Review Article

Capsula Eburnea

EVALUATION OF FIRST SEIZURE IN CHILDHOOD: NEUROIMAGING OVERTURES

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SUMMARY

Seizure is a common presentation in an emergency care setting, and new-onset epilepsy is the most common cause of unprovoked seizures. The neuroradiologic evaluation of patients after a first seizure must be tackled starting from the clinical history, neurological examination and blood tests, followed by an electroencephalographic study. The initial assessment after a single event should determine whether an actual seizure has occurred or if the episode could be attributed to another transitional event; it is necessary to exclude the possibility of the crisis being a manifestation of a possible organic cause, therefore determining whether it was caused by brain injury or a first episode of epilepsy. The role of neuroimaging in a child with new-onset afebrile seizures is controversial. In this article we evaluate the need for neuroradiologic investigation after a first seizure.

Introduction

Seizure is a common presentation in an emergency care setting, and new-onset epilepsy is the most common cause of unprovoked seizures. No single sign, symptom, or test clearly differentiates a seizure from a non-seizure event (e.g., syncope, pseudo-seizure). Electroencephalography (EEG) is recommended for patients presenting with a first seizure, and neuroimaging is recommended for adults (1). Neuroimaging should be performed in children with risk factors such as head trauma, focal neurologic deficits, or a history of malignancy. Magnetic Resonance Imaging (MRI) is preferred over Computed Tomography (CT), except when acute intracranial bleeding is suspected (2). The most common laboratory findings associated with a seizure are abnormal sodium and glucose levels. Patients with a normal neurologic examination, normal test results, and no structural brain damage do not require hospitalization or antiepileptic medications (3).

Epidemiology

Seizures are responsible for approximately 1-2% of all visits to emergency departments (4). Approximately 2-5% of the population of the United States is affected by afebrile seizures. The prevalence of epilepsy is between 1.1% and 2.2%. Most patients (57%) presenting a first seizure, are aged <25 years, with 71% of this subgroup being aged <15 years; moreover, 58% of patients with a first seizure are male (5).

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Potential Etiologies

In evaluating the child after a first seizure, the first consideration should be to determine whether the seizure was provoked or unprovoked (6). In the case of provoked seizures, treatment should include identifying and treating the underlying etiology (7).

The most frequent risk factors for provoked (symptomatic) childhood seizures are:

- Central nervous system (CNS) infections, such as meningitis, encephalitis, and emphyema, that can present with seizures, and identifying and treating the underlying infection is imperative;
- Metabolic alterations that can precipitate seizures and can be directly treatable targets;
- Head trauma that can precipitate seizures and requires an immediate neuroimaging investigation to rule out hemorrhage, contusion, or other serious injuries;
- Structural abnormalities, such as congenital cerebral malformations, ischemic or hemorrhagic strokes, tumors or other mass lesions are less common etiologies causing seizures, but can be ruled out with appropriate neuroimaging studies (8).

If the child is between 6 months and 6 years old, neurologic examination and developmental history result normal, and the patient has a fever without CNS infection, the diagnosis of febrile seizure should be considered (9).

Febrile seizures affect 2-5% of children aged 6 months to 6 years. These occur in association with a high fever, typically above 38.5° C, and in absence of a CNS infection. There is often a family history of febrile seizures. Some believe that the change rate in body temperature is more provoking than the absolute body temperature. A second episode occurs in 33% of children, and only 50% of these have a third episode. Approximately 3-6% of patients with febrile seizures will develop afebrile seizures or epilepsy. EEG and neuroimaging are generally not warranted. Further evaluation may be required for complex febrile seizures, which include seizures lasting longer than 15 minutes, seizures that have a focal onset, or occur multiple times within 24 hours or within the duration of febrile illness (10). Most children with a first afebrile seizure do not have a clear underlying etiology. Many of these children will not develop a second seizure (11). In those children who do develop further seizures, the identification of risk factors or a specific epilepsy syndrome may help with treatment decisions and prognostication. Some childhood epilepsy syndromes include the following:

Infantile spasms. These typically begin in infants aged 4-8 months (though earlier and later presentations do occur) and consist in clusters of myoclonic spasms that typically occur upon awakening or falling asleep. Their presentation can be more subtle and include slight eye flutter or head drop. If suspected, appropriate diagnosis and swift management is essential to improve the developmental outcome.

Absence epilepsy, also known as petit mal epilepsy, is manifested by frequent (as many as 100 per day or more) episodes of brief staring spells, often with fluttering of the eyelids, lasting only a few seconds (typically up to 15 seconds) at a time. Following a typical absence seizure, patients return immediately to their baseline mental status. Absence seizures are usually of a generalized onset. Diagnosis can be assisted by hyperventilation trial, which often provokes the seizures and classic EEG features.

