Nonconvulsive status epilepticus during childhood: clinical and electroencephalographic features

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SUMMARY: Yılmaz Y, Onultan O, Berber M. Nonconvulsive status epilepticus during childhood: clinical and electroencephalographic features. Turk J Pediatr 2008; 50: 449-455.

Nonconvulsive status epilepticus (NCSE) is a medical emergency, which is diagnosed most frequently with the routine use of EEG in the pediatric emergency and intensive care units.

Data from eight patients, ranging from 2.8-15 years old (median 8.7 years), treated with the diagnosis of NCSE were evaluated on clinical basis. The patients attended the hospital with acute confusional state ranging from sudden onset of verbal cooperation insufficiency to aimless-meaningless behavior and confusion without any motor component of seizure. While five of the cases were diagnosed and followed up with epilepsy, the other three had no history of epilepsy. No reason was detected that could cause acute encephalopathy. EEG examinations during acute confusional state showed partial or generalized continuous electrographic seizure activity lasting at least 30 minutes without clinical seizure activity. After administration of intravenous antiepileptic medication, the confusional states of the patients recovered, and the EEG examinations showed normal baseline activity with significantly diminished discharges or complete normal waveform.

Nonconvulsive status epilepticus should be considered in all children admitted to the hospital with acute unexplained encephalopathy, whether they have a history of epilepsy or not. Emergent EEG examination should be a routine part of evaluation in these children for the diagnosis and treatment of NCSE.

Key words: nonconvulsive status epilepticus, childhood.

Nonconvulsive status epilepticus (NCSE), characterized by a cognitive or behavioral change that lasts for at least 30 minutes with electroencephalographic (EEG) evidence of seizures, is a medical emergency, which is diagnosed most frequently with extensive use of EEG in the pediatric emergency and intensive care units[1-4]. However, the diagnostic criteria, classification, EEG findings and treatment strategies are controversial[2,5-7]. We report the clinical findings of eight children treated with the diagnosis of NCSE, and aim to discuss the clinical importance of NCSE during childhood.

Material and Methods

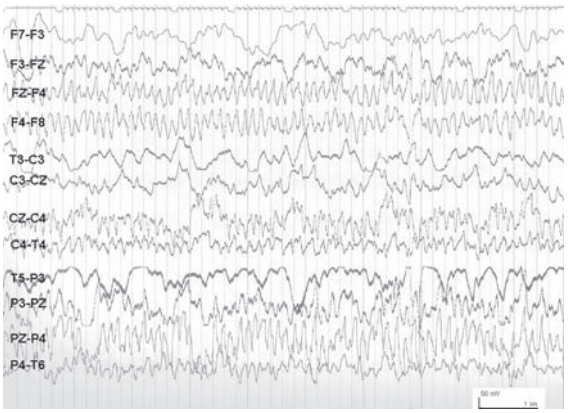
Eight patients, aged between 2.8-15 years (median 8.7 years), admitted to the pediatric emergency unit between April 1999 - January 2004 with acute alteration of consciousness for a minimum of 30 minutes, ranging from lack of verbal cooperation to coma associated with or without behavior change, and unattributable to any etiology, were evaluated. A detailed history including epileptic symptomatology was taken; thorough physical and neurological examinations were performed. Any potential causes of an acute encephalopathy, including intoxication, acute metabolic and infectious etiologies, and any possible causes of acute cerebral damage, were all considered in the differential diagnosis and eliminated.

The EEG recordings were performed during and after an intravenous anticonvulsant medication with a 14-channel electroencephalogram (Nihon Cohden) using the International 10-20 system of electrode placement and clinical follow-up

was done. NCSE was described as "acute confusional state at the time of EEG discharges consistent with electrophysiological status lasting more than 30 minutes, which were abated with intravenous antiepileptic medication". Standard dose intravenous anticonvulsant drugs including diazepam, midazolam, phenobarbital (PB) and diphenylhydantoin (DPH) were selected based on the clinical and EEG findings. The clinical features and electrophysiological findings of the patients were evaluated.

Results

The clinical and ictal EEG findings of patients are presented in Table I. The patients presented with an acute onset of consciousness change ranging from lack of verbal cooperation to coma (n: 7) or bizarre, purposeless behavior despite the ability of limited verbal communication (n: 1). None of the patients had convulsive seizure before the onset of these clinical findings. Motor component consistent with convulsion was not observed. Three patients did not have a previous history of seizure; the other five patients had been treated with the diagnosis of epilepsy. The EEG recordings of the patients revealed generalized (n: 1) or predominant in particular areas (n: 7) continuous slow wave, and spike-and-slow wave discharges with high amplitude. After the administration of intravenous medication, the consciousness and behavior change of the patients resolved and the EEG findings normalized or discharges were significantly diminished within 30 minutes (Figs. 1, 2).



