Continuous Electroencephalographic Monitoring in Critically Ill Patients With Central Nervous System Infections

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Objectives: To determine the prevalence, predictors, and clinical significance of electrographic seizures (ESz) and other continuous electroencephalographic monitoring findings in critically ill patients with central nervous system infections.

Design: Retrospective cohort study.

Setting: Eighteen-bed neurocritical care unit.

Patients: We identified 42 consecutive patients with primary central nervous system infection (viral, 27 patients [64%]; bacterial, 8 patients [18%]; and fungal or parasitic, 7 patients [17%]) who underwent continuous electroencephalographic monitoring between January 1, 1996, and February 28, 2007.

Main Outcome Measures: Presence of ESz or periodic epileptiform discharges (PEDs).

Results: Electrographic seizures were recorded in 14 patients (33%), and PEDs were recorded in 17 patients (40%). Twenty patients (48%) had either PEDs or ESz. Of the 14 patients with ESz, only 5 (36%) had a clinical correlate. Periodic epileptiform discharges (odds ratio = 13.4; $P = .001$) and viral cause (odds ratio = 13.0; $P = .02$) were independently associated with ESz. Both ESz (odds ratio = 5.9; $P = .02$) and PEDs (odds ratio = 6.1; $P = .01$) were independently associated with poor outcome at discharge (severe disability, vegetative state, or death).

Conclusions: In patients with central nervous system infections undergoing continuous electroencephalographic monitoring, ESz and/or PEDs were frequent, occurring in 48% of our cohort. More than half of the ESz had no clinical correlate. Both ESz and PEDs were independently associated with poor outcome. Additional studies are needed to determine whether prevention or treatment of these electrographic findings improves outcome.

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CLINICAL SEIZURES ARE A known complication of central nervous system (CNS) infection, particularly after viral infection[1,2] and less frequently after bacterial infection.[3,4] In previous reports, half of the patients with polymerase chain reaction–confirmed herpes encephalitis had clinical seizures,[1,2] whereas clinical seizures were found in 5% of patients with bacterial meningitis before admission and in 15% during hospitalization.[3,4] In patients with CNS infection, clinical seizures are associated with poor outcome.[4,5] Recent studies emphasize the role of continuous electroencephalographic (EEG) monitoring (cEEG) because it can detect purely electrographic seizures (ESz) activity, including nonconvulsive status epilepticus, in approximately 18% to 40% of patients presenting with an unexplained decreased level of consciousness or clinical seizures.[6] Moreover, ESz and other EEG findings such as periodic epileptiform discharges (PEDs) are associated with worse outcome in patients with acute neurological injuries, such as in the aftermath of convulsive status epilepticus,[7] and in those with intracerebral[8] or subarachnoid[9] hemorrhages. In patients with CNS infections, recent guidelines recommend cEEG for patients with bacterial meningitis with seizures or fluctuations in the level of consciousness.[10]

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Despite these recommendations, we are not aware of any study that has specifically analyzed cEEG findings in patients with CNS infections. Therefore, the prevalence of seizures (clinical and electrographic) and the prognostic value of cEEG findings in patients with primary CNS infections are largely unknown. In this study, we sought to determine the prevalence, predictors, and significance of ESz and other cEEG findings in patients with CNS infections.

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METHODS

STUDY POPULATION

We retrospectively identified all patients with CNS infections who underwent cEEG at the Columbia University Medical Center between January 1, 1996, and February 28, 2007. Indications for cEEG included clinical seizures and a decreased level of consciousness potentially related to nonconvulsive seizures. Patients were identified using the following: (1) the Department of Neurology cEEG log; (2) the Comprehensive Epilepsy Center log of all cEEG reports; and (3) the Columbia University cEEG database.

