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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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Pediatrics 2003;111;1-5

DOI: 10.1542/peds.111.1.1

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<http://www.pediatrics.org/cgi/content/full/111/1/1>

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The Role of Emergent Neuroimaging in Children With New-Onset Afebrile Seizures

Sujit Sharma, MD*; James J. Riviello, MD§; Marvin B. Harper, MD‡; and Marc N. Baskin, MD‡

ABSTRACT. *Objectives.* The objectives of this study were 1) to determine the frequency of clinically significant abnormal neuroimaging in children coming to the emergency department (ED) with new-onset afebrile seizures (ASZ), and 2) to identify children at high or low risk for clinically significant abnormal neuroimaging.

Design/Methods. Five hundred consecutive cases of new-onset ASZ seen in the ED of a tertiary care children's hospital were reviewed. Neuroimaging reports were categorized as normal, clinically insignificant abnormal, or clinically significant abnormal. Recursive partition analysis was used to identify clinical variables that separated children into high- and low-risk groups for clinically significant abnormal neuroimaging.

Results. Ninety-five percent of patients (475/500) with new-onset ASZ had neuroimaging. Clinically significant abnormal neuroimaging was noted in 8% (95% confidence interval [CI]: 6, 11; 38/475) of patients. Recursive partition analysis identified 2 criteria associated with high risk for clinically significant abnormal neuroimaging: 1) the presence of a predisposing condition, and 2) focal seizure if <33 months old. Of the high-risk patients, 26% (95% CI: 17, 35; 32/121) had clinically significant abnormal neuroimaging compared with 2% (95% CI: 0.6, 3.7; 6/354) in the low-risk group.

Conclusions. In this large, retrospective review of children with new-onset ASZ, clinically significant abnormal neuroimaging occurred with relatively low frequency. Emergent neuroimaging should be considered, however, for children who meet high-risk criteria. Well-appearing children who meet low-risk criteria can be safely discharged from the ED (if follow-up can be assured) without emergent neuroimaging, because their risk for clinically significant abnormal neuroimaging is appreciably lower. *Pediatrics* 2003;111:1–5; *afebrile seizures, children, evaluation, neuroimaging, computed tomography.*

ABBREVIATIONS. ED, emergency department; ASZ, afebrile seizures; CT, computed tomography; MRI, magnetic resonance imaging; CI, confidence interval.

The role of emergent neuroimaging (neuroimaging obtained as part of the emergency department [ED] evaluation) in children presenting with new-onset afebrile seizures (ASZ) is not well defined. A practice parameter recently published by the American Academy of Neurology¹ states that insufficient evidence is available to make a recommendation at the level of standard or guideline for the use of routine neuroimaging in children with new-onset ASZ. In contrast, guidelines for obtaining emergent neuroimaging in adult patients presenting with seizures have been recently published.² These guidelines are based on a review of numerous studies, some of which have documented a prevalence of abnormal neuroimaging ranging from 34% to 45%.^{3–5} Because of the large proportion of structural lesions requiring immediate therapy (most often stroke or neoplasm), emergent or urgent neuroimaging has been recommended for most adults with new-onset seizures.²

In the few studies that have reviewed the yield of emergent neuroimaging in children presenting to the ED with new-onset seizures, the prevalence of abnormalities ranged from 0% to 21%.^{6–9} To better estimate the prevalence of abnormal neuroimaging, and specifically, clinically significant abnormal neuroimaging, we investigated a large, consecutive series of children with new-onset ASZ. Our study was also designed to identify clinical variables that could predict which children were at high or low risk for clinically significant abnormal neuroimaging.

METHODS

Study Design/Patients

We performed a retrospective review of 500 consecutive children with new-onset ASZ seen over the 34-month period between October 1996 and July 1998 in the ED of Children's Hospital, Boston, Massachusetts. This ED serves as main emergency care center for a diverse urban population, as well as a referral center for the larger metropolitan area. Patients with possible seizures were identified by the ED *International Classification of Diseases*,

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Received for publication Feb 5, 2002; accepted May 14, 2002.