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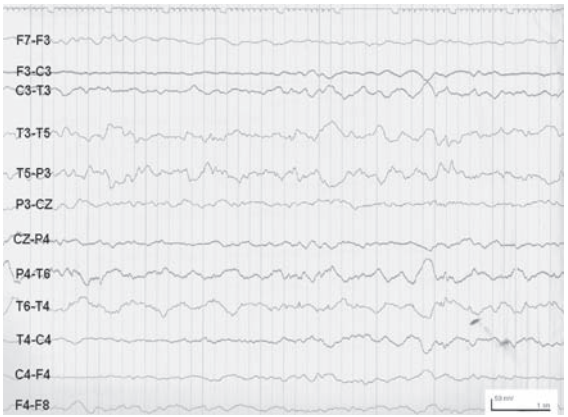

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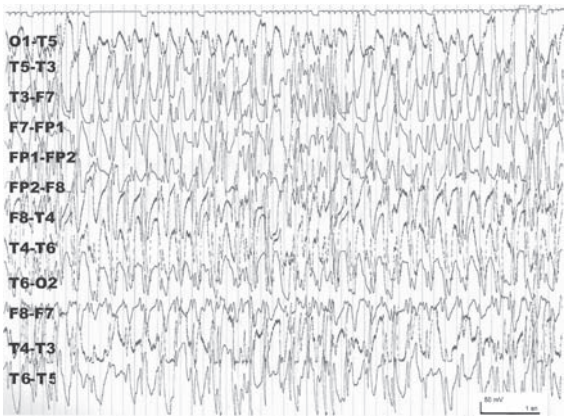
Fig. 2. EEG examination of patient no. 7 (A: Ictal EEG before intravenous antiepileptic drug (IV AED) revealed asymmetry with prominent delta waves on left hemisphere and continuous sharp and spike wave discharges on right hemisphere; B: After IV AED therapy).



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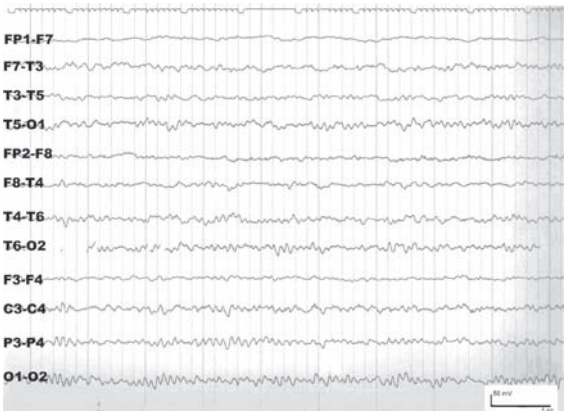

(b)

Fig. 1. EEG examination of patient no. 6 (A: Ictal EEG before intravenous antiepileptic drug (IV AED) showed generalized 3-3.5 Hz spike and wave discharges especially prominent on frontal areas with some irregularly shaped waveform and fragmentations; B: After IV AED therapy).

Table I. Clinical and EEG Findings of the Patients

Pt	Age (Year) /gender	Clinical presentation of NCSE	Ictal EEG	Precipi-tating factor	NCSE time (hr)	Treatment	Pre-existing epilepsy	Classification of epilepsy/etiology	Types of previous seizures	Neurological status	Previous AED
1	6.7/M	Confused, non-responsive to verbal stimuli, no voluntary movement	Continuous, high voltage, slow wave, SSW discharges with bifrontotemporal dominance	None	24	Diazepam, PB, Midazolam	+	Generalized (cryptogenic LGS)	AA, GTC, GT	No neurologic sign, moderate MR	PB, CBZ
2	11.9/M	No response to verbal stimuli, spontaneous eye opening, non-cooperative	Bitemporoparietal continuous slow wave, SSW discharges with high amplitude	Abrupt ces-sation of AED	3	Diazepam, DPH, Midazolam	+	Partial (symptomatic/ Sturge-Weber syndrome)	CP, GT, GTC	Normal	CBZ, VPA, Primidone, VGT
3	2.8/F	Blank expression, non-cooperative, mild palpebral blinking in the eyes (able to walk, could not follow simple commands)	Bitemporoparietal, predominantly in right temporal region, SSW discharges with high amplitude	None	2	PB	–	Partial (cryptogenic)	?	Normal	–
4	10/F	Non-cooperative, no response to verbal stimuli, deviation of eyes to left	Continuous, high voltage, slow wave, SSW discharges with right temporal dominance	None	2	Diazepam, PB	–	Unclassified*	–	Normal	–
5	14/M	Blank expression, non-cooperative	Continuous SSW discharges with high amplitude predominantly in the right temporal	None	12	DPH	+	Partial (symptomatic-operated brain tumor)	CP	Left hemiparesis	CBZ
6	9.5/F	Meaningless talking and laughing, unaimed behavior (could walk without support and obey simple commands)	Generalized, continuous, 3-3.5 Hz slow spike discharges with high amplitude	Head trauma	4	Diazepam	–	Unclassified	–	Normal	–

