

CASE REPORT

Successful treatment of refractory status epileptics with a single dose of IV ketamine in a Saudi child - a case report

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ABSTRACT

Background: Status epileptics are classically defined as seizures that are continuous for 30 minutes or longer or repetitive seizures between which the patient does not regain consciousness. This study reports a case of a boy with a 2-hour seizure.

Case Presentation: We present the case of a 7-year-old boy, who is known to have tuberous sclerosis (TSC2 gene mutation). On the day of presentation, the seizure had started with aura (epigastric pain with weakness in the face), then started to seize in a form left focal jerky movement with generalization associated with rolling up of the eyes, and lasted for 5 minutes; it was aborted clinically by lorazepam 0.1 mg/kg IV. However, the electroencephalography (EEG) showed subclinical seizure. The patient received a loading dose of phenytoin, 20 mg/kg IV, with no changes in the EEG; then Keppra (three doses) with a total of 40 mg/kg IV was given, but subclinical seizure still persisted. The patient was given one dose of Ketamine IV of 1 mg/kg, which resulted in complete cessation of the seizure activity within 3 minutes after injection, which was confirmed by prolonged EEG monitoring. The total duration of the seizure was 2 hours.

Conclusion: Ketamine can be considered as a third-line drug in refractory status epilepticus.

Keywords: Status epilepticus, refractory status epilepticus, seizure, ketamine.

Introduction

A seizure is defined as a transient, involuntary alteration of consciousness, behavior, motor activity, sensation, and/or autonomic function caused by an excessive rate and hypersynchrony of discharges from a group of cerebral neurons. A convulsion is a seizure with prominent alterations of motor activity. Epilepsy, or seizure disorder, is a condition of susceptibility to recurrent seizures [1].

The underlying abnormality in all seizures is the hypersynchrony of neuronal discharges. Cerebral manifestations include increased blood flow, increased oxygen and glucose consumption, and increased carbon dioxide and lactic acid production. If a patient can maintain appropriate oxygenation and ventilation, then the increase in cerebral blood flow is usually sufficient to meet the initial increased metabolic requirements of the brain. This will slow down the rate of neuronal loss, which may still occur due to overstimulation. Systemic alterations may occur with seizures and result from a massive sympathetic discharge, leading to tachycardia, hypertension, and initially stress hyperglycemia. Failure of adequate ventilation, especially in patients in

whom consciousness is impaired, can lead to hypoxia, hypercarbia, and respiratory acidosis. Patients with impaired consciousness may be unable to protect their airway and are at risk for aspiration. Prolonged skeletal muscle activity can lead to lactic acidosis, rhabdomyolysis, hyperkalemia, hyperthermia, and hypoglycemia [1].

A prolonged seizure activity is a true medical emergency. Following stabilization of the ABCs, further treatment is directed at stopping any seizure activity, as prolonged seizures are harder to control. Although certain causes of

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seizures may require specific treatment, anticonvulsant therapy is initiated simultaneously during the evaluation of the seizing patient. The benzodiazepines are the initial drugs of choice for the treatment of seizures. Benzodiazepines work by blocking the GABA receptor, thus increasing the seizure threshold [2]. Phenytoin is a second-line agent for the treatment of seizures; it blocks sodium channels and thus acts by a different mechanism than the benzodiazepines [3]. Phenobarbital is another second-line agent for the treatment of seizures. Valproic acid (Depakene) is a commonly used antiepileptic agent. If all the described therapies fail, the patients may require general anesthesia to abort the seizure [3].

In recent years, many researchers have reported that, during prolonged seizures, the number of activated GABA-A receptors on the postsynaptic membrane gradually decreases, whereas the number of inactive GABA-A receptors increases. These changes cause a significant reduction in the efficacy of antiepileptic drugs (AEDs) that target the GABAergic system, such as diazepam, clonazepam, valproic acid, midazolam, propofol, and phenobarbital. Increased doses of AEDs might restore their efficacy, but the side effects of AEDs on cardiopulmonary function are simultaneously significantly increased, thus limiting the clinical applications of such increased doses. However, a study by Dingledine et al. [4] reported that the number and activities of glutamate-sensitive N-methyl-D-aspartate (NMDA) receptors are significantly increased when the activity of GABA receptors are decreased. Subsequently, this process induced continuously amplified neuronal hyperexcitability, leading to the development of RSE. Ketamine is a noncompetitive NMDA receptor antagonist that might play a role in treating status epileptics by blocking NMDA receptor-mediated glutamatergic neurotransmission. Moreover, by blocking glutamate-mediated NMDA receptor-induced neurotoxicity, ketamine also exerts neuroprotection. Therefore, ketamine has been proposed as a new therapeutic agent for the treatment of status epileptics [5].