Inclusion criteria for this study were a diagnosis of primary CNS infection and elevation of the cerebrospinal fluid (CSF) white blood cell count (>4/μL). Patients with marked immunosuppression and a diagnosis of toxoplasmosis suggested by typical cerebral lesions and response to appropriate treatment were also included, even without elevation of the CSF white blood cell count. Exclusion criteria included postoperative neurosurgical infections and a likely alternative noninfectious cause of CSF pleocytosis. This retrospective analysis was performed with the approval of the local institutional review board.

CLINICAL VARIABLES

Level of consciousness was categorized into normal, abnormal but alert, stuporous, or comatose. Neurological status and the presence of clinical seizures were recorded. Outcome at discharge was evaluated using the Glasgow Outcome Scale, a scale ranging from 1 (death) to 5 (no disability).[11] Poor outcome was defined as a Glasgow Outcome Scale score of 1 to 3 (death, vegetative state, or severe disability, respectively).

CLASSIFICATION OF INFECTIONS

All of the patients underwent CSF analysis and brain imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI). The cause or presumed cause of infection was classified into the following categories according to published criteria[12]: viral, bacterial, and fungal or parasitic.

Viral infection was defined as an acute febrile illness with or without characteristic radiological abnormalities and with either of the following: (1) positive polymerase chain reaction or culture results for a viral agent in the CSF; or (2) a lack of positive polymerase chain reaction and culture results but predominant CSF lymphocytic pleocytosis without evidence of another cause of infection.

Bacterial infection was defined as an acute febrile illness with or without characteristic radiological abnormalities and with either of the following: (1) positive polymerase chain reaction or culture results for bacterial agents in the CSF; or (2) predominant CSF neutrophilic pleocytosis without evidence of another cause of infection.

Fungal or parasitic infection was defined as an acute illness with or without characteristic radiological abnormalities and with either of the following: (1) positive culture or antigen detection results in the CSF; or (2) cerebral lesions compatible with toxoplasmosis in immunocompromised patients with response to appropriate treatment.

TREATMENT

Patients were treated with antiviral, antimicrobial, and antifungal medications as clinically indicated. Patients did not receive prophylactic antiepileptic drugs. Generally after a first clinical seizure or ESz, patients received a loading dose of fosphenytoin sodium. In patients with status epilepticus, initial management consisted of lorazepam and fosphenytoin. If seizures persisted, continuous infusions of midazolam maleate followed by pentobarbital sodium were started.[6]

RADIOLOGICAL VARIABLES

Computed tomographic or MRI scans of the brain were obtained on admission and repeated when necessary. Cortical and meningeal enhancements as well as focal and diffuse white matter abnormalities were recorded.

cEEG RECORDINGS

Continuous EEG monitoring was recorded using 21 electrodes according to the International 10-20 system. Silver/silver chloride electrodes were affixed to the scalp with collodion. The cEEG trace was continuously displayed at the bedside. The ESz and PEDs were recorded. The PEDs were classified according to previously defined criteria[13]: periodic lateralized epileptiform discharges (PLEDs), generalized PEDs (GPEDs), and bilateral independent PLEDs (BIPLEDs). Generally, cEEG was discontinued if seizures were not recorded after 24 hours in awake patients and after 48 hours in comatose patients. In cases with highly epileptiform findings (eg, PLEDs), monitoring was continued for longer periods depending on the treating neurologist.

STATISTICAL ANALYSIS

We first determined whether ESz were associated with any clinical, biological, or radiological variables. We used the χ^2 or Fisher exact test for dichotomized variables. Continuous variables were tested using a 2-tailed *t* test. For non–normally distributed variables, the Mann-Whitney *U* test was performed. Significant variables ($P < .05$) were included in multivariate logistic regression models. We then conducted 3 sets of analyses. First, after controlling for non-EEG variables, we determined whether PEDs were associated with ESz. Second, we repeated the analysis to determine whether poor outcome (Glasgow Outcome Scale score of 1-3) was associated with any clinical, biological, or radiological variables. When evaluating EEG findings (ESz and PEDs), we controlled for non-EEG variables. Third, in a subgroup analysis, we compared patients with each specific type of PED (PLEDs, GPEDs, and BIPLEDs) with those without PEDs to determine whether any of these were associated with seizures. Statistical analysis was performed with SPSS version 12.0 statistical software (SPSS Inc, Chicago, Illinois).

