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Original Article

The Role of Continuous Electroencephalography in Childhood Encephalitis

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ABSTRACT

BACKGROUND: Seizures are a known complication of encephalitis. We sought to determine the incidence of seizures and the relative utility of routine and continuous electroencephalography in children with suspected encephalitis. **METHODS:** Records from all 217 children (ages 0-20 years, enrolled 2004-2011) from our institution who had diagnostic samples sent to the California Encephalitis Project were reviewed. **RESULTS:** One hundred children (46%) had at least one seizure observed clinically or recorded on electroencephalography. Diffuse abnormalities (e.g., generalized slowing) were more common than focal or epileptiform abnormalities (88.9% vs 63.2% and 57.3%, respectively; $P < 0.0001$), but focal and epileptiform abnormalities were more correlated with seizures (91.0% [$P = 0.04$] and 89.2% [$P = 0.05$], respectively vs 76.9%). Fifty-four patients (25%) had at least 1 day of continuous electroencephalography. When used, continuous electroencephalography recorded a seizure in more than half of patients. Six children had no recognized seizure (clinical or electrographic) before continuous electroencephalography was performed. Twenty-two children (10%) had a seizure recorded by continuous electroencephalography after routine electroencephalography did not record a seizure. Overall, continuous electroencephalography was more likely to capture a seizure, capture a subclinical seizure, or rule out a concerning event as a seizure than routine electroencephalography (all comparisons $P < 0.0001$). **CONCLUSIONS:** Children with suspected encephalitis are at high risk for seizures. Continuous electroencephalography is better able than routine electroencephalography to determine whether seizures are present. Further, continuous electroencephalography can guide treatment by classifying a clinical event as seizure or seizure-mimic. Our findings support the expanded use of continuous electroencephalography in children with suspected encephalitis.

Keywords: EEG, encephalitis, seizures, epilepsy, electroencephalography

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Introduction

Encephalitis occurs in 3.5-7.4 cases per 100,000 person-years in the general population with an incidence up to 16 times higher in children.[1] In the National Hospital Discharge Survey between 1988 and1997, encephalitis accounted for 230,000 hospital days and 1400 hospital deaths annually.[2] Children with encephalitis have diverse clinical presentations, with variable signs and symptoms including headache, meningismus, fever, changes in mental status such as lethargy or hallucinations, seizures, abnormal movements, or tremor, and focal neurological signs.[1,3] Children with symptoms consistent with encephalitis undergo medical management with a great deal of ambiguity as to their etiologic diagnosis, and most will never have a

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verifiable etiology for their illness.[4] The California Encephalitis Project (CEP) was an attempt to identify etiologic agents and characterize the clinical course of patients with encephalitis; summaries of the infectious agents found and patient outcomes have been reported previously.[3,5,6]

Seizures, both clinical and subclinical, are common in children with encephalitis. Glaser et al.[5] reported seizures in 42% of children in the CEP. Misra and Kalita[7] reported that 37% of adults and 61% of children with encephalitis in a prospective hospital-based study had seizures. Dubray et al.[6] reported that 62% of children with encephalitis had seizures, and that seizures were correlated with a prolonged illness and worse outcome. However, seizures can be difficult to recognize in patients with encephalitis and it is unclear whether routine electroencephalograph (EEG) is sufficient to rule out seizures in this population; in a study of intensive care unit (ICU) patients (adults and children) with suspected central nervous system infection receiving continuous EEG monitoring (cEEG), 33% had a seizure while on the monitor and 64% of those seizures had no clinical correlate.[8] Several recent reports of children receiving ICU monitoring in pediatric ICUs show that critically ill children frequency have seizures, seizures are frequency subclinical, and seizures are correlated with poor outcomes.[9-15]

In this study, we report EEG and clinical findings from all children who presented to Rady Children's Hospital of San Diego (RCHSD) between 2004 and 2011 and had diagnostic samples sent to the CEP. Our findings suggest that cEEG is important in the diagnosis and management of children with symptoms consist with encephalitis.

