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Anesthetic Management with Propofol in a Patient with Rasmussen's Encephalitis Complicated by Intractable Partial-Onset Epileptic Seizures: A Case Report

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Abstract
Introduction: Rasmussen's encephalitis (RE) is a progressive and chronic ailment characterized by drug-resistant epileptic seizures. RE is uncommon, and no documented accounts of its anesthetic management exist. Anesthetic management without causing epileptic seizures is important in RE. Here, we present a case of safe anesthetic management in a pediatric patient with RE. ***Case Presentation:*** A 7-year-old boy who was diagnosed with RE at the age of 6 years was scheduled for supernumerary tooth extraction under general anesthesia. The patient was being treated with prednisolone, sodium valproate, zonisamide, lacosamide, and famotidine. Despite receiving antiepileptic therapy, the patient experienced partial epileptic seizures several times per week. The seizures presented as numbness in his right hand and progressed to tonic-clonic seizures affecting the right side of his body. On the day of the surgical procedure, the patient was administered regular doses of antiepileptic drugs and prednisolone. Anesthesia was induced and maintained using a combination of propofol, remifentanil, and rocuronium. The surgical procedure was successfully performed, and the patient awakened smoothly from anesthesia. No epileptic seizures were observed intra- or postoperatively. ***Conclusion:*** RE typically presents with drug-resistant seizures and the initial symptoms are usually refractory partial seizures. Propofol is well-established as a treatment option for refractory status epilepticus, and it reduces the frequency of spikes in patients with partial epilepsy. In this case, general anesthesia without epileptic seizures was achieved using propofol.

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Introduction

Rasmussen's encephalitis (RE) is a progressive disorder characterized by intractable focal epilepsy, progressive hemiplegia, and cognitive deterioration with frequent epileptic seizures [1]. Traditionally, patients with RE have had short-term exacerbations of seizures and have undergone hemisphere dissection as a curative procedure. However, the use of immunosuppressive therapy has improved the long-term prognosis of patients, rendering them more likely to receive general anesthesia surgery other than hemispherectomy. RE is uncommon, and no documented accounts of its anesthetic management exist. This study describes a case of RE managed under general anesthesia using propofol.

Case Report

The patient was a 7-year-old male (height: 122.7 cm, weight: 23.2 kg). A supernumerary tooth and interdental avulsion were discovered in the maxillary anterior region; thus, supernumerary tooth extraction was scheduled under general anesthesia. He was born by normal delivery. No abnormalities in growth and development were noted. At 5 years of age, he began experiencing epileptic seizures and was started on antiepileptic drugs; however, his epileptic seizures worsened and the patient was diagnosed with RE at 6 years of age. The seizures were focal, starting with numbness in the right hand and occasionally progressing to tonic-clonic seizures of the right side of the body, lasting 15–30 min. Epileptic waves were frequently observed in the left frontal region during seizures. He received immunosuppressive therapy while continuing antiepileptic medication. The patient was administered a regimen that included prednisolone 38 mg·day^{-1}, sodium valproate 280 mg·day^{-1}, zonisamide 160 mg·day^{-1}, lacosamide 70 mg·day^{-1}, and famotidine 10 mg·day^{-1}. An oral midazolam solution was administered if the seizure lasted longer than 5 min. Despite receiving antiepileptic therapy, the patient continued to experience seizures several times a week. The patient experienced three status epilepticus episodes before the immunosuppressive therapy initiation and did not experience any after the therapy onset. The triggers of seizures remain unknown. The patient underwent regular dental checkups and did not experience any seizures during these visits.

Magnetic resonance imaging of the head showed mild atrophy of the left hemisphere, while the patient's growth and development factors were within normal ranges. No intellectual disability or paralysis was present, and no other complications or malformations were observed. The preoperative electrocardiography, plain chest radiography, and blood test results revealed no abnormalities.