RESULTS

STUDY COHORT

A total of 1078 patients were admitted to the Columbia University Medical Center between January 1, 1996, and February 28, 2007, with the diagnosis of primary CNS infection. Of these, cEEG was performed in 75 patients (7%). Thirty-three patients were then excluded because of CNS infection in the context of an external ventricular drain (n=12), craniectomy or craniotomy (n=9), CNS tumor (n=5), brain biopsy (n=4), and intracranial hemorrhage (n=5). Therefore, 42 patients remained for analysis with the diagnosis of primary CNS infection having undergone cEEG during the study period. The mean age was 39 years (range, 0-82 years) and there were 21 women (50%).

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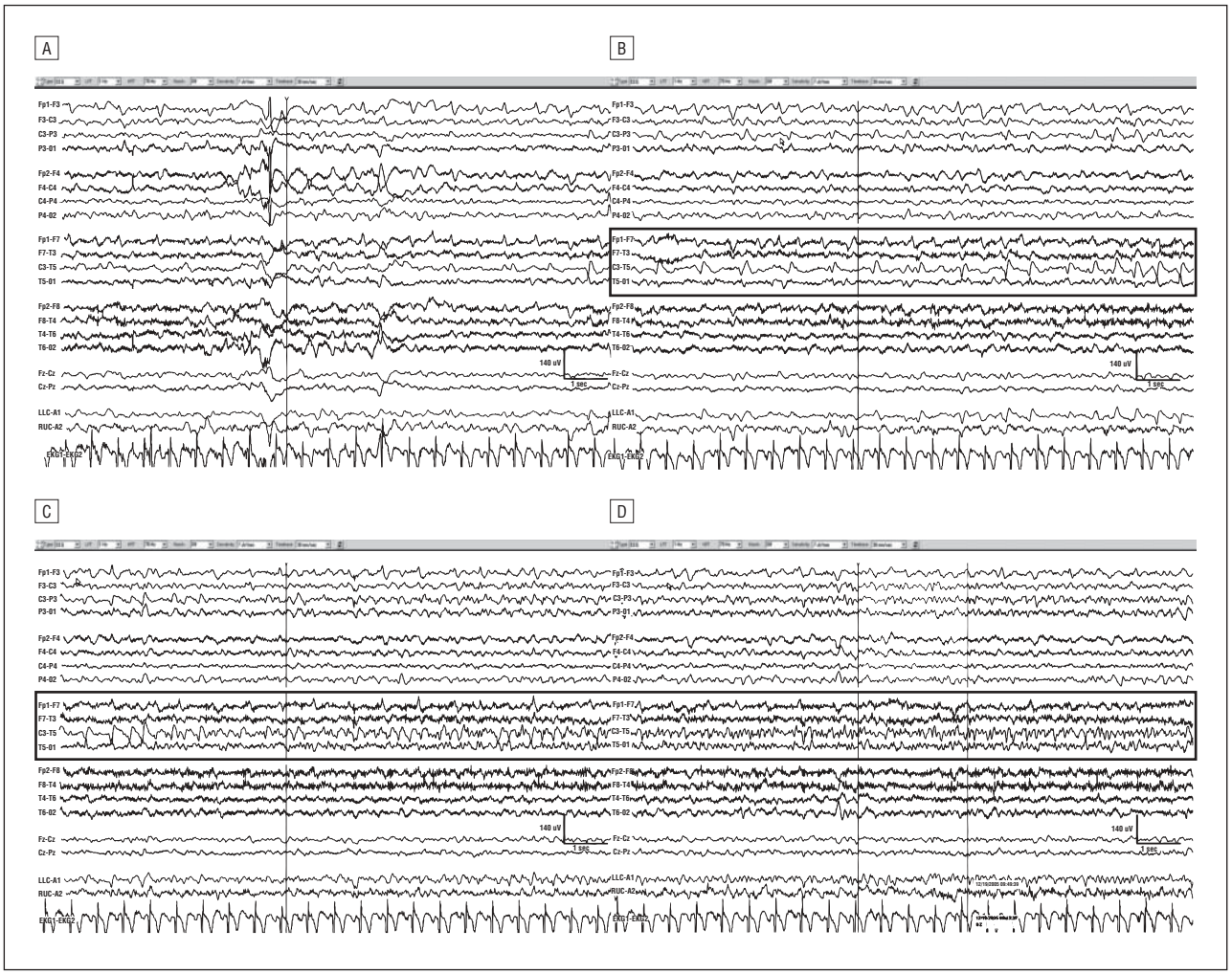

