

Propofol-induced refractory status epilepticus at remission age in benign epilepsy with centrotemporal spikes

A case report and literature review

Lu Lu, MD, Weixi Xiong, MD, Yingying Zhang, MD, Yingfeng Xiao, MD, Dong Zhou, MD, PhD*

Abstract

Rationale: Benign epilepsy with centrotemporal spikes (BECTS) is one of the most common forms of childhood epilepsy, which is expected to resolve before 16 years of age, with mild effects on the cognitive or behavioral functions in adulthood. This study aims to report the first propofol-induced refractory status epilepticus (SE) in patients with BECTS after 16 years of age, and to review SE in BECTS or induced by propofol.

Patient concern: A 16-year-old Chinese girl, who was diagnosed with BECTS at the age of 2 years, developed refractory SE induced by propofol administered during the maintenance stage of general anesthesia during a plastic surgery procedure.

Diagnoses: Considering her medical history, EEG, and magnetic resonance images, and brain computed tomography, a diagnosis of refractory SE in BECTS was confirmed.

Interventions: The patient had been seizure-free for 3 years from treatment with 2 anti-epileptic drugs (AEDs) valproate acid (VPA) and oxcarbazepine (OXC), and had started monotherapy with OXC for 3 months before the seizure incidence. She had undergone blepharoplasty under local anesthesia prior to receiving general anesthesia. During the maintenance state she developed convulsive SE, which was uncontrolled seizure and lasted for 14 hours. The treatment for which included midazolam, diazepam, propofol, VPA, OXC, and levetiracetam (LEV).

Outcomes: The prolonged seizure was controlled by diazepam (4 mg/h), propofol (6 mg/kg/h), VPA (2400 mg/d intravenous injection). Subsequently, she was administered VPA (800 mg/d po), OXC (600 mg/d po), and LEV (1000 mg/d po). Finally, on the 17th day she was discharged, and did not have any seizure recurrence and EEG results were normal as noted during the 3-month follow-up.

Lessons: This was the first report of an SE in BECTS patient past the remission age. This report implied that interventions of sedation or analgesia in a patient after remission age of BECTS might still be at risk of refractory SE and therefore, should be carefully evaluated and monitored during such procedures, especially when an AED medication has been withdrawn or altered.

Abbreviations: ABFEC = atypical benign focal epilepsy of childhood, AEDs = anti-epileptic drugs, BECTS = benign epilepsy with centrotemporal spikes, CSWSS = continuous spike-and-waves during slow sleep, CT = computed tomography, ER = Emergency room, GTCS = generalized tonic-clonic seizure, i.v. = intravenous injection, ICU = intensive care unit, LEV = Levetiracetam, LKS = Landau-Kleffner syndrome, MRI = magnetic resonance imaging, OXC = oxcarbazepine, PICC = peripherally inserted central catheter, SE = status epilepticus, VPA = valproate.

Keywords: anesthesia, benign epilepsy with centrotemporal spikes, neurocritical care, propofol, review, status epilepticus

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The patient and the guardians have provided informed consent for publication of the case.

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Department of Neurology, West China Hospital, Sichuan University, Chengdu, China.

* Correspondence: Dong Zhou, Departments of Neurology, West China Hospital, Sichuan University, No. 37 GuoXue Alley, Chengdu 610041, China (e-mail: zhoudong66@yahoo.de).

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1. Introduction

Benign epilepsy with centrotemporal spikes (BECTS), also known as rolandic epilepsy, is one of the most common form of childhood epilepsy syndromes.^[1] The seizure onset is usually between 3 and 10 years of age. Children can expect terminal remission by the age of 16 years.^[2,3] Although some BECTS patients with atypical evolutions have been reported during the past few decades including atypical benign focal epilepsy of childhood (ABFEC), status epilepticus (SE) of BECTS, Landau Kleffner syndrome (LKS), and continuous spike-and-waves during slow sleep (CSWS) syndrome, which may be parts of a continuum related to BECTS, the age-dependent remission is unexceptional.^[4] The cognitive or behavioral deficits in patients with BECTS have been repeatedly discussed.^[5–7] Impairment can last in patients who have been symptom-free of seizure for years.^[8] Thus, whether there is an underestimated risk of epileptic incidence after remission has been unclear. Until now, no reports have shown the recurrence of an epileptic incidence in BECTS patients after 16 years of age. Herein, we present the case of a 16-year-old girl with typical BECTS clinical features who suffered a prolonged seizure during a plastic surgery procedure under general anesthesia after being seizure-free for 3 years.