TABLE 1.
Demographics and baseline characteristics

Patient number	217	
Age	8.1 Years ± 5.4 yr*	
	0-20 Years	
	n	Percent
Gender		
Male	120	55.3
Race		
White	52	24.0
Hispanic	90	41.5
Asian	19	8.8
African American	9	4.1
Other/undeclared	47	21.7
Fully immunized†	209	96.3
Normal development†	186	85.7
Chromic medical condition‡	42	19.4
CNS disease‡	25	11.5
Systemic disease‡	22	10.1
Psychiatric condition‡	14	6.5
History of seizure§	17	7.8
History of EEG	14	6.5
History of AED use	16	7.4
History of neuroimaging‖	37	17.1

Abbreviations:
AED = Automated external defibrillator
CNS = Central nervous system
EEG = Electroencephalography
* Mean ± standard deviation.
† Self-reported.
‡ See Methods section and Table 2.
§ Any seizure in the past before the presenting case of encephalitis.
‖ Magnetic resonance imaging, computed tomography, or both.

Patients and Methods

Study participants

Between 2004 and 2011, 222 children at RCHSD had diagnostic samples sent to the CEP. To be included in the CEP, children had to be hospitalized with encephalopathy lasting at least 24 hours and meet at least one of the following criteria: fever, seizure, focal neurological signs, pleocytosis, or EEG or neuroimaging evidence concerning to the treating clinicians for encephalitis.[5] At the discretion of treating physicians, children who met these criteria had a standardized panel of blood, cerebrospinal fluid, nasal swap, and rectal swab sent to a reference laboratory for analysis. The CEP and the standardized testing performed have been previously described.[3,5,6] From this prospectively identified cohort, we recovered the complete electronic medical record of 217 patients. For the other five patients, the electronic medical record was either missing in its entirety or severely truncated; therefore, these five patients were excluded from the analysis. This retrospective study was granted approval under the multi-institutional protocol established by the State of California for the CEP and a waiver of consent was granted. Patient demographics can be found in Table 1. Comorbid medical conditions and medical history can be found in Table 2.

Data collection

The electronic medical record was reviewed for 217 children, including the medication administration record and all preceding and antecedent clinic, emergency room, admission, consultation, progress, and discharge notes. Laboratory values, results of neuroimaging tests including magnetic resonance imaging (MRI) and computed tomography (CT) scans, and the results of all EEGs were examined.

TABLE 2.
Comorbid conditions

Cancer (n = 8)	Acute lymphoblastic leukemia (3)
	Medulloblastoma (2)
	Optic gliomas and astrocytoma*
	Ependymoma
	Atypical teratoid rhabdoid tumor
CNS disorder (25)†	Epilepsy (12)
	Autism and/or cerebral palsy (6)
	CNS cancer (5)
	Febrile seizures (4)
	Corpus callosum agenesis
	Microcephaly
	Multiple sclerosis
	Traumatic brain injury
Systemic disease (22)	Recurrent respiratory illnesses (7)
	Autoimmune pancytopenia
	Congenital heart disease
	Congenital insensitivity to pain‡
	Cystic fibrosis
	Diabetes mellitus type 1
	Diabetes mellitus type 2
	DiGeorge syndrome
	Familial progressive cholestasis§
	Hereditary spherocytosis
	Idiopathic thrombocytopenic purpura
Psychiatric disease (11)	Depression/anxiety (7)
	Aggression‖
	Bipolar disorder
	Eating disorder
	Schizophrenia

Abbreviation:
CNS = Central nervous system
* This patient had neurofibromatosis type 1.
† Four children had a history of either meningitis or encephalitis.
‡ Congenital insensitivity to pain led to limb amputation.
§ Familial progressive cholestasis after liver transplant.
‖ Patient with aggression had multiple psychiatric admissions.