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CASE REPORT

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Two cases of anesthetics-induced epileptic seizures: a case report and literature review

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Abstract

Background: Anesthetics like propofol have been reported to be capable of controlling status epilepticus. However, we have observed during daily clinical work that some anesthetics can induce epileptic seizures. Therefore, this study aims to explore the relationships between anesthetics and epilepsy.

Case presentation: We collect and report two cases of anesthetics-induced epileptic seizures, in order to arouse attention towards this critical phenomenon. We also summarize the current research progress on this topic, analyze associations between anesthetics and epilepsy, and discuss the mechanisms underlying the associations. Two females, seizure-free for more than 3 years, presented with anesthetics-induced epileptic seizures and controlled by administration of Midazolam and Diazepam. By literature review, we included six studies which found that the occurrence of epileptic seizures has no relationship with the age/sex of patients, the surgery procedure, nor the type of anesthesia. It is closely related to the decreased blood concentration of antiepileptic drugs (AEDs) and the inadequate preoperative preparation.

Conclusions: Unnecessary surgery should be avoided for patients with epilepsy, and anesthetists should make careful selections on anesthetics and prepare adequately for surgery.

Keywords: Epileptic seizures, Anesthetics, Surgery, Anesthesia-induced seizure

Background

Epilepsy is the second most common chronic neurological disease in the world, associated with high morbidity and mortality and causing a great economic burden [1–3]. There are about 50 million patients with epilepsy worldwide, of whom more than 9 million are in China [4, 5]. Status epilepticus contributes to the rising rate of sudden death among young epileptic patients, and nearly 120,000 people die from epilepsy each year [6–8]. Seizures can be effectively controlled by regular antiepileptic drugs (AEDs) in two-thirds of epileptic patients, but although they have relatively good prognosis, the seizure-free retention rate 5 years after AED withdrawal is only 57% [9, 10]. The other one-third of epileptic patients suffer from drug-resistant epilepsy, and some of them can be cured by epileptic surgery. However, the following questions are usually of surgeons' concern during multidisciplinary discussions on epileptic cases: what kind of patients should receive an epileptic surgery? Whether anesthetics affect the epileptic seizure frequency? What preparations should be made before an operation? Many surgeons underestimate the adverse effects of anesthetics on epilepsy. They think as long as patients continue to take AEDs before surgery, anesthetics have little effect on the rick of epileptic seizures However, anesthetics can induce clinically apparent epileptic seizures in the perioperative period, which increases the risk and difficulty of surgery.

Howe J et al. have reviewed 400 cases with propofol as general anesthesia during craniotomy, and found that intraoperative seizures occurred in two patients who

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did not have a prior history of epilepsy, with an overall frequency of 0.5% [11]. Niesen AD et al. reviewed the medical records of 641 patients with a documented history of a seizure disorder, after receiving an anesthetic, and found that 22 patients (3.4%) experienced perioperative seizure activity [12]. Akavipat P et al. found that the incidence of perioperative convulsion was 3.1 per 10,000 from all 172,592 anesthetics [13]. Hashimoto K et al. showed that 5 (4%) of 125 patients suffered postoperative convulsive seizures after craniotomy with isoflurane or sevoflurane anesthesia [14]. The perioperative seizures are rare, yet very harmful.

In this study, we report two cases of anesthetics-induced epileptic seizures who had been seizure-free for more than 3 years, and then discuss the potential mechanisms underlying the anesthesia-induced seizures.

Case presentation

The study was approved by Ethics Committee of West China Hospital and written informed consent was obtained from all participants. Two patients, seizure-free for more than 3 years, with anesthetics-induced epileptic seizures were enrolled at the Epilepsy Center of West China Hospital of Sichuan University. The detailed case history and auxiliary examination results were collected. Patients were followed up for at least one year. Embase, Medline, Web of Science, CNKI, and WANFANG were searched without language restriction using the terms "epilepsy/seizure", "Anesthetics" and "Anesthesia-induced seizure" for eligible studies. We reviewed the collected papers and summarized the current research progress on this topic. The associations between anesthetics and epilepsy were analyzed and the mechanisms underlying the associations were discussed.

