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Clinical evaluation of neuroimaging abnormality in children suffering from new onset afebrile seizure

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Abstract

The aim of emergent neuroimaging in patients with a first afebrile seizure is to determine a severe cranial pathology that may require immediate intervention and treatment. The American Academy of Neurology states that there is insufficient evidence to support a recommendation at the level of standard or guideline for the use of routine neuroimaging in children with a first afebrile seizure.8 Therefore, emergent neuroimaging is indicated for selected cases according to history and physical examination considering potential risks of radiation, sedation and contrast agent. However, in routine practice, children presenting to emergency department (ED) with a first afebrile seizure are often evaluated with cranial imaging, especially CT. Many factors, such as parental stress and tension, physicians' fear of legal issues that could arise after an incorrect diagnosis and abstaining from life-threatening consequences, are likely to be effective in this decision. Hence based on above findings the present study was planned clinical evaluation of neuroimaging abnormality in children suffered from new onset afebrile seizure.

The study was planned in Upgraded Department of Pediatrics, Patna medical College and Hospital, Patna, Bihar. The study was conducted from the May 2016 to June 2017. The study was conducted on 20 childrens of age 6 months to 12 years of age undergoing the neuroimaging for the new-onset afebrile seizure were evaluated in the present study.

The data generated from the present study concludes that Incidence of neuro-imaging abnormality in children presenting with first afebrile seizure is high in developing countries like India due to high prevalence of NCC and tuberculosis so neuro-imaging should be considered in any child with first afebrile seizure. Although MRI is the accepted imaging modality in children with seizures, CT may be an option in cases if MRI is technically not possible.

Keywords: first onset afebrile seizure, pediatric age group, neuroimaging abnormalities, management, etc

Introduction

A febrile seizure, also known as a fever fit or febrile convulsion, is a seizure associated with a high body temperature but without any serious underlying health issue. They most commonly occur in children between the ages of 6 months and 5 years. Most seizures are less than five minutes in duration and the child is completely back to normal within an hour of the event.

Febrile seizures may run in families. The diagnosis involves verifying that there is not an infection of the brain, there are no metabolic problems, and there have not been prior seizures that have occurred without a fever. There are two types of febrile seizures: simple febrile seizures and complex febrile seizures. Simple febrile seizures involve an otherwise healthy child who has at most one tonic-clonic seizure lasting less than 15 minutes in a 24-hour period. Blood testing, imaging of the brain or an electroencephalogram (EEG) is typically not needed for the diagnosis. Examination to determine the source of the fever is recommended. In otherwise healthy-looking children a lumbar puncture is not necessarily required.

Neither anti-seizure medication nor anti-fever medication are recommended in an effort to prevent further simple febrile seizures. In the few cases that last greater than five minutes a benzodiazepine such as lorazepam or midazolam may be used. Outcomes are generally excellent with similar academic achievements to other children and no change in the risk of death for those with simple seizures. There is tentative evidence that affected children have a slightly increased risk of epilepsy at 2%. Febrile seizures affect two to five percent of children before the age of five [1, 2]. They are more common in boys than girls. After a single febrile seizure there is a 15 to 70% chance of another one [1].

Population-based estimates suggest that every year 25,000–40,000 children in the United States experience a first unprovoked seizure [1]. Using the International League Against Epilepsy (ILAE) definition, this includes multiple seizures within a 24-hour period if the child returns to baseline consciousness between episodes [2].

Most of these children never experience a recurrence. However, a seizure may be the initial presentation of a more serious medical condition or subsequent epilepsy. Historically, epilepsy has been defined as a condition in which a child has 2 or more seizures without a proximal cause for the seizures (unprovoked seizures). In 2013, the ILAE also accepted these 2 alternative conditions: 1) one unprovoked or reflex seizure plus a recurrence risk of at least 60% over the next 10 years; or 2) a diagnosis of an epilepsy syndrome [3].

Identification of the underlying seizure etiology helps to identify appropriate treatment options and the prognosis for the child. In evaluating the child after a first seizure, the first consideration should be determining if the seizure was provoked or unprovoked. In the case of provoked seizures,

treatment should include identifying and treating the underlying etiology. Some etiologies of provoked (symptomatic) childhood seizures include central nervous system (CNS) infections, metabolic alterations, head trauma, and structural abnormalities. CNS infections, such as meningitis, encephalitis, and empyema, can present with seizures. Identifying and treating the underlying infection is imperative.

Metabolic alterations can precipitate seizures and can be directly treatable targets. In children who are receiving intravenous (IV) fluids, are diabetic, or who may otherwise be prone to electrolyte abnormalities, consider evaluating glucose, sodium, and calcium levels. For patients with chronic hyponatremia, rapid sodium correction should be avoided to prevent central pontine myelinolysis. Also consider obtaining toxicology screens to evaluate for medication or toxic exposures.

