizure

Additional neurological investigation is often done in a child presenting with a first afebrile seizure:

Electroencephalogram (EEG)

- The EEG is a useful adjunct to the history and physical examination in establishing the diagnosis of epilepsy, but a routine interictal (between seizures) EEG will show an epileptiform abnormality in only approximately 60% of infants and children; less in adolescents and adults.
- EEGs may be useful to identify epilepsy syndromes based on both the patient's history and EEG pattern (e.g., absence seizures and infantile spasms have characteristic EEG findings such as 3-Hz spike-and-wave pattern and hypsarrhythmia, respectively); identification of these syndromes can lead to effective treatment and prognosis.

Magnetic resonance imaging (MRI)

- MRI is frequently performed in the evaluation of epilepsy.
- Brain MRI is much more likely to be abnormal in children with focal seizures than in generalized or febrile seizures.
- With better resolution than CT scanning, MRI is able to identify brain parenchymal malformations, vascular malformations and temporal sclerosis.

Computed tomography (CT)

- In general, CT is of little use in the evaluation of a child with suspected epilepsy as it provides little useful information for clinical management.
- Exceptions include trauma and the investigation of calcifications, such as in cytomegalovirus (CMV) infections or tuberous sclerosis.

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