Case 1

A 16-year-old girl, complaining of repeated disturbances of consciousness and convulsions, was admitted to our hospital (Table 1). She first presented with a generalized tonic-clonic seizure (GTCS) without obvious inducement 13 years ago, which lasted 1–2 min before self-remission, and recurred more than 10 times intermittently. She was then diagnosed with "epilepsy" in the West China Hospital of Sichuan University. Under regular medication with sodium valproate and oxcarbazepine, she did not experience epileptic seizures during the last 3 years. This patient was scheduled for rhinoplasty and double-eyelid surgery. All the preoperative physical examinations including cardiopulmonary function showed no abnormalities, and no history of hypertension, diabetes, drug allergy, or mental illness was reported. Laboratory analyses and electrocardiogram revealed normal results. Under mask inhalation of oxygen, a total of 100 mg propofol was slowly injected intravenously. After the injection, the vital signs of the patient were stable. During surgery, the patient began to present with spasmodical convulsions, most prominent on the upper and lower extremities. The symptoms were relieved by an intravenous administration of midazolam. But a few minutes later, the continuous convulsions occurred again. After administration of 10 mg midazolam and 20 mg diazepam, the symptoms completely disappeared. She was then transferred to the Neurological Intensive Care Unit. Her body temperature was 36.5 °C, blood pressure 86/66 mmHg, and heart rate 109 beats/min. Results of blood tests were as follows: white blood cell 11.36×10^9/L, hemoglobin 128 g/L. Myocardial markers included creatine kinase 1515 U/L and brain natriuretic peptide 12 pg/mL. The biochemical parameters, blood sugar, serum electrolytes, arterial blood gas analysis, and brain magnatic resonance imaging (MRI) showed no abnormalities. The patient gradually felt better. She followed the prescription of 300 mg oxcarbazepine and 500 mg sodium valproate twice a day. During 1 year follow-up, no epileptic seizures occurred.

Case 2

A 34-year-old woman was scheduled for bilateral tonsillectomy due to severe chronic tonsillitis (Table 1). The patient suddenly developed clonic seizures on limbs, unconsciousness with head swaying, eyes turning up, and trismus, which lasted 2–4 min, after a quarrel 5 years ago. She regained consciousness within 10 min, but could not recall the experience. This attack occurred 1–2 times a day, more frequently in the afternoon. She was diagnosed with epilepsy in our hospital. After treatment with sodium valproate and oxcarbazepine, her symptoms were under control. Lamotrigine (75 mg bid) was taken regularly for 5 years without recurrence of epilepsy. No other noteworthy medical history was reported. At the time of admission, physical examination and laboratory data all showed normal results. No discomfort was reported at the start of operation. Immediately after administration of 160 mg lidocaine, the patient experienced a GTCS, which lasted for about 20 min. She presented with general muscle contraction and rigidity, loss of consciousness, tooth clenching, tongue biting, and upper-gazing. The patient regained consciousness after an intravenous administration of diazepam. The epileptic seizure occurred three times. Laboratory tests had normal results. Magnetic resonance imaging of the brain revealed slight enlargement of the left ventricle temporal horn. Abdominal ultrasonography showed fatty liver. Cerebrospinal fluid examination had negative results. Electroencephalogram showed increases of slow waves in both hemispheres. The patient still babbled intermittently. Discharge medications included lamotrigine 75 mg

Table 1 Two cases of anesthetics-induced epileptic seizures who had a history of epilepsy