2. Methods

2.1. Ethical approval and consent for publication

The ethics committee of West China Hospital has approved this study. Written informed consent was obtained from the patient and her guardians.

2.2. Collection of the data

We identified a Han Chinese female patient as diagnosed with BECTS at our center 13 years ago. The patient's previous medical records, medical history, and electronic medical records during the course of the SE were collected and considered for this report.

2.3. Review of the literature

We have searched the literatures for BECTS with recurrence after 16 years of age, SE in BECTS, and propofol-induced SE in PubMed. We have included studies that reported of SE or recurrence in BECTS patients or studies that followed more than 50 BECTS patients, by reading the full content. Additionally, we have also reviewed literatures that reported SE induced by propofol.

3. Case report

The patient was a 16-year-old girl who had her first unprovoked seizure at 2 years of age. Within half hour of sleep, she had awakened with bilateral numbness of legs and arms, which developed to be generalized tonic-clonic seizure (GTCS) that lasted for around 3 to 5 minutes. Symptoms including hemifacial clonic manifestations and sialorrhea were reported by the parents. She used to experience a seizure attacks monthly prior to medical treatment. A 3T magnetic resonance imaging (MRI) investigation showed no remarkable disorders (Shown in Fig. 1A). EEG showed typical features of BECTS. There was no remarkable history before seizure onset. No developmental deficits were found during the entire course. The patient

experienced seizure yearly during treatment with anti-epilepsy drugs (AEDs) until treatment with valproate (VPA, 1000 mg/d) and oxcarbazepine (OXC, 750 mg/d) was initiated at the age of 13 years. The EEG results were negative during the same period. VPA dosage was gradually reduced during the seizure-free 3 years. Eventually, monotherapy with daily 600 mg OXC was continued for 4 months until the incidence of SE.

This patient was presented to the Emergency room (ER) with uncontrolled tonic-clonic convulsions lasting for at least 4 hours. Prior to SE, she had undergone blepharoplasty under local anesthesia with no complications. Thereafter, when she was undergoing an augmentation rhinoplasty, she developed convulsive SE under general anesthesia induced by propofol (1.5 mg/kg). The local anesthetics were made of 2% lidocaine, 0.5% bupivacaine, 1/1000 of adrenaline, and saline. The infusion of propofol was 4 mg/kg. A prolonged trembling symptom was noted at first which was not treated by the operator until it developed to a convulsive SE. At first it was controlled with repeated midazolam injections (40 mg), but recurred after the withdrawal of the endotracheal intubation. Treatments including midazolam (extra 20 mg) and diazepam (20 mg), propofol (4 mg/kg/h), VPA (2400 mg/d intravenous injection) were used in the ER, and the seizure episode continued for over 14 hours before ceasing. The prolonged seizures were controlled by diazepam (4 mg/h), propofol (6 mg/kg/h), VPA (2400 mg/d i.v.), and the oral AEDs used were VPA (800 mg/d), OXC (600 mg/d), and LEV (1000 mg/d). The emergency Computed tomography (CT) showed diffuse cerebral edema. The consciousness could not be evaluated under narcotism. The machinery applied were ventilator, peripherally inserted central catheter (PICC), and circulation supporting treatment in intensive care unit (ICU) 5 hours after the onset. Her vital signs were stable under the ICU care, the blood pressure was varied around 80–120/60–90 mmHg and the SpO₂ was between 98% and 100%. The blood PH was around 7.46–7.44, and was within the normal limit after the withdrawal of propofol.

She was treated with sedative and AEDs for the following 12 days. Her consciousness had not returned to the baseline, while repeated convulsive seizures were stopped. She had recurrences of 2 GTCSs on the 3rd and the 10th day during the withdrawal of IV diazepam and VPA. The EEG recording showed continual slow waves in all leads with little spikes in the F3, T3, T5 leads (shown in Fig. 2). She had the tracheal intubation removed on the 11th day. Dexmedetomidine and propofol were stopped 2 days after. On the 13th day time point, cognition functions test, calculation and orientation, showed slightly impaired memory. Defective perception was noted during this transient period. CT scan showed hydrocephalus on the 7th and 15th day after the attack (shown in Fig. 1B and C). She was given 3 types of oral AEDs including VPA, OXC, and LEV until the 15th day of the onset. Then a dual therapy of OXC (600 mg/d po) and VPA (1000 mg/d po) was prescribed. She was discharged on the 17th day, the MRI result is shown in Fig. 1D).