Benign Rolandic epilepsy occurs in children aged 3-13 years. A typical presentation is a seizure characterized by perirolandic or perisylvian sensorimotor features including speech arrest, or guttural sounds and facial numbness or twitching, which may progress to generalized tonic-clonic activity. The majority of seizures occur during sleep or upon awakening. Classic EEG features can aid in diagnosing this syndrome.

Other benign partial epilepsies of childhood include benign occipital epilepsy of childhood (Gastaut Syndrome), in which visual symptoms predominate, as well as Panyiotopoulous syndrome, with prominent autonomic symptoms.

Juvenile myoclonic epilepsy (JME) occurs in the teen years. In JME, individuals may present with generalized tonic-clonic seizures, myoclonic jerks (typically seen within hours of awakening), and staring spells (12).

Clinical management of a first seizure

Because medical personnel often do not witness the first seizure, medical history may be the most important part in the

evaluation of a patient. A thorough description of the event from start to finish from a primary witness should be obtained. Information should be collected on what the patient was doing just before the seizure, as well as on postictal symptoms, such as confusion or hemiparesis. An accurate description of seizure semiology, including whether consciousness was affected, lateralizing signs or automatisms, and other behaviors is important because different tests and treatments may be indicated (or contraindicated) for specific seizure types. An accurate description of seizure semiology at onset is particularly important, as this might give clues as to whether a generalized seizure actually had a partial onset (3). There are no specific symptoms to discriminate between epileptic seizures and non-epileptic events. Several studies have investigated prolactin or creatine kinase levels in blood, that may help distinguish epileptic from non-epileptic events, but neither approach is reliable enough for routine diagnostic use (13). Details of possible fever history, chronic medical conditions (eg, diabetes), medications (eg, clozapine), behavioral or dietary changes, and recent or remote history of head trauma or CNS infection must be collected. A family history of epilepsy or febrile seizures, particularly among first-degree relatives, should be obtained. A developmental history is important in assessing possible etiologies and likelihood of future events (2).

Differential Diagnosis

Many disorders can mimic seizures in children and should therefore be considered in the differential diagnosis of a first seizure in a child. The most common nonepileptic paroxysmal disorders include the following:

- Syncope or breath-holding spells
- Migraine
- Benign paroxysmal vertigo
- Behavioral events such as nonepileptic staring spells, jitteriness, self-stimulation, or stereotypies
- Gastrointestinal reflux (Sandifer syndrome)
- Movement disorders such tics, benign myoclonus, dyskinesias, or dystonias
- Sleep disorders such as night terrors or confusional arousals
- Psychogenic pseudoseizures or panic attacks (14).

Laboratory and Diagnostic Evaluation

Initial laboratory evaluation of a first seizure can include serum studies for glucose, electrolytes, calcium, and magnesium, as well as toxicology studies (15). A CT scan should be performed if the patient has had recent head trauma, or presents a significantly altered mental status, significant headache, papilledema or bulging fontanelle, or an abnormal neurologic examination. A lumbar puncture (LP) should be considered in patients who have fever and a stiff neck, or who have fever and are unconscious. If increased intracranial pressure is suspected, non-contrast CT scan should be obtained prior to a LP, as there may be the risk of inducing cerebral herniation with space-occupying lesions or obstructive hydrocephalus. If a CNS infection is suspected, an appropriate empiric antibiotic and antiviral medications should be administered promptly. Steroids are currently thought to improve the outcome in some forms of bacterial CNS infection, in particular Haemophilus influenzae type b, and should be administered before the antibiotics as a rapid infusion, unless this would entail a delay in the initiation of antibiotic therapy (16). LP is best obtained prior to antibiotic administration, but it can also be obtained during, or after, administration, if technical factors would otherwise cause a substantial delay of treatment. Particular attention should be paid to the laboratory evaluation of neonatal patients, since glucose and calcium abnormalities can be observed in the first week of life. When a metabolic abnormality is suspected in a neonate, a basic metabolic evaluation should be considered, involving testing for serum ammonia, serum lactate and pyruvate, serum for amino acids, and urine for organic acids. Further metabolic studies should be guided by the patient's medical history, examination and clinical course (17). Electroencephalograms are an important tool in determining prognosis for future seizures and should be strongly considered for all children with a first seizure. If the child is clinically stable, it may not be necessary to perform an EEG on an emergent basis. An EEG does not prove whether or not the patient has had a seizure, as this is a clinical diagnosis. In healthy individuals, 10% have an abnormal EEG, whereas 50% of patients with epilepsy