Figure 1. Continuous clips of a seizure in a 47-year-old patient with a viral central nervous system infection. Cerebrospinal fluid analysis reveals 18 white blood cells, a glucose level of 118 mg/dL, and a protein level of 60 mg/dL. In the final second of A and most of B, periodic lateralized epileptiform discharges can be seen from the left posterotemporal region (primarily T5; see box in B), evolving into rhythmic delta/theta in C (box), then rhythmic alpha in D (box).

BASELINE CLINICAL VARIABLES

The median CSF white blood cell count was 29/μL (interquartile range, 11-242/μL). Infections were diagnosed as viral in 27 patients (64%), bacterial in 8 (18%), and fungal or parasitic in 7 (17%). The infectious agent was identified in 6 of 27 patients with viral infection (22%) (herpes simplex virus [n=2], varicella-zoster virus [n=1], JC [n=1], Coxsackie B4 virus [n=1], and human herpes virus 6 [n=1]), in 6 of 8 patients with bacterial infection (75%) (*Mycobacterium tuberculosis* [n=4], *Streptococcus pneumoniae* [n=1], and *Streptococcus* group B [n=1]), and in 6 of 7 patients with fungal or parasitic infection (86%) (*Cryptococcus* [n=2], toxoplasmosis [n=3], and a fungus that was found in cultures but without further identification [n=1]). Overall, 8 patients were human immunodeficiency virus positive.

RADIOLOGICAL VARIABLES

Overall, 40 patients underwent brain MRI and 38 patients had at least 1 CT scan performed. Meningeal enhancement was seen in 9 patients. This enhancement was diagnosed on MRI in 8 patients (and also noted on CT in 3 of these patients) and on CT only in 1 patient who did not undergo MRI. All cases with cortical enhancement had the cortical enhancement diagnosed with MRI (n=6), and it was also seen on CT in 4 patients. All of the focal or diffuse intraparenchymal lesions were diagnosed with MRI (n=20) and were also seen on CT in 10 patients.

SEIZURES AND EEG FINDINGS

The median duration of cEEG was 2.5 days (range, 1-153 days). Overall, 14 of the 42 patients (33%) had ESz. An example of an ESz is presented in **Figure 1**. Of the 14 patients with ESz, 12 (86%) had clinical seizures prior to EEG, compared with 17 of the 28 patients without ESz (61%) (*P*=.16). Only 5 of 14 patients with ESz (36%) had a clinical correlate during any ESz. Periodic epileptiform discharges were recorded in 17 patients (40%) (PLEDs in 14 patients, GPEDs in 11 patients, and BIPLEDs in 4 patients). Twenty patients (48%) had either ESz or PEDs. Twenty patients had convulsive status epilepticus before EEG, which persisted in 3 of them during EEG. Eight patients (19%) had nonconvulsive status epilepti-

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Table 1. Clinical, Biological, Radiological, and Electroencephalographic Findings in Patients With and Without Electrographic Seizures