Head trauma can precipitate seizures and requires immediate evaluation with appropriate neuroimaging studies 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 of seizures but can be ruled out with appropriate neuroimaging studies. Focal cortical dysplasias are a frequent cause of medically refractory epilepsy.

Febrile seizures are convulsions in infants and children triggered by a fever in the absence of CNS infection. Febrile seizures affect 4–5% of children aged 6 months to 6 years. These occur in association with a high fever, typically above 38.5°C (101.3°F), although some believe the rate of change in body temperature is more provoking than the absolute temperature in febrile seizures. There is often a positive family history of febrile seizures in other family members. A second episode occurs in 33% of children, and only 50% of those have a third episode. Few children, approximately 3–6%, with febrile seizures develop afebrile seizures or epilepsy. Electroencephalography (EEG) and neuroimaging are generally not warranted [4]. Further evaluation may be required for complex febrile seizures, which include seizures that are greater than 15 minutes in duration, have focal onset, or occur multiple times within 24 hours or within a febrile illness.

An exhaustive list of seizure types and pediatric epilepsy syndromes is beyond the scope of this article. However, familiarity with some of the most common seizure syndromes can aid the clinician in obtaining an appropriate workup and evaluation. Infantile spasms typically begin in infants aged 4–8 months (although earlier and later presentations do occur) and consist of clusters of myoclonic spasms, typically upon awakening or falling asleep. The presentations can be more subtle and include slight eye flutter or head drop. If infantile spasms are suspected, appropriate diagnosis and swift management is essential to improve developmental outcome.

Absence epilepsy, also known as petit mal epilepsy, is manifested by frequent (as many as 100 times 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 primarily generalized in onset. The diagnosis can be assisted by classic EEG features and hyperventilation trial, which often provokes the seizures.

Benign rolandic epilepsy occurs in children aged 3–13 years [5]. The 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 the diagnosis of this syndrome. Other benign partial epilepsies of childhood include benign occipital epilepsy of childhood (Gastaut syndrome), in which visual symptoms predominate, and Panayiotopoulos syndrome, in which autonomic changes, vomiting, sweating, and pallor are prominent ictal symptoms.

Juvenile myoclonic epilepsy (JME) may present 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 [6].

Because medical personnel often do not witness the first seizure, eyewitness accounts are a crucial step in evaluation. Collect information on what the patient was doing just before the seizure (eg, association with sleep onset or arousal from sleep). Seizure while watching television or flickering lights may suggest a photosensitive seizure.

An accurate description of seizure semiology can help differentiate between specific seizure types. One should ask about alteration of consciousness, lateralizing signs (eg, eye deviations, head turning, focal clonus) or automatisms (eg, lip smacking, picking at clothes, gestures such as fumbling or tapping) [6]. An accurate description of seizure semiology at onset is particularly important, as this might give clues to whether a generalized seizure actually had a partial onset [2].

If possible, getting the patient's account of the event can provide further diagnostic clues. For example, olfactory or epigastric aura are suggestive of temporal lobe epilepsy, while visual hallucinations can occur with occipital lobe seizures. In addition to events immediately surrounding the seizure, it is important to gather any history of recent illnesses, antibiotic treatment (which may raise suspicion for a partially treated meningitis), recent travel, recent head injury, chemical or toxin exposures, and intake of medications, supplements, alcohol, and/or illicit drugs. Obtain a family history of epilepsy or febrile seizures, particularly among first-degree relatives. Elicit a history of fever, chronic medical conditions (eg, diabetes), medications, behavioral or dietary changes, and recent or remote history of head trauma or CNS infections. A developmental history is important in assessing possible etiologies and risk of future events.

Initial laboratory evaluation of a first seizure can include serum studies for levels of glucose, electrolytes, calcium, and magnesium and for toxicology. The American Academy of Neurology (AAN) recommends that clinicians use their clinical judgment [5]. While it is not routinely tested, prolactin may help to distinguish seizures from nonepileptic events [7]. Give particular attention to the laboratory evaluation of the neonate, as glucose and calcium abnormalities can be observed in the first week of life. When a metabolic abnormality is suspected in the neonate, consider a basic metabolic evaluation with serum ammonia, serum lactate and pyruvate, serum for amino acids, and urine for organic acids. Further metabolic studies should be guided by the history, examination, and clinical course.

The role of neuroimaging in a child with new-onset afebrile seizures is controversial. Emergent neuroimaging should be performed when there is a high clinical suspicion for a

condition requiring immediate intervention, such as recent head trauma, recurrent seizures, focal or new neurologic deficits, and papilledema. Neuroimaging should also be considered if the patient has not returned to baseline. In marked distinction to the adult population seen in the emergency department, afebrile seizures in children are not commonly associated with abnormal neuroimaging [8].