A follow-up was performed 3 months after the discharge and no seizure recurrence with normal EEG were reported under the same dual therapy (shown in Fig. 2).

4. Discussion

We report a BECTS patient aged sixteen who developed refractory SE after being seizure-free for 3 years. To the best of our knowledge, this case is the first report of a refractory SE

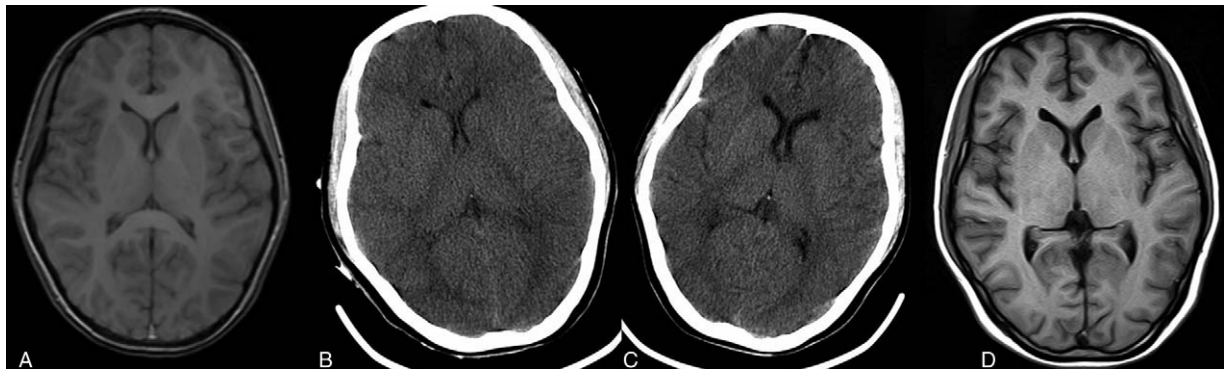


Figure 1. A: Magnetic resonance imaging (MRI), in T1 Flair at age 12; B: Computed tomography (CT) scan on the 7th day, showed severe hydrocephalus, C: CT scan on the 15th day, D: MRI scan in T1 Flair at the discharge.