Variables	No Electrographic Seizures (n=28)	Electrographic Seizures (n=14)	Univariate Analysis		Multivariate Analysis	
			OR	*P* Value	OR	*P* Value
Clinical						
Demographics						
Age, mean (SD), y	41 (27)	33 (17)		.30		
Male, No. (%)	15 (54)	6 (43)	0.7	.51		
Clinical seizures, No. (%)						
Prior to admission	8 (29)	8 (57)	3.3	.07		
Prior to EEG	17 (61)	12 (86)	3.9	.16		
Stupor or coma at neurological examination on admission, No. (%)	14 (50)	7 (50)	1.0	>.99		
Stupor or coma at neurological examination prior to EEG, No. (%)	16 (57)	12 (86)	4.5	.09		
Temperature, mean (SD), °C	38.4 (1.2)	38.5 (1.0)		.71		
Biological						
Blood, median (IQR)						
WBC count, /μL	8600 (6800-12 700)	9550 (6900-11 375)		.95		
Glucose level, mg/dL	113 (88-142)	156 (100-276)		.06		
CSF, median (IQR)						
WBC count, /μL	33 (10-274)	64 (7-156)		.52		
Protein level, mg/dL	106 (65-191)	59 (29-113)		.04		.08
Glucose level, mg/dL	51 (33-79)	65 (54-92)		.13		
Cause, No. (%)						
Viral	14 (50)	13 (93)	13.0	.007	13.0	.02
Bacterial	7 (25)	1 (8)	0.2	.23		
Fungal or parasitic	7 (25)	0		.08		
Radiological						
Meningeal enhancement, No. (%)	8 (29)	1 (7)	0.2	.23		
Cortical enhancement, No. (%)	5 (18)	1 (7)	0.4	.65		
Focal or diffuse intraparenchymal lesions, No. (%)	13 (46)	7 (50)	1.2	.83		

Abbreviations: CSF, cerebrospinal fluid; EEG, electroencephalography; IQR, interquartile range; OR, odds ratio; WBC, white blood cell.
SI conversion factor: To convert blood glucose to millimoles per liter, multiply by 0.0555.

cus. Of those 8 patients, 2 did not manifest clinical signs of status epilepticus before or during cEEG.

Overall, 21 patients received a loading dose of fosphenytoin and 1 received a loading dose of phenytoin sodium.

Before or during cEEG, 38 patients were receiving valproate sodium and/or phenytoin/fosphenytoin. Three patients did not receive any antiepileptic medication and 1 additional patient received levetiracetam only. Other adjunctive antiepileptic agents based on the preference of the treating physician included carbamazepine (n=7), oxcarbazepine (n=2), levetiracetam (n=7), gabapentin (n=4), topiramate (n=2), and lamotrigine (n=1). Treatment of refractory status epilepticus included midazolam (n=6), pentobarbital (n=6), phenobarbital sodium (n=8), propofol (n=3), and ketamine hydrochloride (n=1).

ASSOCIATION OF CLINICAL, BIOLOGICAL, AND RADIOLOGICAL VARIABLES WITH ESz

In the univariate analysis, a lower CSF protein level and a viral cause were associated with ESz, and the CSF protein level was lower in patients with viral infection vs nonviral infection (median [interquartile range], 60 [45-116] vs 151 [66-233] mg/dL). In the multivariate analysis, only a viral cause (odds ratio=13.0; 95% confidence interval, 1.5-113.3; *P*=.02) was independently associated with ESz (**Table 1**).

ASSOCIATION OF EEG VARIABLES WITH ESz

Periodic epileptiform discharges were more frequent in patients with ESz (11 of 14 patients [79%]) compared with patients without ESz (6 of 28 patients [21%]) (*P*<.001). In patients with ESz as compared with those without ESz, PLEDs were more frequent (8 of 14 patients [57%] vs 6 of 28 patients [21%], respectively; *P*=.04), as were GPEDs (9 of 14 patients [64%] vs 2 of 28 patients [7%], respectively; *P*<.001) and BIPLEDs (4 of 14 patients [29%] vs 0 of 28 patients [0%], respectively; *P*=.009). Eleven of 17 patients (65%) with PEDs had ESz compared with 3 of 25 patients (12%) without PEDs (8 of 14 patients [57%] with PLEDs vs 6 of 28 patients [21%] without PLEDs; 9 of 11 patients [82%] with GPEDs vs 5 of 31 patients [16%] without GPEDs; and 4 of 4 patients [100%] with BIPLEDs vs 10 of 38 patients [26%] without BIPLEDs) (**Figure 2**). After correction for a viral cause and the CSF protein level, PEDs were independently associated with ESz (odds ratio=13.4; 95% confidence interval, 2.8-64.2; *P*=.001).