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Ninth Revision diagnosis codes for convulsions (febrile and generalized), grand mal seizures, status epilepticus, partial seizures, and epilepsy. Medical records were reviewed, and patients with recurrent seizures, febrile seizures, or with primary diagnoses other than seizures were excluded.

Data Collection

Historical, clinical, and neuroimaging data were abstracted from the medical record. Historical data included the following: age, sex, presence of any predisposing conditions, known toxic ingestion, length of seizure, focality of seizure, report of a focal deficit, whether the patient was seen initially at another medical institution, and number of seizures before evaluation. Children with multiple seizures of recent onset were included if they had not had any previous medical evaluation.

Predisposing conditions were defined a priori as conditions placing the patient at increased risk for abnormal neuroimaging (Table 1). Predisposing conditions were defined as sickle cell disease, bleeding disorders, cerebral vascular disease, malignancy, human immunodeficiency virus infection, hemihypertrophy, hydrocephalus, travel to an area endemic for cysticercosis (ie, Mexico, Central or South America, Africa, Asia, Spain, or Portugal), or recent significant closed-head injury. Closed-head injury was considered significant if it occurred in close temporal relationship to the seizure and was associated with any of the following: loss of consciousness, persistent headache, vomiting, change in mental status, or visit to a health care provider. Previous febrile seizures, developmental delay, attention-deficit/hyperactivity disorder, or Tourette's syndrome were not considered predisposing conditions.

Clinical data abstracted included temperature, abnormal mental status (if patient was described as lethargic, sleepy, toxic, ill-appearing, irritable, or obtunded by the most senior physician examining the patient), focal neurologic signs, seizures during the ED evaluation, endotracheal intubation, and hospital admission. Laboratory or ancillary data included serum chemistries, urine toxicological screen, electrocardiogram, and lumbar puncture.

Final computed tomography (CT) and magnetic resonance imaging (MRI) reports were categorized as normal, clinically insignificant abnormal, clinically significant abnormal, or not done. Clinically significant abnormal neuroimaging results were those that resulted in a change in the patient's management (eg, tumor or stroke) or prognosis (eg, lissencephaly), and not just a new investigation. Clinically insignificant findings were those considered to be incidental to the patient's seizure (eg, slight asymmetry of the lateral ventricles, small increases in the extra-axial fluid space, or no change from a prior study). All of the charts were reviewed by 1 investigator (S.S.). Charts of all patients whose neuroimaging was abnormal were reviewed by 3 authors (S.S., M.N.B., J.R.), and any disagreements were resolved by consensus. All abnormal neuroimaging reports (clinically insignificant as well as clinically significant) were reviewed by a pediatric neurologist (J.R.).

The timing of neuroimaging was categorized as 1) during the ED evaluation, 2) after discharge from the ED but within 24 hours, 3) 24 to 72 hours after presentation, or 4) >72 hours after presentation.

Statistical Analysis

Statistical analyses were conducted using Statistical Program for the Social Sciences, version 6.1.1 (SPSS Inc, Chicago, IL). Median values and associated ranges were reported for nonnormal data. Confidence intervals (CIs) for proportions were calculated using Stata Version 6 (Stata Inc, College Station, TX).

Recursive partition analysis was used to identify variables that could be associated with higher or lower risk for clinically significant abnormal neuroimaging. Recursive partition analysis is a tree-structured analysis (CART software, Salford Systems, San

Diego, CA) that partitions data into groups by categorical outcomes. In this analysis, potential predictors are analyzed to predict a single binary outcome variable (in our study, clinically significant abnormal neuroimaging). Splitting rules are developed in a stepwise fashion by analyzing each potential predictor and all possible cutpoints. Splits are made to minimize false-negative and false-positive assignments for the outcome variable at each step. Partitioning is repeated until any of the subgroups contain a homogenous group or the subgroups are too small for further subdivision. A parameter representing the significance of misclassifications can be modified such that the model maximizes sensitivity or specificity. Finally, the model is tested by V-fold cross-validation, whereby the data set is divided into 10 equal parts with similar distribution of dependent variables. Then, the model is derived with 9 parts (the learning set) and tested with 1 part (the validation set). This cross-validation is repeated 10 times, and the results are combined to develop the predictive accuracy and error rates for the tree. Previous medical publications have used recursive partition analysis to develop prediction rules to aid in the diagnosis of systemic lupus erythematosus, as well as myocardial infarction, and to predict vaccination status in children.¹⁰⁻¹³

