Seizure 20 (2011) 723–726

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Case report

Oral ketamine controlled refractory nonconvulsive status epilepticus in an elderly patient

Poh-Shiow Yeh [a,b,*], Hsiu-Nien Shen [c], Tai-Yuan Chen [d]

[a] Department of Neurology, Chi-Mei Medical Center, Tainan, Taiwan
[b] Department of Neurology, Taipei Medical University, Taipei, Taiwan
[c] Department of Intensive Care Medicine, Chi-Mei Medical Center, Tainan, Taiwan
[d] Division of Neuroradiology, Department of Radiology, Chi-Mei Medical Center, Tainan, Taiwan

ARTICLE INFO

Article history:
Received 16 January 2011
Received in revised form 24 April 2011
Accepted 7 June 2011

Keywords:
Nonconvulsive status epilepticus
Ketamine

ABSTRACT

Nonconvulsive status epilepticus (NCSE) is a heterogeneous disorder with different seizure types and diverse etiologies, and is mainly characterized by altered consciousness. The recognition of NCSE is more challenging than generalized convulsive SE, and diagnosis and treatment are often delayed. Therefore, some cases can evolve into refractory SE and become pharmacoresistant even with GABAergic anesthetics. Herein we report the successful clinical experience of pharmacoresistant complex partial SE treated with ketamine. An elderly woman was profoundly stuporous and had relentless clonic movements of the right hand and forearm. Electroencephalography revealed repetitive periodic lateralized epileptiform discharges (PLEDs). There was a poor clinical response to standard anticonvulsants and GABAergic anesthetics. Both the clinical and electroencephalographic SE were controlled after intravenous ketamine therapy. Rebound refractory NCSE occurred about six days after discontinuing the intravenous ketamine, which was successfully terminated by oral ketamine treatment. There were no adverse effects observed.

1. Introduction

Nonconvulsive status epilepticus (NCSE) often manifests as altered consciousness accompanied with subtle focal motor twitches or ambiguous behavior changes, and the diagnosis has to be based on electroencephalography (EEG).[1,2] It is easily misdiagnosed clinically without evidence of continuous epileptiform activities on EEG, and attempts to terminate NCSE are frequently delayed. Unfortunately, a number of such cases with prolonged and persistent seizures will become malignant and self-sustaining refractory to standard pharmacotherapy. To date, there is no consensus on treating comatose patients with refractory NCSE, and the treatment mostly follows the guidelines on management of refractory generalized convulsive SE (GCSE).[3–5] When anesthetic agents involving γ-aminobutyric acid (GABA) receptors fail to stop ongoing seizures and prevent their recurrence, a non-competitive N-methyl-D-aspartate (NMDA) antagonist, ketamine, has been successfully used in animal models and a few human cases, based on the theory of an imbalance of neuronal transmission by a predominance of excitatory receptors if seizures are continued.[6–8] Ketamine is currently used as an anesthetic agent for short operations, pediatric or veterinary surgeries, and also for chronic pain control. In the past, the clinical use of ketamine in control refractory SE was mostly via an intravenous route, and oral ketamine therapy has been documented only in pediatric patients with NCSE.[9] Herein we report the successful experience of oral ketamine use in terminating refractory complex partial status epilepticus in an elderly patient.

2. Case report

A 76-year-old woman was admitted to our neurological ward for prolonged disturbed consciousness over 12 h after cessation of a generalized convulsion by intravenous (IV) lorazepam at the emergency unit. She had recurrent ischemic, hemorrhagic strokes and bilateral traumatic subdural hemorrhages before this admission, and vascular dementia and a dependent life for 1 year. She had complex partial seizures characterized by right hand twitches and blank staring for 2 months, and used carbamazepine intermittently. Upon admission, she was in a profound stuporous state and had persistent clonic twitches or choreatic movements of her right hand and forearm at a frequency of about 1–2 Hz. An emergency electroencephalogram (EEG) showed periodic lateralized epileptiform discharges (PLED) with high-amplitude polyspikes recurring

* Corresponding author at: Department of Neurology, Chi-Mei Medical Center, 901, Chung-Hwa Road, Yung-Kang City, Tainan 71004, Taiwan.
Tel.: +886 6 2812811x53744/53740; fax: +886 6 2828928.
E-mail address: poh.shiow@msa.hinet.net (P.-S. Yeh).