Table I. Clinical and EEG Findings of the Patients (cont'd)

Pt	Age (Year) /gender	Clinical presentation of NCSE	Ictal EEG	Precipi-tating factor	NCSE time (hr)	Treatment	Pre-existing epilepsy	Classification of epilepsy/etiology	Types of previous seizures	Neurological status	Previous AED
7	6/M	No response to verbal stimuli, minimal spontaneous activity	Continuous sharp and spike wave discharges on right hemisphere, delta waves on left hemisphere	None	12	Diazepam, PB, Midazolam	+	Partial (cryptogenic)	CP	No neurologic sign, moderate MR	PB, CBZ
8	3.5/M	Non-cooperative, no response to verbal stimuli, mild palpebral blinking	Continuous, high voltage, slow wave, SSW discharges predominantly on right parietal region spreading to right temporal, left frontotemporoparietal regions	None	24	Diazepam, PB	+	Partial (symptomatic-focal cortical dysplasia on right parietal region)	CP	Left hemiparesis	TPX

LGS: Lennox-Gastaut syndrome. AED: Antiepileptic drug. VPA: Valproate. PB: Phenobarbital. DPH: Diphenylhydantoin. CBZ: Carbamazepine. VGT: Vigabatrin. TPX: Topiramate. GT: Generalized tonic. GTC: Generalized tonic-clonic. AA: Atypical absence. CP: Complex partial. SSW: Slow and spike wave. MR: Mental retardation. (*): case w/o follow-up.

Discussion

Status epilepticus (SE) is "longer than 30 minutes of continuous seizure activity or two or more sequential seizures without full recovery of consciousness between the seizure", and SE is divided into convulsive SE and NCSE[2,8]. NCSE is defined as "the presence of seizure activity on EEG associated with changes of consciousness and/or behavior without convulsive movements and often showing a good response to anticonvulsant medication", but the definition and diagnostic criteria differ between some authors[2,3,9-11]. According to Kaplan[1], NCSE is "an epileptic state in which there is some impairment of consciousness associated with ongoing seizure activity on EEG". The current definition reported by Kaplan[12] is "multiple seizures or continuous seizure activity on EEG with a nonconvulsive clinical correlate (typically cognitive or behavioral change with minor facial myoclonus unaccompanied by frank convulsive movements) without return to baseline state".

There is a clear overlap of encephalopathies with different etiologies; patients with metabolic, infectious, toxic encephalopathies and acute cerebral injury also show the same or a very similar clinical picture considering consciousness and EEG findings, including partial or generalized continuous epileptiform discharges[12-14]. However, as Kaplan[1] indicated, NCSE should be considered as an epileptic state. The patients with metabolic, toxic or infectious encephalopathies and acute intracranial pathologies were not included in this series. The mainstay of our study was to consider NCSE as a differential diagnosis in patients with encephalopathy that is not caused by any metabolic or infectious or another identifiable etiology. Although these etiologies readily show a similar clinical picture and EEG patterns, the underlying cause of change in consciousness is difficult to claim, whether a result of the underlying cause or a result of the electrophysiological discharges. The diagnosis of NCSE is difficult in some cases because there are no specific clinical features or laboratory test other than EEG examination. For the accurate diagnosis, the presence of seizure activity on EEG in addition to variable clinical findings without convulsive movements should be demonstrated[1,2].

The real incidence of NCSE is unknown and it is accepted that NCSE is an underestimated clinical entity due to failure to diagnose[1,3,4,15]. Another problem in determining the incidence is the confusion regarding its definition. It is postulated that 25% of patients who experience SE have NCSE, either absence or complex partial SE[3,16]. In the study of Towne et al.[15], which was conducted in unselected comatose patients, NCSE was found as an under-recognized cause of coma, occurring in 8% of all comatose patients without signs of seizure activity. Alehan et al.[4] investigated the role of EEG in the pediatric emergency unit, and reported that seven patients of a total of 56 children with new-onset seizures or known epilepsy presenting with worsening seizures and altered mentation or with acute confusional states were diagnosed as NCSE. Saengpattrachai et al.[17] reported that the diagnosis of NCSE was made in 23 of 141 children with an unexplained decrease in level of consciousness and no overt clinical seizures.