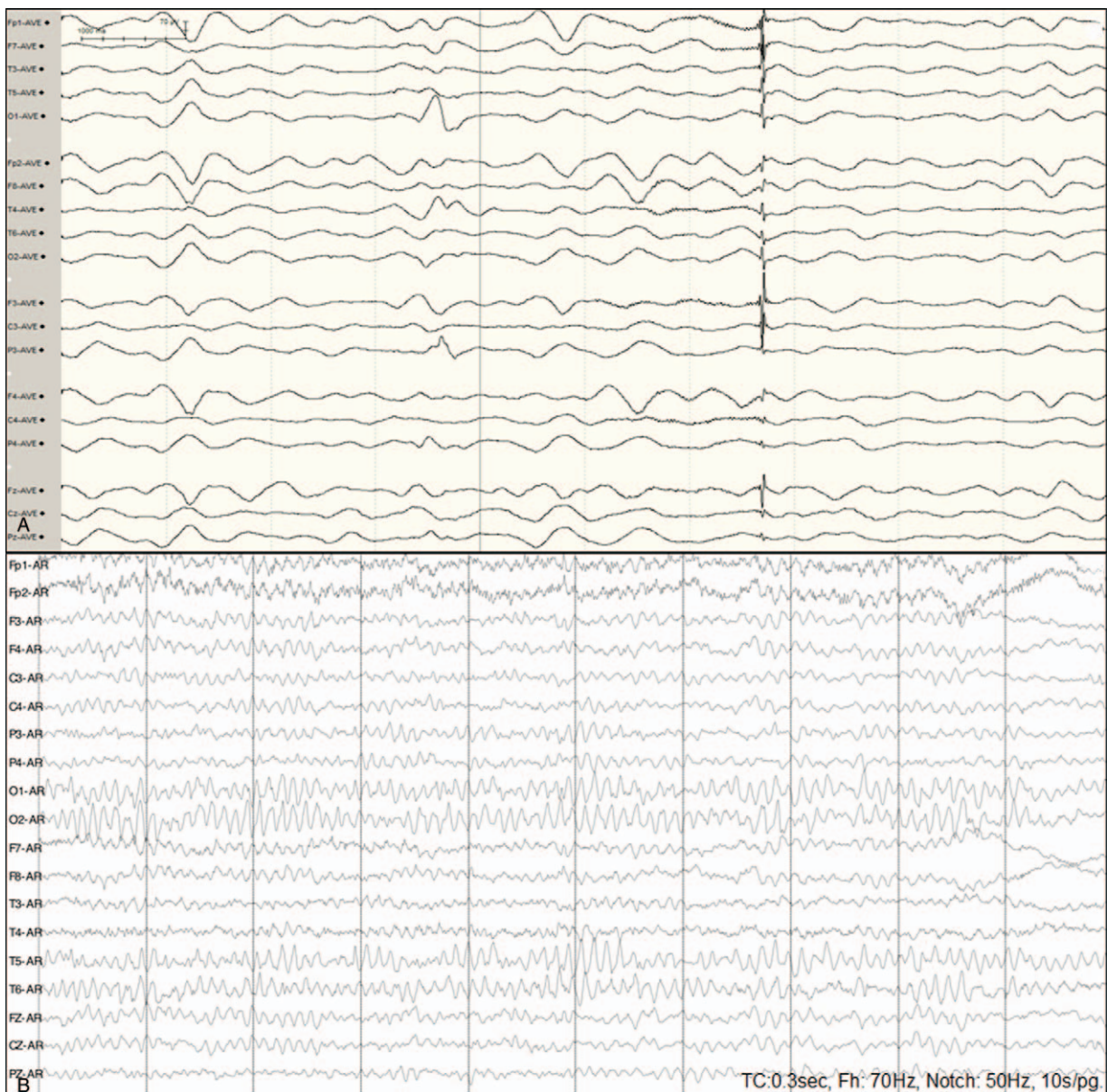


Figure 2. A: Video electroencephalogram (VEEG) recording of the 7th day, showed the continuous slow wave and spikes in T3, T5, F3 leads; B: VEEG recording 3 months after status epilepticus showed normal background.

after remission age in patients with BECTS, presenting the risk of epileptic incidence in a more severe form in patients with BECTS after “terminally resolved.”

SE has been recognized as an atypical form of benign rolandic epilepsy since the report in 1987^[9]; most of the SE phenomenon was describe as a prolonged focal onset seizure, which is typical in BECTS patients including intermittent drooling and oromotor dyspraxia or other motor symptoms of the face.^[10–12] Secondary GTCS in SE was only seen in one case in previous reports.^[13] Most of the cases were found at the beginning of the course or during the first 5 years of seizure onset. Awareness was reported in only few cases. No SE events were reported in patients with BECT older than 13 years old, nor did the study report of any refractory SE. No SE was reported after anesthesia. In recent population studies in BECTS patients, the incidence rate of SE has dramatically decreased, in most of them, no SE event had occurred.^[14–16] The population studies and case reports are shown in Table 1.

The recurrence rate of seizure in BECTS patients was relatively low compared to other childhood epilepsy syndromes, the recurrence risk after drug withdrawal ranged from 6% to 24%.^[19–21] Seizure recurrence was mostly seen at 6 to 8 years old. Evident improvement was usually seen by the age of 12. At puberty, most patients with BECTS would be seizure-free with few cases reporting to have focal onset motor symptoms during this period. No study reported SE as a recurring incidence among all the studied population.

The primary reasons for relapse after 2-year remission in children with epilepsy was considered to be the tapering off of medication, including the tapering initiated before a child achieved a 2-year remission.^[20] There are no recommendation to follow or treat young adults with BECTS for any epilepsy-related social or medical issues.^[22] Our case indicated the possibility of an epileptic incidence in adolescent patient during the tapering or withdrawal of AEDs, cautioning the neurologists or psychiatrists of the management of these patients adapting to relative circumstances including anesthesia.

The prognosis of BECTS patients has been excellent, and adults who had recovered from BECTS did not have general negative outcomes in the field of development, education, employment, and social adaptation.^[14] The recent studies have questioned the highly prevalent cognitive and behavioral limitations of BECTS patients after a long-lasting seizure-free period. While the mechanism behind the post-epileptic effect was under investigation, we did see this patient with early seizure onset and long

duration develop unfavorable outcome during the seizure-free period, whether it underlines a possible change in susceptibility in anesthesia-induced epilepsy would require more population for confirmation.