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doi:10.1016/j.seizure.2011.06.001

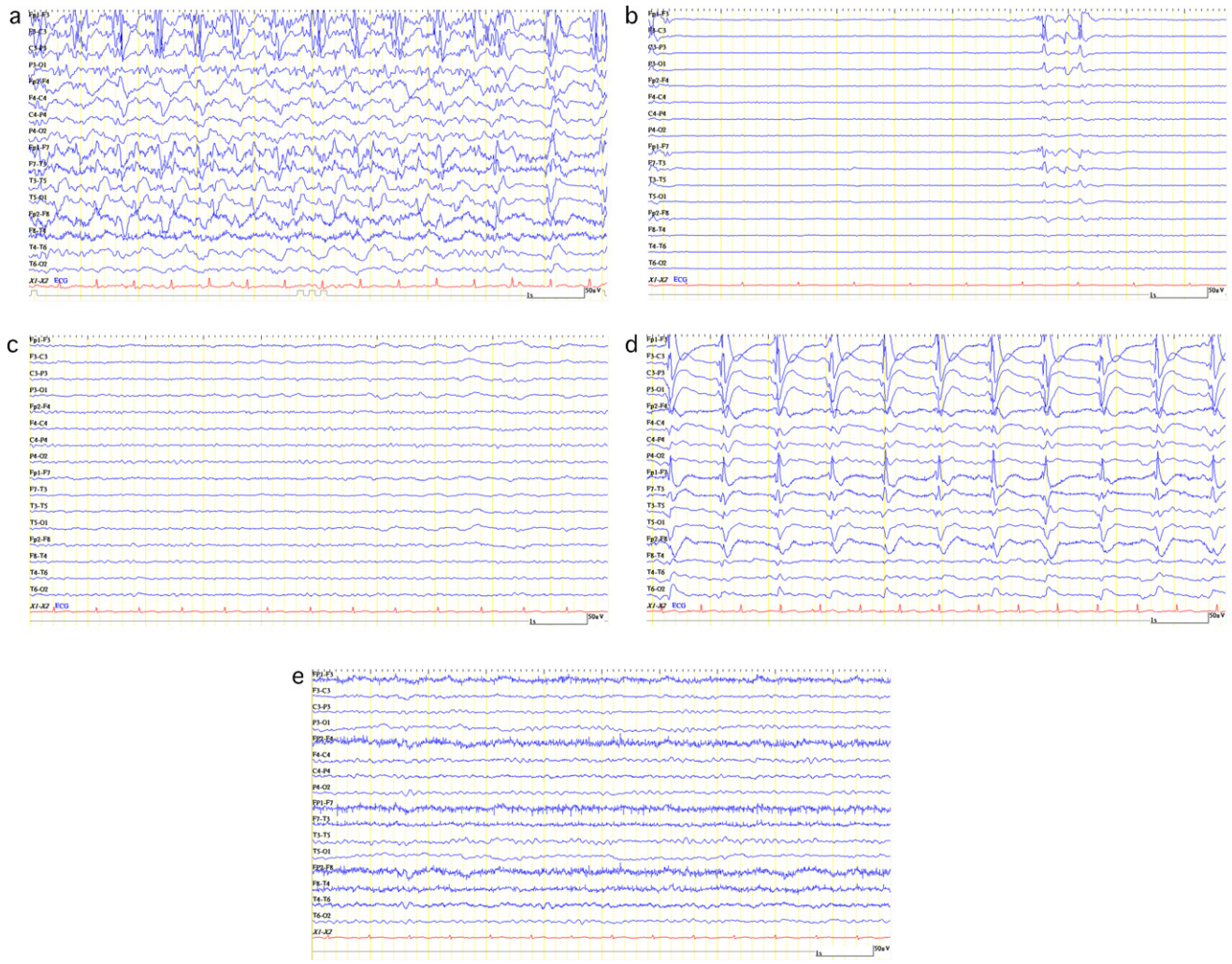

Fig. 1. Electroencephalographic recordings during the time course of treatment. (a) Before GABAergic anesthetic treatment, periodic lateralized epileptiform discharges were seen over the left hemisphere with the highest amplitude on the left anterior frontal area. (b) After propofol-induced coma, the burst period of burst–suppression patterns consisted of lateral periodic epileptic discharges over the left anterior frontal area. (c) After intravenous ketamine with a cumulative dose of about 2500 mg, PLEDs disappeared and diffuse low amplitude slow waves were seen on the left hemisphere. (d) Reappearance of PLEDs on the left hemisphere after withdrawal of intravenous ketamine. (e) After oral ketamine with a cumulative oral dose of about 1500 mg, diffuse irregular theta waves on both hemispheres were seen.

every 1–2 s on the left hemisphere, and main epileptic focus on the left anterior frontal area (Fig. 1a). Brain magnetic resonance images (MRI) revealed old ischemic and hemorrhagic lesions, residual subdural hematoma and diffuse brain atrophy. A series of hematological, biochemistry and hormone studies revealed only a urinary tract infection. Under the impression of complex partial status epilepticus (CPSE) provoked by systemic infection and inadequate medicine control, she was first treated with intravenous (IV) valproic acid (bolus of 40 mg/kg, then 400 mg every 6 h with a blood level reaching 98 μg/mL) with no clinical improvement. Midazolam anesthesia (initial dose of 0.4 mg/kg/h) was added soon after her airway had been protected, but it failed to reach burst–suppression (BS) on EEG even under a higher dosage (up to 1 mg/kg/h). Oral levetiracetam (2000 mg/d/os) on day 2 and IV phenytoin (bolus of 20 mg/kg, then 300 mg/d) on day 3 were tried, however SE continued. In order to achieve