

Nonconvulsive Seizures of Traumatic Brain Injury Patients

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Objective: Seizures are common consequence of traumatic brain injury and have been reported in clinical series as an incidence of 15% to 22%. Among them, nonconvulsive seizures (NCS) are often unrecognized during the early period of neurosurgical hospitalization because their clinical presentations can be misunderstood as consequent symptoms of clinical course, and the diagnosis can be confirmed only by the electroencephalographic (EEG) recording.

Methods: We retrospectively reviewed our clinical database of traumatic brain injury (TBI) patients admitted between March 2008 and September 2012. Twenty one patients with suspicious symptoms of NCS, such as decrease of consciousness, aphasia or irritability, were included. Routine wake and sleep EEG or bedside continuous EEG monitoring were done in all patients.

Results: Ten out of twenty-one patients showed abnormal activities on EEG. Ictal discharges were documented on four patients. Based on clinical symptoms and EEG findings, these four patients were diagnosed as NCS. Two out of four NCS patients showed EEG findings of nonconvulsive status epilepticus (NCSE). Another six patients with abnormal EEG activities were considered as 'suspicious NCS' because only interictal activities were recorded on EEG but increasing dose or adding on antiepileptics relieved their symptoms. All NCS/NCSE were successfully controlled by appropriate antiepileptic therapy.

Conclusion: Our result showed that NCS was diagnosed in about 20% of patients with suspicious symptoms. There's a possibility that actual NCS might have happened more. Because untreated NCS/NCSE might cause worse clinical outcome, careful observation and urgent EEG recordings should be considered in a patient with suspicious NCS symptoms.

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KEY WORDS: Traumatic brain injury · Nonconvulsive seizure · Status epilepticus · Electroencephalography.

Introduction

Seizures are common consequence of traumatic brain injury (TBI) and have been reported in clinical series as an incidence of 15% to 22% in patients of traumatic brain injury.^{5,11)} Nonconvulsive seizures (NCS) are also common that approximately 10% of patients have been suffered from electroencephalographically detected seizures during the acute period of TBI.¹¹⁾ Early posttraumatic seizures are one cause of clinical deterioration and may worsen the resultant outcome.^{2,10,11)} NCSs are often unrecognized during the early period of hospitalization because it often presented

as changes of consciousness, which can be misunderstood as a clinical deterioration owing to such as brain edema. Furthermore, NCS can only be confirmed by electroencephalographic (EEG) recording which is not always possible for all traumatic brain injury patients.^{6,8)} The purpose of this study is to investigate clinical manifestations of NCS during the early period of hospitalization in the traumatic brain injury patients with or without brain surgery.

Materials and Methods

We retrospectively reviewed our TBI patients between 2008 and 2012, who were taken EEG. Twenty-one TBI patients with suspicious NCS symptoms within two weeks after injury with or without cranial surgery were included. Decrease of consciousness, aphasia, lethargy, confusion, tremor, or facial twitching were considered as suspicious NCS symptoms.⁶⁾ We included chronic subdural hemorrhage

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(SDH) patients who underwent burr-hole drainage surgery. All patients enrolled showed no structural interval changes on follow-up imaging studies. Routine wake and sleep EEGs were performed in all ambulatory patients and continuous EEG monitoring were done in patients in the intensive care unit. Each patient's demographic findings such as sex, age, type of injury, initial Glasgow Coma Scale (GCS), clinical symptoms, EEG findings, and the day of onset of NCS after injury were reviewed. An experienced epileptologist reviewed all EEGs.

Results

Patients

There were 13 men and 8 women in the study. The mean age was 65.7 years ranging from 10 to 87 years. The mean initial GCS score was 12.7, ranging from 4 to 15. All patients received valproate as a prophylactic anticonvulsant. The type of injuries and the number of patients with each injury were as follows: acute SDH (6), chronic SDH (10), acute epidural hemorrhage (EDH) (2), cerebral contusion (2) and depressed skull fracture (1) (Table 1). Among these, thirteen patients underwent surgery. The two EDHs were located on left occipital lobe and left frontal lobe respectively, and two cerebral contusions were on bilateral frontal lobe. Skull fracture was on right temporal bone with

TABLE 1. Demographics of the study population

Total	21
Sex	
Male : Female	13 : 8
Total	21
Age (years)	65.7 (10–87)
GCS score	12.7 (4–15)
Type of injury	
ASDH	6
CSDH	10
EDH	2
HCONT	2
Skull fracture*	1
Symptoms	
Aphasia	4
Twitching	4
Confusion	4
Lethargy	1
Tremor	2
Decreased consciousness	6