Clinically significant neuroimaging abnormalities have been reported in 2% of children presenting with first afebrile seizure without focal features or predisposing conditions. [9] The decision of whether or not to obtain neuroimaging in these cases should be made on an individual basis, and an electroencephalogram (EEG) can be helpful. For example, a focal EEG may increase suspicion for a structural abnormality. Patients who have clearly defined epileptic syndromes, such as absence epilepsy or benign rolandic epilepsy, do not necessarily require neuroimaging. American Academy of Neurology (AAN) practice parameters recommend nonurgent imaging after initial seizure in situations in which there is a significant cognitive or motor impairment, unexplained abnormalities on the neurological examination, partial-onset seizures, an EEG inconsistent with a benign or primary generalized epilepsy, and in patients younger than 1 year [5].

If neuroimaging is obtained, MRI is the preferred method of imaging to avoid radiation exposure while providing more detailed diagnostic information [7]. However, CT is still frequently obtained based on available resources. According to one study, CT in the emergency department for children presenting with first seizure will change acute management in approximately 3 to 8% of patients [10].

The aim of emergent neuroimaging in patients with a first afebrile seizure is to determine a severe cranial pathology that may require immediate intervention and treatment. The American Academy of Neurology states that there is insufficient evidence to support a recommendation at the level of standard or guideline for the use of routine neuroimaging in children with a first afebrile seizure.8 Therefore, emergent neuroimaging is indicated for selected cases according to history and physical examination considering potential risks of radiation, sedation and contrast agent [11, 13]. However, in routine practice, children presenting to emergency department (ED) with a first afebrile seizure are often evaluated with cranial imaging, especially CT. Many factors, such as parental stress and tension, physicians' fear of legal issues that could arise after an incorrect diagnosis and abstaining from life-threatening consequences, are likely to be effective in this decision. Hence based on above findings the present study was planned clinical evaluation of neuroimaging abnormality in children suffered from new onset afebrile seizure.

Methodology

The study was planned in Upgraded Department of Pediatrics, Patna medical College and Hospital, Patna, Bihar. The study was conducted from the May 2016 to June 2017. The study was conducted on 20 childrens of age 6 months to 12 years of age undergoing the neuroimaging for the new-onset afebrile seizure were evaluated in the present study.

Demographic features, predisposing conditions (high risk factors for seizure such as neonatal hypoglycemia, perinatal asphyxia, bleeding disorders, malignancy, immune deficiency, previously known hydrocephalus or cranial tumor, recent head injury or operation), characteristics of the seizures (seizure type, duration, number of seizures), neurologic examination after seizure, baseline neurologic status, and neuroimaging results were recorded.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: 1. Children between the age of 6 months-12 years presenting with first onset of unprovoked seizures.
2. No h/o fever.
3. Informed consent given by parents.

Exclusion Criteria: 1. Contraindications to MRI such as metallic clips etc.
2. Age less than 6 months or more than 12 years.
3. Patients with febrile seizures or with CNS infections

Results & Discussion

Afebrile seizures are one of the most common neurological emergencies among children. There are multiple causes of seizure, but new-onset epilepsy is the most common cause of a first afebrile seizure. The patient history and physical examination should direct the type and timing of laboratory and imaging studies [14]. The role of neuroimaging is not well defined in children presenting to ED with a first seizure. Neuroimaging was done after stabilization and sedation given if needed to reduce motion artefacts. Neuroimaging was done either as urgent or non-urgent study. MRI was preferred in most situations as it better detected the abnormality compared to other imaging modalities.

Neuroimaging is usually obtained to establish etiology and to plan appropriate clinical cure.3 The purpose of performing an urgent neuroimaging study in a child with first afebrile seizure is to detect a serious condition that may require immediate intervention. The purpose of performing a non-urgent neuroimaging study, which can be deferred to the next few days or later, is to detect abnormalities that may affect prognosis and therefore have an impact on long-term treatment and management [15, 16].

Patients with a clinical history and EEG findings consistent with an idiopathic epilepsy, such as childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, and benign childhood epilepsy with centrotemporal spikes (benign rolandic epilepsy), do not require brain imaging. Brain imaging should, however, be performed in children who have had two or more afebrile epileptic seizures and who do not have the clinical or EEG features of an idiopathic epilepsy. Although MRI is superior to CT in demonstrating subtle brain developmental abnormalities, the choice of imaging modality will be influenced by the availability of MRI and the need to administer a general anesthetic to young children during the MRI. Although neuroimaging abnormalities occur in up to one-third of children with a first afebrile seizure, only 2% demonstrate clinically significant abnormalities that influence management [17]. Seizures are an uncommon presenting symptom of a brain tumor in children.