have a normal first EEG. Repeating the EEG a second time may increase the sensitivity to 80-90%. EEGs may be helpful in classifying seizure types and identifying particular epilepsy syndromes, such as benign rolandic epilepsy or JME. This classification system can help with both the prognosis and determining appropriate anticonvulsant therapy. For more information regarding EEG findings in specific childhood epilepsy syndromes, see EEG in Common Epilepsy Syndromes (18). If clinical concern arises for non-convulsive status epilepticus following a clinical seizure, an EEG can help to determine if the patient is still having electrographic seizure activity. An EEG is important if a nonreactive patient who has received paralytics for intubation does not show awakening in the critical care unit after the expected timeframe. Clinical signs, such as appropriate pupil reactivity and withdrawal reflex in response to pain/stimulation, can be helpful clues indicating that the patient is not in continuous non-convulsive status epilepticus (19).

Neuroimaging

The selection of imaging techniques depends on the clinical features, the age of the patient and, if present, the type of epilepsy suspected (4). According to evidence in the literature, structural alterations visible with neuroradiological imaging techniques (CT-MRI) are present in approximately 10% of adults with a first seizure, suggesting an etiological diagnosis (cerebral hemorrhage, cerebral edema, cerebral post-traumatic complications, intracranial expansive process) and may be relevant in determining a possible risk of recurrence of seizures (20). MRI of the brain is the test of choice to identify structural brain lesions. In acute situations and in poorly cooperative patients, as well as in patients with contraindications for an MRI scan, a CT scan is a viable alternative (21). In the case of new-onset seizures it is recommended to perform an MRI scan to determine the etiology of seizures in the following situations (22):

- focal-onset seizures suspected on the basis of medical history or EEG;
- unclassifiable seizures debut or apparently generalized crisis in the first year of life or in adult patients;
- presence of focal neurological or neuropsychological deficits;
- difficulty in obtaining seizure control with first line drugs (23);
- changes in the characteristics of the crisis, indicating the presence of a progressive disease (24).

The celerity with which MRI should be performed depends on the clinical context, and should not exceed 2 weeks post-seizure.

In patients with seizures or epilepsy, an urgent CT or MRI scan is recommended under these conditions:

- new postictal neurological deficit;
- recent trauma, persistent headache, cancer, bleeding disorders, history of immunodeficiency (25).

Functional imaging including SPECT (Single Photon Emission Computed Tomography), PET (Positron Emission Tomography) fMRI and other techniques providing information on metabolism and cerebral blood flow can be used in the study of seizure disorders, but are of limited clinical utility in most patients with epilepsy. However, they have an important complementary role in evaluating patients undergoing surgery (26).

Role of neuroimaging in children

The evidence in favor of or against performing neuroimaging investigations in children who present with a single unprovoked seizure, are insufficient (27). Neuroimaging examinations are recommended in children with focal neurological deficits or in children who do not return to pre-attack neurological function within a few hours, as well as in children with head trauma or a history of malignancy. A non-urgent Magnetic Resonance Imaging (MRI) procedure should be considered in children who are under one year old (28). If the child has had recent head trauma, recurrent seizures, focal or new neurologic deficits, and/or papilledema, neuroimaging should be obtained. Patients who have clearly defined epileptic syndromes, such as petit mal epilepsy or benign rolandic epilepsy, do not necessarily require a brain MRI. The necessity for neuroimaging in a child with new onset afebrile seizures is controversial (29). Without stratifying based on history and neurologic examination findings, a recent meta-analysis reported that emergent head CT resulted in a change in acute management in 3-8% of children presenting at an emergency department with a seizure. Clinically signifi-

cant neuroimaging abnormalities have been reported in 2% of children with a single afebrile seizure without focal features or predisposing conditions. The decision on whether or not to obtain neuroimaging in these cases should be made on an individual basis and an EEG can be helpful. For example, a focal EEG may increase the suspicion of a structural abnormality (30).

Conclusion

Seizures in children are relatively common clinical occurrences. These are usually self-limiting, with severe and longer lasting episodes being rather rare (5). It is always of paramount importance to obtain personal and family medical history, details on seizure characteristics (duration, location, any physical symptoms such as bladder or bowel incontinence), body temperature and relevant symptoms, as well as any history of head injuries (9).