Our major outcome variable was clinically significant abnormal CT, or MRI if CT was not performed. In our model, normal and clinically insignificant abnormal CT results were grouped together as normal. Potential predictor variables entered into the analysis included age, sex, presence of any predisposing conditions, duration of seizure, focality of seizure, report of a focal deficit, number of seizures before evaluation, temperature, mental status, neurologic examination, and need for endotracheal intubation.

This study was approved by the institutional review board at Children's Hospital, Boston.

RESULTS

There were 139 316 patients seen in the ED during the 34-month study period. Two percent (2832) had an *International Classification of Diseases, Ninth Revision* code of seizure. Five hundred (18%) of these patients had new-onset ASZ and formed our study group. The remaining 2332 patients were excluded for diagnoses of recurrent seizures (1312; 46%), febrile seizures (779; 28%), and nonseizure diagnoses (232; 8%), such as gastroesophageal reflux, breath-holding spells, and syncope.

The median age of the patients with their first ASZ was 46 months (range: 0–21 years; mean: 62 months; standard deviation: 59 months). Forty-seven percent of the patients were female. Fifty-eight percent (291/500) were admitted to the hospital, and the remainder were discharged from the hospital.

Neuroimaging was obtained in 95% (475/500) of cases. CT was the initial study performed in 91% (454/475) and MRI in 4% (21/475) of the cases. Ninety-two percent (437/475) had neuroimaging obtained while in the ED; 3% (13/475) had neuroimaging obtained after the ED visit, but within 72 hours of presentation; and the remaining 5% (25/475) had neuroimaging obtained >72 hours after presentation. No neuroimaging was obtained in 25 of the 500 cases. Clinical follow-up was available for 16 of these patients. No adverse events or new findings were noted in any of these patients at the time of follow-up. Overall, a neuroimaging result or clinical follow-up was available in 98% (491/500) of the cases we reviewed.

Normal neuroimaging results were reported in 83% (95% CI: 80, 86; 395/475). Clinically insignificant neuroimaging results were reported in 9% (95% CI: 6.4, 11.8; 42/475), whereas clinically significant neuroimaging abnormalities were reported in 8% (95% CI: 5.7, 10.8; 38/475). The 38 clinically significant abnormal neuroimaging cases are categorized in Ta-

TABLE 1. Predisposing Conditions Defined A Priori

Sickle cell disease
Bleeding disorders
Cerebral vascular disease
Malignancy
Human immunodeficiency virus infection
Hemihypertrophy
Hydrocephalus
Travel to an area endemic for cysticercosis
Closed-head injury

TABLE 2. Neuroimaging Abnormalities

Abnormality	Number of Patients (n = 38)
Hemorrhage	8
Contusion (1)	
Epidural (1)	
Subarachnoid (3)	
Subdural (2)	
Straight sinus thrombosis (1)	
Vascular	7
Acute infarction (3)	
Old infarction (4)	
Structural	6
Arachnoid cyst (2)	
Cavernous angioma (1)	
Tuberous sclerosis (1)	
Tumor (2)	
Infectious/inflammatory	4
Cysticercosis (3)	
Acute disseminated encephalomyelitis (1)	
Cortical dysgenesis	4
Hydrocephalus	3
Other	6
Abnormal mineralizations (4)	
Focal area of low density (2)	

ble 2. Of the 38 patients with abnormal neuroimaging, 8% (3/38) expired. Two of these patients suffered anoxic brain injury after presenting in prolonged status epilepticus. The other had suffered a severe closed-head injury. Thirteen percent (5/38) required operative interventions. These interventions included ventriculo-peritoneal shunt revision, intracranial pressure monitor placement after a closed-head injury, hemispherectomy (done 7 months after presentation) in a patient with an old middle cerebral artery territory infarct that led to intractable seizures, resection of benign frontal tumor 6 weeks after presentation, and resection of temporal lobe glioma.