Few studies comment on the duration or number of seizures upon presentation in infants. Infants appear less likely to have prolonged seizures than older children and adolescents [18]. In contrast, the seizure recurrence rate during admission was considerably higher than previous reports of 20% in children

of all ages [19]. The high risk of recurrence supports policies for prolonged observation either in the ED or on inpatient wards in this population.

In a large retrospective study of children with new-onset afebrile seizure, 2 criteria were found to be associated with high risk for clinically significant abnormal neuroimaging: 1) presence of a predisposing condition (sickle cell disease, bleeding disorders, cerebral vascular disease, malignancy, human immunodeficiency virus infection, closed-head injury, hydrocephalus), and 2) focal seizure if the patient is <33 months old. In high-risk patients, 26% had clinically significant abnormal neuroimaging compared with 2% of patients in the low-risk group [20]. Warden *et al*. [21] reported that neuroimaging results were always normal when the patient did not have an underlying high-risk condition (malignancy, neurocutaneous disorder, recent closed-head injury, or recent cerebrospinal fluid shunt revision), was older than 6 months, had sustained a seizure of 15 minutes or less, and did not have a history of a new-onset focal neurologic deficit.

Table 1: Neuroimaging abnormalities of studied cases

Neuroimaging	No. Of cases
Normal	6
Abnormal	14
Total	20

Table 2: Neuroimaging abnormalities

Neuroimaging report	Frequency
Normal	7
NCC	6
Tuberculoma	3
Infract	1
Tumor	1
Misc.	2
Total	20

Table 3: Correlation between type of seizure and abnormal neuroimaging

	Seizure		
Neuroimaging	**Focal**	**General**	**Total**
Abnormal	10	5	15
Normal	1	4	5
Total	11	9	20

Table 4: Correlation between neurological examination (GCS) and neuroimaging abnormalities.

Neuroimaging	GCS<9	GCS>9	Total cases
Normal	3(12%)	22(88%)	25
Abnormal	10(20%)	40(80%)	50

In weighing choice of imaging modalities, several factors need to be considered. Accessibility of imaging modality is often a major determinant; CT is more widely available especially in urgent circumstances. CT involves the risk of radiation exposure while MRI involves the risks of sedation in most infants. Proper diagnosis, however, provides therapeutic and prognostic implications. Symptomatic epilepsies in the first year can correlate with more difficult-to-control seizures.35 In addition, the developmental outcome is reported to be poorer in symptomatic epilepsies beginning in the first years of life, as opposed to cryptogenic epilepsies [22, 24]. The higher rate of localization-related seizures in this age range, the higher rate of abnormalities in infants vs older children, the prognostic implications, and the superior yield of MRI compared to CT in identifying and defining abnormalities support the view that MRI should be obtained in all infants under 2 years old presenting with a new-onset afebrile seizure. An argument can be made for cases in which urgent neuroimaging is not indicated and the infant can be observed, to avoid CT, and thus unnecessary radiation, and instead arrange for a brain MRI.

Khodapanahandeh and Hadizadeh [25] suggested the use of neuroimaging studies for children who present with focal seizures, abnormal neurological findings or who are younger than 2 years of age. The AAN guidelines [26] recommend the use of emergency neuroimaging for any child of any age who exhibits a postictal focal deficit (i.e. Todd's paresis) that does not resolve quickly or who has not returned to baseline within several hours after the seizure. In other reports [27, 28] nonurgent MRI should be considered for any child with a significant cognitive or motor impairment of unknown etiology, unexplained abnormalities on neurological examination, a seizure of focal onset with or without secondary generalization, an electroencephalography result that does not represent a benign partial epilepsy of childhood or primary generalized epilepsy, or in children <1 year of age. Unfortunately, following the AAN guidelines, neuroimaging studies were ordered for 47 of the patients (94%) despite the absence of Todd's paresis. This resulted in performing unnecessary, expensive and, in some cases, high-radiation tests on the children based on our findings.

Afebrile seizures are one of common problem in children of all ages. This might be due to birth asphyxia, neurocysticercosis and nervous system infections and other risk factors [29, 30]. The basis of incidence can be evaluated by EEG. It is mostly useful in investigating afebrile epileptic seizures and its risk of recurrence. It is advantageous to perform neuroimaging (CT or MRI) in children who had two or more afebrile epileptic seizures and who do not have EEG features of an idiopathic epilepsy. MRI is superior to CT in demonstrating elusive brain developmental abnormalities [31, 32].

Conclusion

The data generated from the present study concludes that Incidence of neuro-imaging abnormality in children presenting with first afebrile seizure is high in developing countries like india due to high prevalence of NCC and tuberculosis so neuro-imaging should be considered in any child with first afebrile seizure. Although MRI is the accepted imaging modality in children with seizures, CT may be an option in cases if MRI is technically not possible.

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