References

1. Adams SM, Knowles PD: Evalutation of a first seizure. Am Fam Physician 2007; 75:1342-1347.
2. Hitz D, Berg A, Bettis D :Practice parameter: treatment of the child with a first unprovoked seizure: report of the quality standards subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2000; 60:166-175.
3. Soto-Ares G, Jissendi Tchofo P, Szurhaj W,Trehan G, Leclerc X: Management of patients after a first seizure. J Neuroradiol. 2004; 31:281-288.
4. Andriola MR, Ettinger AB : Pseudoseizures and other nonepileptic paroxysmal disorders in children and adolescents. Neurology 1999; 53:S89-95.
5. Shinnar S, TA Glauser: Febrile seizures. J Child Neurol. 2002; 17: S44-52.
6. Adams SM, Knowles PD. Evaluation of a First Seizure. American Family Physician. 2007; 75:1342-1347.
7. van Gaal JC, Petru R, Sie LT: An infant with unexplained epilepsy. Ned Tijdschr Geneeskd. 2010;154-50:A2420.
8. Sharieff GQ, Hendry PL: Afebrile pediatric seizures. Emerg Med Clin North Am. 2011; 29:95-108.
9. Maytal J, Krauss JM, Novak G, Nagelberg J, Patel M: The role of brain computed tomography in evaluating children with new onset of seizures in the emergency department. Epilepsia. 2000; 41-8:950-954
10. Reuter D, Brownstein D: Common emergent pediatric neurologic problems. Emerg Med Clin North Am. 2002;20:155-176.
11. Mustafić N, Tahirović H, Trnovcević J :Frequency of recurrent convulsions after a first febrile seizure: two-year observation results. Lijec Vjesn. 2010; 132:227-231.
12. Harden CL, Huff JS, Schwartz TH, Dubinsky RM, Zimmerman RD, Weinstein S: Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2007;69:1772-1780.
13. Sharma S, Riviello JJ, Harper MB, Baskin MN: The role of emergent neuroimaging in children with new-onset afebrile seizures. Pediatrics 2003;111:1-5.
14. Shinnar S, Glauser TA: Febrile seizures. J Child Neurol. 2002;17:S44-52.
15. Shinnar S, O'Dell C, Berg AT: Distribution of epilepsy syndromes in a cohort of children prospectively monitored from the time of their first unprovoked seizure subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Epilepsia. 1999;40:1378-1383.
16. Pillai J, Sperling MR: Interictal EEG and the diagnosis of epilepsy. Epilepsia. 2006;47-S1:14-22.
17. Musicco M, Beghi E, Solari A, Viani F: Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. Neurology. 1997;49:991-998.
18. Stroink H, Brouwer OF, Arts WF: The first unprovoked, untreated seizure in childhood: a hospital based study of the accuracy of the diagnosis, rate of recurrence, and long term outcome after recurrence. Dutch study of epilepsy in childhood. J Neurol Neurosurg Psychiatry 1998;64:595-600.
19. Expert Committee on Pediatric Epilepsy, Indian Academy of Pediatrics: Guidelines for diagnosis and management of childhood epilepsy. Indian Pediatr. 2009;46:681-698.
20. Freeman JM: Less testing is needed in the emergency room after a first afebrile

seizure. Pediatrics 2003;111:194-196.
21. Beghi E, Leone M, Solari A: Mortality in patients with a first unprovoked seizure Epilepsia.2005, 46, suppl 11:40-42.
22. Braunwald E, Fauci AS, DL Kasper, SL Hauser, DL Longo, JL Jameson: Malattie del sistema nervoso centrale. Eds. Harrison Principi di Medicina Interna 15a ed. It. New York, 2001:2354-2369.
23. Beghi E: Prognosis of first seizure. Prognosis of Epilepsies, Jallon P (ed). John Libbey Eurotext, Paris, 2003:21-28.
24. Annegers JF, Hauser WA, Lee JR, Rocca WA: Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia 1995; 36:327-333.
25. Berg AT, Shinnar S: The risk of seizure recurrence following a first unprovoked seizure: A quantitative review. Neurology 1991; 41: 965-972.
26. Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, Camfield P, Crumrine P, Elterman R, Schneider S, Shinnar S: Practice parameter: evaluating a first nonfebrile seizure in children: Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society. Neurology 2000; 55:616-623.
27. Hirtz D, Berg A, Bettis D, Camfield C, Camfield P, Crumrine P, Gaillard WD, Schneider S, Shinnar S: Practice parameter: treatment of the child with a first unprovoked seizure. Neurology 2003; 60:166-175.
28. Hoefnagels WA, Padberg GW, Overweg J, van der Velde EA, Roos RA: Transient loss of consciousness: the value of the history for distinguishing seizure from syncope. J Neurol 1991; 238:39-43.
29. King MA, Newton MR, Jackson GD, Fitt GJ, Mitchell LA, Silvapulle MJ, Berkovic SF: Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. Lancet 1998; 352: 1007-1011.
30. Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D: Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. Lancet 2005; 365:2007-2013.