OUTCOME

Glasgow Outcome Scale scores at discharge were obtained in 40 of 42 patients (95%). Twenty-one patients (53%) had a poor neurological outcome (Glasgow Out-

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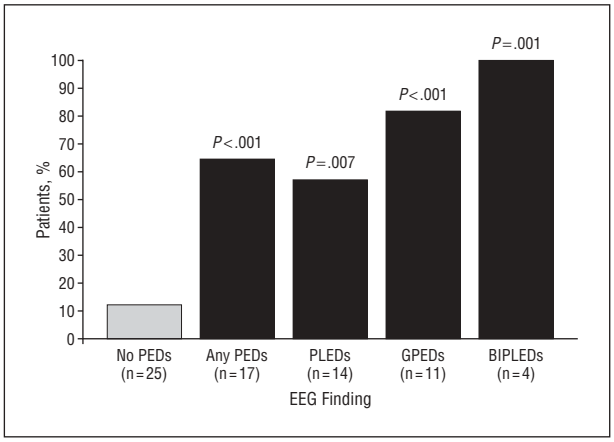

Figure 2. Difference in prevalence of electrographic seizures among patients with and without the corresponding periodic epileptiform discharges (PEDs). *P* values are in comparison with the group with no PEDs. PLEDs indicates periodic lateralized epileptiform discharges; GPEDs, generalized PEDs; BIPLEDs, bilateral independent PLEDs; and EEG, electroencephalographic.

come Scale score of 1-3; 13 had severe disability, 3 were in a coma or vegetative state, and 5 died). In the univariate analysis, poor outcome was associated with poor neurological status (stupor or coma) at the beginning of cEEG as well as ESz and PEDs. After correction for neurological status, PEDs (odds ratio = 6.1; 95% confidence interval, 1.5-25.0; $P = .01$) and ESz (odds ratio = 5.9; 95% confidence interval, 1.3-26.3; $P = .02$) each remained significantly associated with poor outcome (**Table 2**). The detailed distribution of outcomes according to the different EEG findings is presented in **Table 3**.

COMMENT

In this study, we found that ESz occurred in 14 patients with primary CNS infection who underwent cEEG (33%), and most of the seizures were without a clinical correlate. A viral cause and PEDs were independently associated with ESz. Additionally, ESz and PEDS were the only variables independently associated with poor outcome at discharge.

The prevalence of ESz in this cohort was higher than in the overall population of patients who undergo cEEG at our center (19% based on a prior study).[6] It was particularly high in our patients with a confirmed or presumed viral cause (48%). The prevalence was also higher than in patients with intracerebral hemorrhage,[14] subarachnoid hemorrhage,[11] ischemic infarct,[15] or severe traumatic brain injury.[16] The higher incidence in our cohort likely reflects the highly selected nature of the patients, only including those in whom cEEG was performed.

In our study, no clinical variable was associated with ESz. Clinical seizures before EEG were found in 69% of the population, a frequency higher than that previously reported in less-selective cohorts of patients with bacterial meningitis[3,4] or herpes simplex infection.[1] However, clinical seizures before EEG were not associated with ESz. Additionally, of the 14 patients with ESz, only 5 (36%) showed a clinical correlate. In contrast with a previous study of patients who underwent cEEG for an unexplained decrease in the level of consciousness or management of seizures,[6] patients with poor neurological status were not more likely to have ESz. Prospective studies are needed to determine whether the lack of association between EEG findings and clinical features reflects a selection bias or true findings in patients with CNS infections; if it is the latter, it may justify a broader use of cEEG in patients with CNS infections.