	Sex/ age	History of epilepsy	AEDs before surgery	Seizure-free duration	Surgery	Anesthesia	Epileptic seizure	Treatment	EEG	CT/MRI	AEDs after surgery	One year follow-up
Case 1	Female/16	GTCS 13 years ago, lasting 1–2 min and repeated more than 10 times intermittently	Sodium valproate and oxcarbazepine	3 years	Rhinoplasty and double-eyelid surgery	Propofol (100 mg) General anesthesia	During surgery, the patient began to present with spasmodical convulsions, more prominent on the upper and lower extremities .	Midazolam (10 mg) and Diazepam (20 mg)	Normal	Normal	Oxcarbazepine (300 mg bid), Sodium valproate (500 mg bid)	No seizure
Case 2	Female/34	Limb clonic seizures 5 years ago, lasting 2–4 min. This attack occurred 1–2 times a day, more frequently in the afternoon.	Sodium valproate, oxcarbazepine, and lamotrigine	5 years	Bilateral tonsillectomy	Lidocaine (160 mg) Local anesthesia	Immediately after local anesthesia, the patient suffered from a GTCS, which lasted for about 20 min.	Diazepam (10 mg)	Increase of slow waves in both hemispheres	Slight enlargement of the left ventricle temporal horn	Lamotrigine (75 mg bid), Sodium valproate (500 mg bid)	No seizure

AEDs Antiepileptic drugs, *EEG* Electroencephalography, *CT* Computed tomography, *MRI* Magnetic resonance imaging, *GTCS* Generalized tonic-clonic seizure

Table 2 Anesthetics induced seizures in patients without a history of epilepsy in different studies

Study	Sex/Age	Surgery	Anaesthetic	Anesthesia type	Epileptic seizure	Duration	Period	Treatment	Epilepsy history	Family history	EEG	CT/MRI
Mark 2017 [15]	M/34	Craniotomy for arteriovenous malformation resection	Propofol	G	TCS	100 s	During operation	Propofol and levetiracetam	N	N	Abnormal	Normal
Hsieh 2015 [16]	F/10	Elective tenectomy	Lidocaine	L	GTCS	3 min	After anesthesia	Non	N	N	Abnormal	Normal
Tuna 2012 [17]	F/65	Endoscopic procetures	Propofol	G	GTCS	40 min	Awakening period	Benzodiazepine	N	N	NA	Normal
Yanaru 2010 [18]	M/23	Removal of the nails in his upper arm	Propofol	G	GTCS	20 min	After anesthesia	Midazolam	N	N	NA	NA
Dorf 2006 [19]	F/94	Fracture reduction	Lidocaine	L	GTCS	2 min	After anesthesia	Non	N	N	NA	Normal
Takeuchi 2005 [20]	NA	Obturator nerve blockade	Ropivacaine	L	GTCS	2 min	After anesthesia	Non	N	N	NA	NA

F Female, *M* Male, *G* General anesthesia, *L* Local anesthesia, *TCS* Tonic-clonic seizure, *GTCS* Generalized tonic-clonic seizure, *s* seconds, *min* minutes, *NA* Not available, *N* No, *Y* Yes, *EEG* Electroencephalography, *CT* Computed tomography, *MRI* Magnetic resonance imaging

bid, sodium valproate 500 mg bid, risperidone 3 mg bid, benzhexol hydrochloride 2 mg tid, and clonazepam 1 mg qn. The patient did not experience epileptic seizures during 1 year follow-up.

Discussion

The anesthetics-induced seizures in patients without a history of epileptic seizures have been reported previously (Table 2) [15–20]. In these reports, all of the patients suffer from a tonic-clonic seizure (TCS) after receiving anesthetic drugs. Epileptic seizure occurs immediately in patients with local anesthesia, and develops during any period of anesthesia in patients with general anesthesia. This phenomenon has no relationship with the age or sex of patients. The occurrence of epileptic seizure has nothing to do with the type of surgery, anesthesia or procedure [12]. In this study, the two cases were seizure-free for more than 3 years with regular AEDs, suggesting that the recurrence of epileptic seizure is attributed to the anesthetics. Thus, they were asked to continue AEDs in case of relapse.