*depressed skull fracture with open wound. GCS: Glasgow Coma Scale, ASDH: acute subdural hemorrhage, CSDH: chronic subdural hemorrhage, EDH: epidural hemorrhage, HCONT: hemorrhagic contusion

TABLE 2. The clinical characteristics in patients of NCS and 'suspicious NCS' group

	Case no.	Sex	Age	Type of injury	Initial GCS* score	Surgery	Day of seizure	EEG finding	Symptoms
NCS	1	M	68	HCONT	7 (2/1/4)	None	1	Cont gen ictal spikes	Decreased consciousness
	2	M	60	ASDH	15 (4/5/6)	None	4	Cont gen delta slowing	Decreased consciousness
	3	F	81	ASDH	13 (3/4/6)	Decomp & H/R	14	Focal ictal spikes	Facial twitching, Nystagmus
	4	F	83	ASDH	14 (3/5/6)	None	11	Gen ictal spikes	Decreased consciousness
Suspicious NCS	5	M	72	CSDH	15 (4/5/6)	Burr hole drainage	13	TIRDA	Aphasia
	6	F	64	CSDH	15 (4/5/6)	Craniotomy & H/R	15	FIRDA	Aphasia
	7	F	75	CSDH	15 (4/5/6)	Burr hole drainage	9	Focal interictal spikes	Lethargy
	8	M	36	ASDH	4 (1/1/2)	Decomp & H/R	8	PLEDs	Facial twitching
	9	M	72	CSDH	8 (2/1/5)	Burr hole drainage	11	Focal interictal spikes	Decreased consciousness
	10	M	71	ASDH	11 (3/3/5)	None	3	PLEDs	Decreased consciousness

*total score (eye/verbal/motor response), *postinjury day 0 indicates the day of injury. EEG was taken at the 'day of seizure' in all patients. EEG: electroencephalographic, NCS: nonconvulsive seizures, GCS: Glasgow Coma Scale, HCONT: hemorrhagic contusion, ASDH: acute subdural hemorrhage, CSDH: chronic subdural hemorrhage, Decomp: decompressive craniectomy, H/R: hematoma removal, Cont: continuous, Gen: generalized, TIRDA: temporal intermittent rhythmic delta activity, FIRDA: frontal intermittent rhythmic delta activity, PLEDs: periodic lateralized epileptiform discharges

depression. Each patient showed symptoms of decreased consciousness, lethargy, aphasia, facial twitching, and/or confusion (Table 1). All patients showed no structural interval changes on follow-up images. In all patients, EEG monitoring was taken when suspicious symptoms were presented.

Nonconvulsive seizures

Ten out of twenty-one patients (48%) showed abnormal findings on EEG. Ictal discharges were documented on four patients (19%)(Table 2). All ictal events were recorded by a continuous EEG monitoring. Presented symptoms were deterioration of consciousness on three patients, and facial twitching with ictal nystagmus in one patient. Based on clinical symptoms and the EEG findings, these four patients were diagnosed as NCS. The level of serum valproic acid was evaluated in all patients with abnormal EEG findings, and if it was below the therapeutic range, additional doses were given. If increasing dose did not resolve symptoms, other antiepileptic drugs were added such as levetiracetam or phenytoin. Especially, two out of four NCS patients showed prolonged ictal EEG findings more than 30 minutes and diagnosed as nonconvulsive status epilepticus (NCSE)(Figure 1, Table 2). The types of injuries of these two patients were bilateral frontal hemorrhagic contusion and right sided acute subdural hemorrhage, respectively. These two patients were treated using a stepwise protocol for status epilepticus. They were given a lorazepam 0.1 mg/kg intravenous (IV) with simultaneous loading of phenytoin (20 mg/kg IV). When seizures continued, additional doses of phenytoin were maintained. If seizures continued more than 30 minutes, general anesthesia was started with midazolam (0.05–0.4 mg/kg/hr drip). Seizures of NCS/NCSE patients were successfully controlled by conventional antiepileptics and free with seizures during the follow-up period more than 6 months, except one patient of NCSE. This patient was admitted with frontal hemorrhagic contusion, and showed recurrent complex partial seizures with secondary generalization, which was medically refractory. Most of patients maintained conventional antiepileptics for more than one year on average, and tapered drugs.

Another group of six patients showed only interictal activities on EEG, and these findings were insufficient for the diagnosis of NCS. However given that the EEG was not continuous monitoring and their symptoms were improved after increasing doses or adding on other antiepileptic drugs, these patients were grouped as ‘suspicious NCS’.

The type of injuries in these two groups were mostly SDHs (9/10), three in NCS group and six in ‘suspicious NCS’ group. Acute SDH were dominant type of injury in NCS group (3/4), while chronic SDH were dominant in ‘suspicious NCS’ group (4/6). Most patient in ‘suspicious NCS’ group underwent surgery (5/6), and suspicious NCS symptoms also occurred postoperatively.