In our study, we found that ESz were more frequent after viral vs nonviral infections. The more extensive parenchymal involvement after viral encephalitis, due to neurotropism of the viral agent with direct entry into the CNS, parenchymal damage, and subsequent host immune response,[17,18] may be responsible for the significant difference in the ESz incidence between viral and bacterial infections as previously reported for clinical seizures.[19] Additionally, we found in the univariate but not multivariate analysis that a lower CSF protein level was related to seizures, probably because CSF protein levels were lower in patients with viral infections. Although both viral and bacterial infections affect the blood-brain barrier, the physiopathologic mechanism related to a higher CSF protein level in patients with bacterial infections may be related to the more extensive damage to the blood-brain barrier caused by bacterial infections.[20-22]

Not surprisingly, PEDs, including BIPLEDs, GPEDs, and PLEDs, were associated with ESz, with 65% of patients with any PEDs having ESz. These findings and similar results in prior investigations[23,24] suggest that when PEDs are initially detected on cEEG, prolonged monitoring is warranted.

PREDICTORS OF OUTCOME

We found that ESz and PEDs were the only independent risk factors for poor outcome. It is not clear whether the cEEG findings simply reflect the severity of disease or contribute to poor outcome; this study cannot address that important issue. However, there is increasing evidence of potentially harmful effects of seizures on brain tissue as supported by animal[25] and human[26] studies. Additionally, our findings show that PEDs are related to poor outcome in CNS infections as was previously reported in subarachnoid and intracerebral hemorrhages.[8,9] To date, however, there is no consensus on whether to treat patients with these findings and, if so, how aggressively.[27] If replicated in a larger prospective data set, our results may provide an argument toward a more aggressive management of periodic or ictal EEG activities because both were independently associated with worse outcome. The fact that a decreased level of consciousness when EEG was started was a predictor of outcome confirms the prognostic value of the clinical evaluation in critically ill patients with CNS infections. However, the lack of independent significance after adjustment for EEG findings may indicate that the decreased level of consciousness reflects previously unnoticed epileptic activity.

LIMITATIONS

The main limitation is the selection bias in that only patients in whom cEEG was requested were included. Thus,

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Table 2. Clinical, Biological, Radiological, and Electroencephalographic Findings in Patients With and Without Poor Outcome

Variables	Poor Outcome[a] (n=21)	Good Outcome[b] (n=19)	Univariate Analysis OR	Univariate Analysis *P* Value	Multivariate Analysis OR	Multivariate Analysis *P* Value
Clinical						
Demographics						
Age, mean (SD), y	40 (15)	40 (28)		.98		
Male, No. (%)	9 (43)	11 (58)	0.5	.34		
Clinical seizures, No. (%)						
Prior to admission	7 (33)	7 (37)	0.9	.82		
Prior to EEG monitoring	14 (67)	13 (68)	0.9	.91		
Stupor or coma at neurological examination on admission, No. (%)	11 (52)	9 (47)	1.2	.75		
Stupor or coma at neurological examination prior to EEG monitoring, No. (%)	18 (86)	10 (53)	5.4	.04		.07
Temperature, mean (SD), °C	38.6 (1.1)	38.3 (1.2)		.38		
Biological						
Blood, median (IQR)						
WBC count, /µL	10 300 (6050-11 750)	8800 (7750-12 950)		.77		
Glucose level, mg/dL	117 (91-198)	118 (92-148)		.86		
CSF, median (IQR)						
WBC count, /µL	38 (13-153)	29 (7-306)		.81		
Protein level, mg/dL	84 (56-189)	90 (60-173)		.71		
Glucose level, mg/dL	58 (34-91)	58 (41-84)		.68		
Cause, No. (%)						
Viral	16 (76)	10 (53)	2.9	.12		
Bacterial	2 (10)	6 (32)	0.2	.12		
Fungal or parasitic	3 (14)	3 (16)	0.9	>.99		
Radiological						
Meningeal enhancement, No. (%)	4 (19)	5 (26)	0.9	.58		
Cortical enhancement, No. (%)	3 (14)	3 (16)	1.0	>.99		
Focal or diffuse intraparenchymal lesions, No. (%)	10 (48)	9 (47)	1.0	>.99		
EEG findings[c]						
Electrographic seizures, No. (%)	11 (53)	3 (16)	5.9	.02	5.9	.02
Any PEDs, No. (%)	13 (62)	4 (21)	6.1	.01	6.1	.01