Anesthetics like propofol are effective drugs to treat convulsive status epilepticus, but they also cause seizures sometimes. The occurrence of anesthetics-induced epileptic seizures in epilepsy patients is related with some factors. The most commonly accepted mechanism of this phenomenon is that the blood concentrations of AEDs are reduced by anesthesia [21–23]. Patients are prepared to abstain from drinking and fasting before anesthesia, which may mislead them to quit antiepileptic medication. Besides, the gastrointestinal absorption of AEDs is altered. These changes lead to the decreased blood concentration of AEDs, thus inducing seizures. Another reason may be that anesthesia disrupts the circadian rhythm, since sleep deprivation can induce epileptic seizures [24]. Moreover, anesthesia can cause hypercapnia and hypoventilation, which result in the elevated susceptibility to seizures and prolonged duration of seizures [25]. Other potential causes include fatigue, stress, menstruation, and electrolyte disturbances. Therefore, more studies are needed to figure out the underlying mechanisms.

In the following, we summarize a procedure as a guidance for surgeons to reduce and deal with anesthesia-induced epileptic seizures. For patients without a history of seizures, adequate preparations can reduce the risk of anaesthesia-induced seizures. For epileptic patients, unnecessary operation should be avoided. If epileptic patients ask for a plastic and anesthetic surgery, doctors should be cautious and let them know both benefits of the surgery and the risks of epileptic seizures. The attack of seizures will hinder the operation, increase the risk, and reduce the success probability of surgery. Anesthesia can cause relapse of epileptic seizures in pregnant women with a history of seizures. For them it is better to choose vaginal birth instead of cesarean delivery, unless there are surgical pointers for cesarean section [26]. Obstetricians and epileptologists should meet to discuss and decide the way of delivery. Epileptic patients including the seizure-free patients, should have adequate preanesthesia preparations before operations with local anesthesia like ophthalmic surgery, nerve block and puncture operation. The use of the following anaesthetic drugs should be avoided for epileptic patients, including alfentanil, remifentanil and sevoflurane [27]. Due to the possibility of occurrence of perioperative seizures, it is essential to prepare emergency drugs to deal with sudden epileptic seizures regardless of the surgical procedure or anesthetic technique. If the seizure lasts less than 5 min, there is no need for such treatment. But if it continues longer than 5 min, a benzodiazepine like diazepam can be injected intravenously, following the guidelines for the treatment of convulsive status epilepticus [28]. Further, a benzodiazepine combined with phenytoin can be administered to the patients with uncontrolled seizures [29].

Conclusions

Patients with epilepsy should avoid unnecessary operations. For pregnant women with controlled epilepsy vaginal birth is recommended, but in the case of epileptic pregnant women having other diseases that require cesarean delivery, obstetricians and epileptologists should discuss together and decide the way of delivery. If a surgery must be done, adequate preparations should be made before anesthesia. The type of anesthesia does not influence the frequency of seizures, but the plasma level of AEDs does. An emergency drug should be at hand for sudden epileptic seizures.

Abbreviations

AEDs: Antiepileptic drugs; CT: Computed tomography; EEG: Electroencephalography; GTCS: Generalized tonic-clonic seizure; MRI: Magnetic resonance imaging.

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Authors' contributions

Wanling Li reviewed the articles online and drafted the manuscript. Wanlin Lai collected the information of the two cases. Anjiao Peng reviewed related articles and extracted the data. Professor Lei Chen conceived the study idea and revised the manuscript for intellectual content. All authors have read and approved the final manuscript.

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Availability of data and materials
The data sets supporting the results of this article are included within the article. All data are fully available without restriction.

Declarations

Ethics approval and consent to participate
The study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, approved by Ethics Committee of West China Hospital (2018 (257)). The written informed consent was obtained from all participants.

Consent for publication
The written informed consent for publication was obtained from all participants.

Competing interests
The authors declare that they have no competing interests.

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