The results of partition analysis are shown in Fig 1. Partition analysis identified 3 variables that partitioned the patients into 4 groups: the presence of a predisposing condition, focality of seizure, and age.

TABLE 3. Combined Risk Group Association With Clinically Significant Abnormal Neuroimaging

Risk Group	Patients (N = 475)	Clinically Significant Abnormal Neuroimaging	95% CI
High	121 (25%)	32 (26%)	17–35
Low	354 (75%)	6 (1.7%)	0.6–3.7

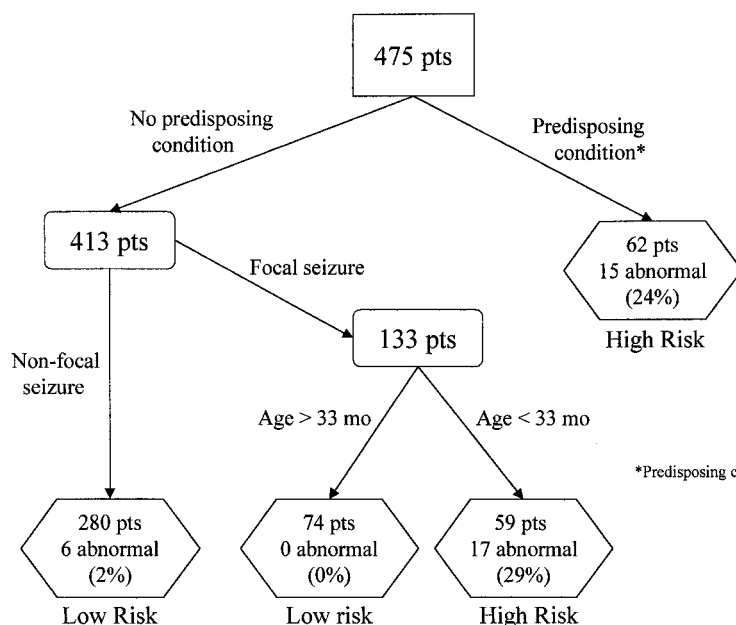
Two of these groups were at high risk for clinically significant abnormal neuroimaging, and 2 groups were at low risk. The prevalence of clinically significant abnormal neuroimaging for these combined high- and low-risk groups are shown in Table 3. Six patients with clinically significant abnormal neuroimaging met low-risk criteria according to partition analysis. Details of the clinical presentation, diagnosis, and outcome for these 6 patients are shown in Table 4.

DISCUSSION

Approximately 4% to 6% of children will have a seizure by 16 years of age.¹⁴ For those children coming to the ED with a new-onset ASZ, the role of neuroimaging is not well defined, because the prevalence of neuroimaging abnormalities in this population of children has not been extensively studied. In contrast, an abundance of such literature pertaining to adult patients exists, some of which report a prevalence of CT abnormalities between 34% and 45%.^{3–5} In 2 of these studies, the incidence of a neoplastic lesion or an acute infarction ranged between 22% and 26%.^{3,4} Recommendations have subsequently been published to obtain emergent or urgent neuroimaging in a large proportion of adults presenting with their first seizure.² Our study shows an 8% (95% CI: 6, 11) prevalence of clinically significant neuroimaging abnormalities in children with new-onset ASZ, with tumor or acute infarction occurring in only 1% (5/475). This drastic difference we describe underscores the need for different guidelines for the use of emergent neuroimaging in children presenting with new-onset ASZ.

Four studies have reported the prevalence of ab-

Fig 1. Recursive partition analysis of 475 patients with new-onset ASZ to identify clinical variables associated with high or low risk for clinically significant abnormal neuroimaging.