Discussion

By definition, NCS or NCSE is not a clinical but an elec-



FIGURE 1. A case of nonconvulsive status epilepticus in 80-year-old woman. She showed repeated episodes of facial twitching and nystagmus. A: Computed tomography demonstrating acute subdural hematoma on right fronto-temporo-parietal area with hemorrhagic contusion. B: Typical EEG findings of nonconvulsive seizure. Ictal activities are seen on right fronto-temporal (F8-T4, T4-T6) and right fronto-parietal (F4-C4, C4-P4) area. Note that during the ictal period, there is no artifact from muscle contraction in other surface electrodes, which is normally accompanied by convulsive seizures. EEG: electroencephalographic.

troencephalographic diagnosis.⁷⁾ The clinical characteristics of NCS are ambiguous, subtle and nonspecific, thus the diagnosis is often delayed or missed.^{1,7)} The clinical spectrums include anorexia, aphasia/mutism, amnesia, lethargy, agitation/aggression, blinking, confusion, facial twitching, nystagmus, and tremulousness.⁶⁾

The present study showed all four NCS patients were diagnosed by continuous EEG monitoring. In case of convulsive seizure, a physician or nursing staff can easily notice it. However, if a patient present only decreased level of consciousness in acute period of traumatic brain injury, the detection of seizures is not always possible.^{8,11)} In patients with TBI, seizures during acute period could be a stimulus for secondary injury, causing poor outcome and high mortality rate.⁹⁻¹¹⁾ Therefore prompt diagnosis and treatment of seizures are important for patients with TBI, especially during the acute period.

Our study showed that the rate of SDH was high among NCS and 'suspicious NCS' patients, and most of seizures occurred postoperatively. Interestingly, high rate of chronic SDH was found in 'suspicious NCS' group. The occurrence of seizures immediately or during the 2 weeks after burr hole drainage has been well recognized as an incidence of about 5% in chronic SDH.^{3,12)} In our study, six patients were considered as 'suspicious NCS' because only interictal activities were shown on 30 minutes routine EEG recordings and their clinical symptoms were disappeared after adjusting antiepileptic medications. Without continuous monitoring, it is difficult to record ictal activities during the clinical symptoms. There is a possibility that actual NCS might have been diagnosed more if continuous EEG monitoring was performed. However, continuous EEG monitoring in all TBI patients is practically not feasible in usual environment of neurosurgical department. Aphasia, delirium, or decreased consciousness is commonly seen in acute phase of TBI. Because these symptoms are various and nonspecific, detection and diagnosis of NCSs are difficult in patients with acute TBI.⁶⁾ If these symptoms do not correlate with the findings of follow-up images, the possibility of NCS should be considered. Because NCS occurs with a high frequency in case of TBI, the prompt EEG monitoring should be performed for the diagnosis when NCS is suspected.^{2,9-11)} In case of NCSs, non-coma inducing agents such as IV fosphenytoin and intermittent benzodiazepines could be used in addition to the oral AEDs such as valproate, levetiracetam, and topiramate.⁶⁾ All patients in our study were treated as such, and no recurrence was found, except one patient of NCSE.

NCSE is a common complication of acute TBI.^{7,11)} NCSE

is diagnosed when EEG-recorded episodes of NCS are continuous or recurrent for greater than 30 minutes without improvement in the patient's clinical state, nor is there a return to a preictal EEG pattern between seizures.⁷⁾ The clinical characteristics of NCSE are also ambiguous and nonspecific, making the diagnosis difficult and uncertain.^{1,4,6,7,11)} In the absence of continuous EEG monitoring, the diagnosis is likely to be missed or delayed. Because the morbidity and mortality of NCSE are largely determined by duration and delay to diagnosis, improving its outcome will require the availability and timely use of EEG testing.⁷⁾ NCSE is more refractory to treatment and has a higher mortality than GCSE.⁷⁾ NCSE may be terminated by intravenous benzodiazepines. Intravenous long-acting phenytoin may be helpful in cases of NCSEs refractory to benzodiazepines. If these medications are not effective, induction of burst suppression could be done with pentobarbital or propofol.^{4,7,11)}

Conclusion

NCS can be unrecognized during the acute period for the treatment of TBI because its symptoms are usually nonspecific. As seen in our result, NCS is common than expected during the early period of TBI though all patients were given prophylactic antiepileptics. With careful observation and prompt EEG recordings, NCS/NCSE can be diagnosed and prevent TBI patients from worse clinical outcome due to untreated seizures.

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