Abbreviations: CSF, cerebrospinal fluid; EEG, electroencephalographic; IQR, interquartile range; OR, odds ratio; PEDs, periodic epileptiform discharges; WBC, white blood cell.

SI conversion factor: To convert blood glucose to millimoles per liter, multiply by 0.0555.

[a] Glasgow Outcome Scale score of 1 to 3.

[b] Glasgow Outcome Scale score of 4 or 5.

[c] Controlled for non-EEG variables.

Table 3. Distribution of Outcome According to Electroencephalographic Findings

EEG Finding	No. (%)[a] GOS Score of 1, Death (n=5)	GOS Score of 2, Vegetative State (n=3)	GOS Score of 3, Severe Disability (n=13)	GOS Score of 4, Slight Disability (n=18)	GOS Score of 5, No Disability (n=1)
Any PEDs (n=17)	3 (18)	2 (12)	8 (47)	3 (18)	1 (6)
PLEDs (n=14)	2 (14)	1 (7)	8 (57)	2 (14)	1 (7)
GPEDs (n=11)	3 (27)	2 (18)	5 (46)	1 (9)	0
BIPLEDs (n=4)	1 (25)	1 (25)	2 (50)	0	0
ESz (n=14)	2 (14)	3 (21)	6 (43)	3 (21)	0

Abbreviations: BIPLEDs, bilateral independent periodic lateralized epileptiform discharges; EEG, electroencephalographic; ESz, electrographic seizures; GOS, Glasgow Outcome Scale; GPEDs, generalized periodic epileptiform discharges; PEDs, periodic epileptiform discharges; PLEDs, periodic lateralized epileptiform discharges.

[a] Percentages indicate the percentage of patients among those with the corresponding EEG finding.

these findings cannot be extrapolated to all patients with CNS infections. However, our findings probably do apply to those with CNS infections and impaired mental status as most of these patients at our center undergo cEEG. Additionally, the Columbia University Medical Center is a large academic medical center and may have more complex cases or sicker patients than in community hospitals. Another limitation of our retrospective study is the classification of the presumed infectious agent in the viral, bacterial, and fungal or parasitic categories. Our classification may be questioned because the infectious agent was conclusively determined in only 18 of 42 patients (43%).

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CONCLUSIONS

In our study of critically ill patients with CNS infections and undergoing cEEG, ESz were found in 33% of the patients. Most of the patients had no clinical correlate to their ESz. A viral cause was independently associated with ESz. Both ESz and PEDs were independently associated with worse outcome. Our results suggest that cEEG should be considered in patients with CNS infections. Only a prospective study, most likely multicenter, can lead to more definitive information to help determine whether and when to treat or prevent these EEG patterns.

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Author Contributions: Dr Carrera had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Carrera, Claassen, and Hirsch. *Acquisition of data:* Carrera, Claassen, Emerson, and Hirsch. *Analysis and interpretation of data:* Carrera, Claassen, Oddo, Emerson, Mayer, and Hirsch. *Drafting of the manuscript:* Carrera. *Critical revision of the manuscript for important intellectual content:* Carrera, Claassen, Oddo, Emerson, Mayer, and Hirsch. *Statistical analysis:* Carrera, Claassen, and Hirsch. *Obtained funding:* Carrera. *Administrative, technical, and material support:* Oddo and Hirsch. *Study supervision:* Claassen, Oddo, Emerson, Mayer, and Hirsch.
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