Nonconvulsive status epilepticus may be the first seizure in healthy children without a history of epilepsy; on the other hand, epileptic children may present NCSE with or without any preceding factor[2,3,9,18]. Three of our eight patients had no previous history of seizure, whereas five of them had been treated with the diagnosis of epilepsy; three of these five patients had symptomatic epilepsy (Sturge-Weber syndrome, operated brain tumor and focal cortical dysplasia), whereas the etiology of epilepsy was unknown in the other two patients. NCSE may occur as both generalized and partial epilepsies, similarly both in symptomatic and non-symptomatic epilepsies.

Clinical findings of NCSE are quite variable during childhood; children with NCSE may be admitted to the emergency units because of strange behavior, acute confusional state, or coma[3,9]. One of our patients (patient number 6) presented with only bizarre behaviors, meaningless talking and laughing, but she could obey simple commands and limited verbal communication was possible. The other seven patients were non-cooperative, ranging from mild-moderate confusional state to coma. Current pediatric emergency practice for a confused child includes investigations to detect any metabolic, toxic or infectious etiology, as well as intracranial pathologies. Children admitted to the hospital with acute, unexplained consciousness or behavior change, with or without a history or diagnosis of epilepsy, should be evaluated by EEG for the diagnosis and treatment of NCSE. Emergent EEG was defined as any EEG examination requested for immediate performance during non-business hours or any EEG done to exclude NCSE with 24-hours-a-day, 7-days-a-week availability and after approval by the neurology or neurosurgery services[19-21]. The role of emergent EEG has been studied both for adults and children[4,19,22]. EEG monitoring has been an inevitable part of pediatric intensive units[23]. We believe that emergent EEG examination should be a part of diagnostic studies in the pediatric emergency units.

The EEG findings of NCSE are heterogeneous; generalized or focal (temporal, temporo-frontal) spike-and-slow wave complexes, polyspike discharges, irregular sharp or slow waves may be seen[2,3]. Classification of NCSE is not yet clear[3,5,6]. Previously, NCSE has been generally divided into two types: absence SE and complex partial SE[3]. With the advent of electrophysiological and neuroradiological methods, new classification schemes have been proposed. According to Kaplan[7], NCSE may be classified as 1) localization-related NCSE, 2) generalized NCSE, and 3) indeterminate or intermediate NCSE. Moreover, partial (localization-related) NCSE has been classified based on the localization of epileptic discharges as NCSE of temporal origin and NCSE of extratemporal origin, and electroclinical varieties of NCSE subtypes have been reported[23]. The accurate subclassification of NCSE can be difficult, not only in children without previous diagnosis of epilepsy but also in patients with localization-related epilepsy[18]. Emergent EEG examinations of seven of our eight patients revealed epileptic discharges with focal dominance, whereas only one patient had bilateral synchronous discharges. Based on the emergent EEG findings, we could not make thorough sub-classification of NCSE free of any doubt. Clinical data including types of new seizures obtained during a long-term follow-up period, as well as ictal and interictal video EEG monitoring may be helpful for the classification.

The therapy regimens of NCSE are controversial; benzodiazepines, DPH and PB are believed to be effective[3,12,25-27]. Midazolam, propofol, and

topiramate have been found as effective in patients with refractory status epilepticus[25,28,29]. In our series, diazepam was selected as the drug of first choice in six patients, but clinical and EEG findings disappeared only in one patient. In four patients unresponsive to diazepam, PB or DPH had to be administered as second drug, and in four patients, midazolam was used as third anticonvulsant. Our experiences do not allow us to propose the drug of first choice; however, it should be taken into consideration that diazepam might not be effective as the first choice in the treatment of NCSE.

The prognosis of NCSE is still inconclusive[30-34]. A few basic scientific studies demons-trated that NCSE may produce long-term behavioral deficits and functional changes in neurons that alter electrical excitability in neuronal circuits despite the absence of neuronal damage[35,36]. Recently, persistent abnormality on magnetic resonance imaging after NCSE was reported[37]. The outcome from de novo NCSE in ambulatory patients has not been studied in detail. All children with NCSE should be followed carefully, since the data collected to the present is not satisfactory.

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