*Predisposing conditions listed in table 1

TABLE 4. Patients With Clinically Significant Neuroimaging Abnormalities Categorized as Low Risk by Partition Analysis

Case No.	Age	History	Physical Examination	Admission	Diagnosis	Management
1	2 mo	6-min seizure	Abnormal mental status	Yes	Subdural hematoma	Child abuse evaluation. No surgery or medications. Normal at age 5 mo.
2	3 y	Idiopathic status epilepticus	Abnormal mental status	Yes	Anoxic brain injury	Intensive care unit admission. Patient expired.
3	9 y	4-min seizure	Normal	No	5-mm arachnoid cyst	Anticonvulsants initiated.
4	10 y	10-min seizure	New right hemiparesis	Yes	Benign frontal lobe tumor	Resection 6 wk later.
5	12 y	5-min seizure	Normal	No	Grey matter heterotopia	Anticonvulsants initiated.
6	16 y	4 seizures	Hypertension	Yes	Hypertensive encephalopathy	Antihypertensive and anticonvulsants initiated.

normal neuroimaging in children with new-onset seizures coming to an ED. Landfish et al⁶ reviewed 56 patients with new-onset seizures. Only 16 patients (29%) had a new-onset ASZ, whereas the remainder (71%) were evaluated for febrile seizures. Twenty-five patients had neuroimaging performed with no abnormalities reported, although it is unclear which patients had neuroimaging. Maytal et al⁷ reviewed 66 children seen in the ED with new-onset seizures. Thirteen (20%) of these patients had complex febrile seizures. Abnormal neuroimaging was found in 21% overall. No attempt was made to differentiate between clinically significant and insignificant findings. Garvey et al⁸ reviewed 99 children with new-onset seizures, excluding patients with underlying neurologic disorders. Seventeen patients (17%) had complex febrile seizures. Nineteen percent overall were found to have abnormal neuroimaging, but only 7% had abnormal neuroimaging that “received further investigation or intervention,” and by our definition would be categorized as clinically significant abnormal neuroimaging. Warden et al⁹ reviewed 203 children with seizures. Fifteen percent had a chronic seizure disorder and 21% had febrile seizures (predominately complex febrile seizures). Abnormal neuroimaging was found in 12% overall. They did not differentiate between clinically significant and insignificant neuroimaging findings.

The prevalence of abnormal neuroimaging in these studies ranged between 0% and 21%. The proportion of children with febrile seizures ranged between 17% and 71%. Children with febrile seizures (simple or complex) are at low risk for neuroimaging abnormalities.^{15,16} Inclusion of these patients, along with relatively small sample sizes, may explain the variation in prevalence of abnormal neuroimaging in the studies. Also, in the larger 3 studies noted above, patients were included only if neuroimaging was obtained as part of the ED evaluation; a presumably large number of patients with new-onset ASZ in whom neuroimaging was not obtained were therefore excluded. This selection bias decreases the power of their calculations. In the study by Warden et al,⁹ CT scans were obtained in only 9% of the patients presenting with seizures during the study period. Although Warden et al⁹ performed a systematic analysis (recursive partition analysis) of the data in search of predictors for abnormal neuroimaging, they included children with febrile seizures as well as children with chronic seizure disorders. Inclusion of these children in their analysis is problematic, because children with febrile seizures and children

with chronic seizure disorders pose different diagnostic and management challenges (with different risk for abnormal neuroimaging) compared with children with new-onset ASZ.

Our study reviewed a large, consecutive series of patients presenting to the ED with new onset ASZ. Children with underlying disorders, including those who suffered head trauma, were not excluded. We did choose to exclude children with febrile seizures (simple or complex) as well as those presenting with recurrent seizures so that we could focus on those children in whom the yield of emergent neuroimaging was most controversial. We also chose to distinguish between clinically significant and insignificant neuroimaging findings to increase the clinical applicability of our results. Neuroimaging was obtained in 95% of the children presenting with a new-onset ASZ in our study (with clinical follow-up available on an additional 3% of the children). Therefore, our reported prevalence of 8% (95% CI: 6, 11) clinically significant abnormal neuroimaging may be more reliable than previous studies in which neuroimaging was not obtained in such high proportion of patients. Of the clinically significant abnormalities, tumor or acute infarction occurred in only 1% overall (5/475), whereas acute operative intervention was required in <1% of the children overall (3/475).