Anesthesia-induced SE has been commonly studied during the past few decades with respect to a few anesthetics. If anesthesia is necessary in patients with epilepsy, anesthetics with higher seizure-inducing properties should be avoided, such as ketamine, sevoflurane, desflurane etc. Propofol was recommended in patients with epilepsy as an anesthetic.^[23] Thus, only a few cases of propofol-induced SE have been published. The very first case report of a patient with epilepsy was reported in 1987 in which the patient suffered a partial SE for 40 mins during recovery state following propofol (3.02 mg/kg).^[24] Similar reports were also seen in the 1990s, reports from Finland demonstrated a patient that developed symmetric tonic-clonic seizure, and was hardly managed after 3 days.^[25] In a systematic review, 4 patients with epilepsy developed SE after propofol, with no exceptions beyond recovery stage. A report from Japan stated that prolonged GTCS was initiated 10 minutes after propofol infusion after brachial plexus block.^[26] Although the prognoses of these seizures were not clear, persistent seizures and SE were likely to lead to postoperative dysfunction in patients.^[27]

The effect of propofol is dose-dependent, low dose propofol is epileptogenic.^[28] Study among mechanisms suggest the involvement of 4-aminopyridine pathway, protein kinase C (PKC) pathway and glycine-antagonist mechanism. A high dose of propofol is antiepileptic and has been recommended as third line in SE rescue.^[29,30] and the first line treatment in refractory SE related to anesthesia.^[31] The relationship between anesthesia and epilepsy is complicated and requires further research. Studies should not only consider the types of anesthetics, but also hypercapnia and hypoventilation that occur during anesthesia^[32] cause seizures and prolong the duration of it.

The management of patient with epilepsy was a huge challenge for the anesthesiologist during the preoperative period. Anesthesia in epilepsy surgery for more precise location of the seizure onset zone has been frequently discussed.^[33] It is now common to evaluate patients with epilepsy in non-epilepsy surgery. Safe administration of anesthesia requires a high attention to detail. The preoperative investigations and preanesthetic evaluations were recommended. Patients in these non-epilepsy surgeries requiring general anesthesia, induction was suggested to be done with propofol or thiopentone, and blood levels of antiepileptics should be obtained to adjust the doses accordingly.^[34] Although

Table 1
Previous study of SE reports in typical or atypical BECTS population.

Author	Year	Region	Study population	Number of SE	Mean age of SE onset	Refractory SE	Key symptoms
Carol et al ^[14]	2014	Canada	42	3	7.7	No report	NA
Tovia et al ^[6]	2011	Israel	196	0	NA	NA	NA
Callenbach et al ^[16]	2010	Dutch	29	0	NA	NA	NA
Datta et al ^[34]	2007	Canada	126	0	NA	NA	NA
Ma et al ^[35]	2003	China	50	0	NA	NA	NA
Verrotti et al ^[3]	2002	Italy	85	0	NA	NA	NA
Gregory et al ^[10]	2002	Canada	3	3	5	No report	Secondary generalized seizure, unilateral facial twitching
Fejerman et al ^[11]	2000	Argentina	26	7	7.5	No report	Unilateral motor seiures, anarithria and sialorrhea.
Camfield et al ^[12]	1995	Canada	42	3	5	No report	Todd's paralysis
Fejerman et al ^[9]	1987	Argentina	2	2	8	No report	Unilateral motor seiures,sialorrhea and speech arrest

the patients with poorly controlled seizures in perioperative period were under higher risk of anesthesia-induced SE, our case represents a rare case in a well-managed patient. If convulsions persist over 5 minutes, it requires a precise recognition and treatment initiation that offers to lower both morbidity and mortality.^[35]

5. Conclusion

In this case report, we presented a patient with BECTS at the terminal remission age who developed refractory SE under anesthesia. We suggested that anesthesia or other sedation and analgesia involving treatments in patients past the remission age of BECTS have a risk of refractory SE and should be carefully evaluated and monitored during such procedures, especially when treatment with AEDs have been withdrawn or changed.

Author contributions

Data curation: Yingfeng Xiao.

Funding acquisition: Weixi Xiong, Dong Zhou.

Investigation: Lu Lu, Weixi Xiong, Yingfeng Xiao.

Methodology: Lu Lu, Weixi Xiong, Yingying Zhang.

Project administration: Dong Zhou.

Writing – original draft: Lu Lu.

Writing – review & editing: Weixi Xiong, Yingying Zhang, Dong Zhou.

Dong Zhou orcid: 0000-0001-7101-4125.

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