a better suppression of clinical and EEG seizure activities, propofol anesthesia (up to 5 mg/kg/h) was substituted on day 4. The patient fell into a deeper coma state but there were still relentless subtle focal motor seizures of the right hand, and meanwhile her EEG showed near-total suppression and intermittent bursts of high-voltage spikes at the left frontal area (Fig. 1b). From the initiation of propofol treatment, remarkable hypotension and stagnant bowel movements were observed, and an inotropic agent had to be given to stabilize the hemodynamic condition. The systemic side effects worsened and propofol anesthesia was withdrawn on day 6. Because thiopental was not available and the generic brand of phenobarbital in our hospital could not be given through an IV route, intramuscular (IM) phenobarbital was administered (100 mg every 4 h) after propofol had been stopped. In the meantime, IV valproic acid and lamotrigine (slow titrating dose starting with 50 mg/d/os) were maintained, and other standard anticonvulsants including oral carbamazepam (600 mg/d/os) and vigabatrin (2000 mg/d/os) were ineffective. Unfortunately, acute hepatitis with elevated liver enzymes and skin rash developed subsequently, and we had to discontinue the valproic acid and lamotrigine. Ultimately, she was maintained on phenobarbital (IM, 600 mg/d) and topiramate (200 mg/d/os) and the clinical and EEG SE persisted. Follow-up image studies including diffusion weighted images (DWI) and fluid-attenuated inversion recovery images (FLAIR) disclosed an edematous change with a faint bright signal on the left frontal cortex after prolonged seizures (Fig. 2a and b), which was not enhanced by contrast medium.

Intravenous ketamine was added on the ninth day with the family's consent. The initial dose of ketamine was 1.5 mg/kg IV bolus continuously infused with a gradual dose titration from 0.05 mg/kg/h to 0.4 mg/kg/h. The SE pictures on EEG resolved