In this report, a successful treatment of refractory status epilepticus (SE) is described, using a single dose of IV Ketamine in a Saudi child who presented at a tertiary pediatric ER in Saudi Arabia.

Case Presentation

This is a case of a 7-year-old boy, who is known to have TUBEROUS SCLEROSIS (TSC2 gene mutation) with the following features: multiple angiomyolipoma, subcortical tubers and subependymal nodules, retinal hamartoma, cardiac rhabdomyoma, and epilepsy. The family refused to give him AEDs for the fear of side effects. The patient had two seizures over the past year prior to presentation.

On the day of presentation, during a routine electroencephalography (EEG) procedure in the neurophysiology laboratory, there was subclinical seizure, followed by an active clinical seizure. The patient was transferred immediately to the ER for further management.

The seizure had started with aura (epigastric pain with weakness in the face), then started to seize in a form left focal jerky movement with generalization associated with rolling up of the eyes, and lasted for 5 minutes; it was aborted clinically by lorazepam 0.1 mg/kg IV. However, the EEG showed a subclinical seizure. The patient received a loading dose of phenytoin 20 mg/kg IV, with no changes in the EEG, then Keppra (three doses) with total of 40 mg/kg IV was given, but the subclinical seizure still persisted.

The patient was given one dose of Ketamine IV 1 mg/kg, which resulted in complete cessation of the seizure activity within 3 minutes after injection. This was confirmed by prolonged EEG monitoring (Figure 1). The total duration of the seizure was 2 hours.

There was no history of fever, recent infection, URTI, or sleep disturbance. On examination after injection, the patient was postictal sleeping, arousable with painful stimuli, and having withdrawing and localizing pain. The vital signs are shown in Table 1.

The patient's skin had multiple ash leaf spots, and his pupils were 3 mm equal with sluggish reaction; there was no tachycardia (HR = 100 B/M), and blood pressure was maintained; there was good perfusion with warm extremities. Clear equal bilateral air entry was present, and saturation on room air was maintained. Abdomen was soft and lax with no tenderness. Brain CT showed no interval changes of the subependymal tubers in keeping with tuberous sclerosis, and no evidence of acute brain insult was present.

The patient was admitted for observation with no more seizure activity. He was discharged home in good condition to be followed-up in the neurology clinic.

Discussion

The Parke-Davis (USA) pharmaceutical company developed Ketamine in 1962. Three years later, McCarthy et al. [6] found the first evidence that ketamine exerts an anticonvulsant effect in epileptic animal models that were electrically or chemically created. These results were soon confirmed in patients, raising the possibility of treating SE using ketamine, although this possibility was soon questioned.

The present index case was a 7-year-old boy, whose 2-hour SE was successfully aborted by IV Ketamine with no side effects related to the drug.

Ketamine is a noncompetitive antagonist of glutamatergic NMDA receptors, and its anticonvulsant effects have previously been confirmed [7]. Additionally, ketamine exerts neuroprotective effects that could ameliorate RSE-induced neuronal damage. Therefore, in recent years, ketamine has become increasingly used in clinical practice [5].

This drug has great potential for the treatment of RSE; however, further robust prospective studies to investigate the regimens, efficacy, and safety of ketamine for the treatment of RSE are highly needed.