Our partition analysis model was developed with the goal of high sensitivity as well as clinical applicability (Fig 1). Two criteria associated with high risk for clinically significant abnormal neuroimaging were identified: 1) the presence of a predisposing condition, and 2) both focal seizure and age <33 months. Twenty-five percent of the patients overall were categorized as high risk, and 26% (95% CI: 17, 35) of these patients had clinically significant abnormal neuroimaging compared with 1.7% (95% CI: 0.6, 3.7) of those in the low-risk group (Table 3). Table 4 reviews the latter group of 6 children in whom clinically significant neuroimaging abnormalities were present despite not meeting high-risk criteria. In 4 of these children (cases 1, 2, 4, and 6), one of the following physical examination features was present: abnormal mental status, focal neurologic examination, or hypertension. The sensitivity of our partition analysis model could have been increased, as described in our methods, and would likely include these intuitively worrisome examination findings. However, the clinical applicability of the decision tree would be hampered, because these examination findings in unison occur in such low frequency.

It was not unexpected that recursive partition

analysis identified the presence of a predisposing condition to be associated with high risk for clinically significant abnormal neuroimaging. As outlined in our methods, this category was meant to represent conditions known to be associated with intracranial abnormalities for which a new-onset seizure could signify an intracranial lesion as the cause. The new finding we do identify is that the history of a focal seizure in a young child (<33 months old) is also associated with a higher risk for abnormalities. Other pediatric studies have suggested that a focal new-onset seizure is more often associated with abnormal neuroimaging.^{7,17} In our study, 33% (167/500) of the children presented with a focal seizure in their history. Using history of a focal seizure alone as a criterion for obtaining emergent neuroimaging may therefore be unwarranted, because it may lead to the performance of many unnecessary scans. Applying an age criterion, however, could allow us to limit these emergency scans to those children at increased risk for clinically significant abnormalities.

As this study was retrospective, clinical data were limited to what was available in the ED record and we could not ensure that clinical data were entered before obtaining the neuroimaging results. The investigators were not blinded from the clinical data when reviewing the final neuroimaging reports for significance. Results of our partition analysis should be validated on another patient population or by a prospective trial.

The use of neuroimaging modalities for the evaluation of seizures in children continues to be controversial. Although CT is more readily available in the ED setting, MRI is accepted as the more sensitive neuroimaging modality for children with seizures.^{18,19} Many pediatric neurologists will request MRI even after CT has been performed for this reason. In fact, of the 374 cases where CT was initially read as normal in our patient population, 163 (43%) went on to have MRI performed as well. In six of these cases (3.7%), the MRI showed a clinically significant abnormality. For patients who go on to develop epilepsy syndromes (at least 2 seizure episodes), Berg et al²⁰ have shown neuroimaging to be an important part of the evaluation, especially as specific epilepsy syndromes have higher likelihood of abnormal neuroimaging. Neurologic follow-up, including electroencephalogram analysis, is an important part of identifying specific epilepsy syndromes. Our study complements the Berg study well, because we identify those children with new-onset ASZ in whom additional evaluation could be safely deferred to the outpatient setting. This practice could help avoid the risk of sedating the child in the ED (often needed for neuroimaging), and save the cost of an unnecessary emergent CT in favor of more definitive MRI.

Based on our findings, we suggest that emergent neuroimaging should be considered for the following children with new-onset ASZ: 1) those with conditions predisposing them to intracranial abnormalities, and 2) those children with focal seizures who are <33 months old. Given the low frequency of abnormalities requiring immediate intervention in

children, those in the latter high-risk group could potentially have more sensitive MRI performed on an urgent outpatient basis if they are otherwise well-appearing, ie, intuitively concerning examination findings such as abnormal mental status or focal neurologic examination are absent. Well-appearing children with new-onset ASZ for whom these high-risk criteria do not apply can be safely discharged from the ED, without neuroimaging, if follow-up can be assured.

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Pediatrics 2003;111;1-5

DOI: 10.1542/peds.111.1.1

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