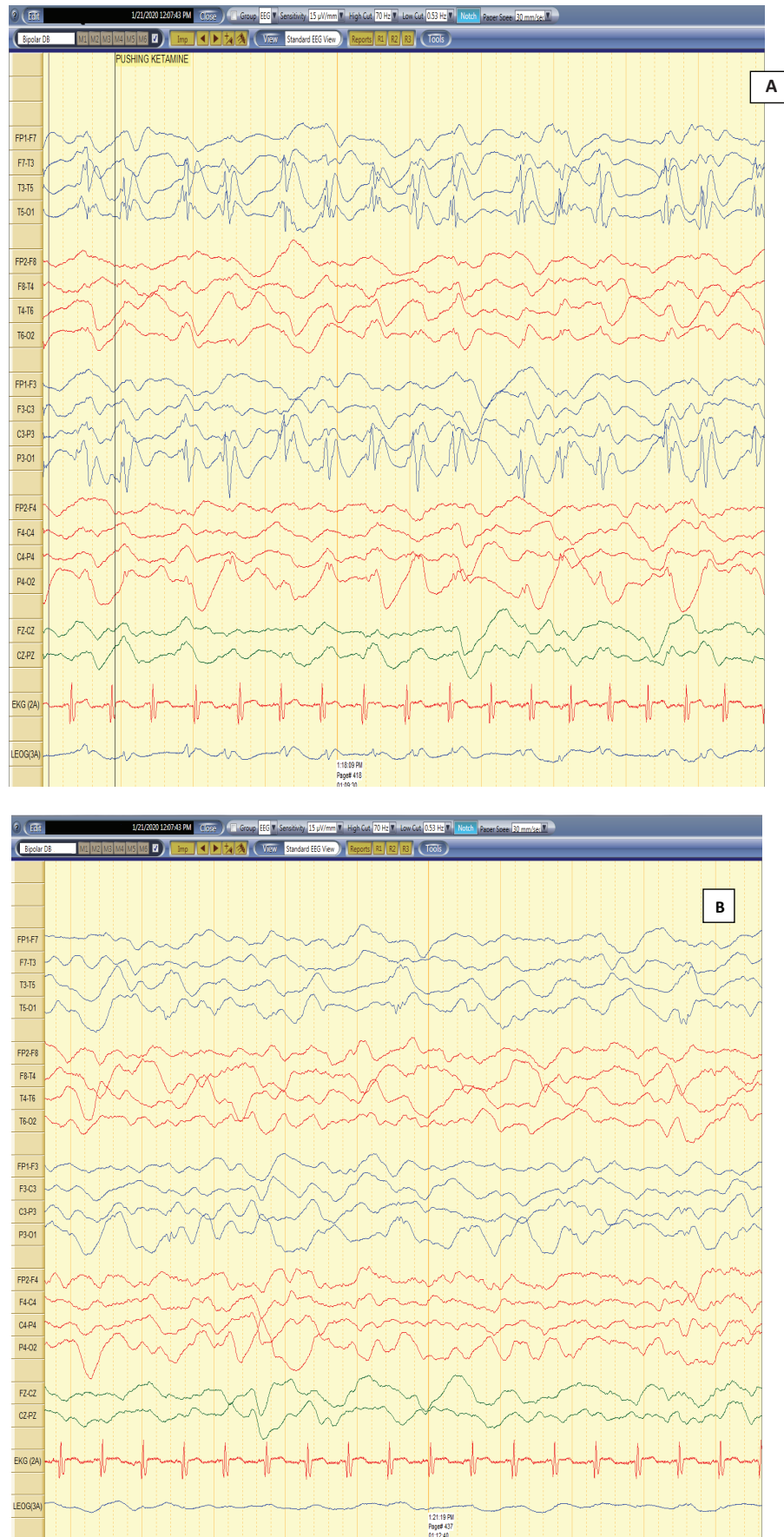


Figure 1. EEG shows (A) epileptic activity in the left hemisphere (blue channels) before and during the Ketamine injection; (B) 3 minutes after injection, epileptic activity resolved and was replaced by diffuse postictal slowing.

Table 1. Vital signs of the patient.

SBP	DBP	Mean BP	HR	RR	Temp	O2 saturation
102 mmHg	50 mmHg	66 mmHg	100 beats/minute	27 breaths/minute	37.0 ° C	96%

Conclusion

Ketamine can be considered as a third-line drug in refractory SE, potentially sparing the need of intubation and hemodynamic instability related to other general anesthetic drugs.

List of Abbreviations

EEG Electroencephalography
SE Status epilepticus

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Informed consent was obtained from the parents of the patient.

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