On the morning of the surgical procedure, the patient was administered the usual doses of prednisolone and antiepileptic drugs. Additional methylprednisolone was not administered. Midazolam (10 mg) was administered orally as premedication 30 min before the operation, and the patient was admitted to the operating room with established peripheral venous access. Noninvasive sphygmomanometry, electrocardiography, percutaneous oxygen saturation (SpO_2) monitoring, and bispectral index (BIS) monitoring were performed during the procedure. BIS levels were recorded at 80–90 upon awakening. As the seizures originated in the right hand, the right upper limb was closely observed during anesthesia. Propofol (50 mg), rocuronium (20 mg), and remifentanil 0.28 μg·kg^{-1}·min^{-1} were administered intravenously. Intubation was accomplished using a cuffed endotracheal tube (5.5 mm inner diameter) with a video laryngoscope (McGRATH™, Covidien, Dublin, Ireland). Anesthesia was maintained using a combination of air, oxygen, propofol, and remifentanil, with propofol administered at 4 mg·kg^{-1}·h^{-1} and remifentanil at 0.07–0.2 μg·kg^{-1}·min^{-1}. The BIS levels ranged from 45 to 65 throughout the procedure. Postoperative analgesia was achieved by infiltrating the surgical wounds with

2.7 mL 2% xylocaine. Postoperatively, propofol and remifentanil were discontinued, and sugammadex (100 mg) was administered intravenously. The patient was extubated upon confirmation of spontaneous eye opening and breathing. The patient remained calm even after extubation. No epileptic seizures were observed intra- or postoperatively.

The patient received antiepileptic drugs on the night of surgery and continued to take them during hospitalization. The postoperative period was uneventful, and the patient was discharged on the second postoperative day. No exacerbation of seizures was observed after discharge from the hospital.

Discussion

RE, first reported by Rasmussen et al. in 1958, is a slowly progressive, autoimmune, chronic inflammatory neurological disease [2]. It typically manifests at the mean onset age of 8.3 ± 9.5 years and primarily affects children; however, it may also occur in adults [1]. The prevalence rate in Japan is estimated to be 0.04 cases per 100,000 individuals [3]. The initial symptoms are usually refractory partial seizures, and approximately half the patients develop epilepsia partialis continua [2]. Diagnosis is challenging at disease onset and is suspected when the seizure frequency gradually increases or epilepsia partialis continua appears [3]. The diagnosis is made using Bein's criteria based on clinical symptoms, electroencephalography (EEG), magnetic resonance imaging, and histological findings [4]. Cytotoxic T lymphocytes play a major role in RE pathogenesis; however, the primary cause remains unknown [1]. In untreated cases, seizures become more frequent, and hemiplegia, hemianopsia, and cognitive decline may develop within 1 year [1].

The treatment options include oral antiepileptic drugs, immunosuppressive therapy, and surgery [1]. Antiepileptic drugs alleviate symptoms but do not provide a definitive cure; however, they aim to reduce seizure severity and frequency and improve long-term functional prognosis [5]. The prevention and management of perioperative epileptic seizures are crucial because patients with RE typically have drug-resistant seizures. Antiepileptic drugs should not be discontinued during the perioperative period, and patients should resume their usual medications as soon as possible [6]. Parenteral antiepileptic drugs should be administered in cases when multiple doses are likely to be missed [7].

There are several reports of anesthetic management for patients with epilepsy; nevertheless, there are no reports of general anesthesia for patients with RE. In pediatric populations, sevoflurane is frequently used for induction and maintenance of general anesthesia; however, its use is not recommended for patients with RE because of the convulsant effects associated with high concentrations of the agent [8]. Alternatives, such as desflurane, thiopental, propofol, and benzodiazepines, can be safely used in individuals with epilepsy [7]. In this case, we used propofol for three reasons. First, it has been well-established as a treatment option for refractory status epilepticus [7]. Second, a case of safe sedation surgery using propofol in a patient with refractory epilepsy secondary to Lennox-Gastaut syndrome has been reported [9]. Third, Fujimoto et al. [10] reported that the frequency of spikes was significantly reduced in patients with refractory partial epilepsy who were treated with a target-controlled infusion of propofol. RE is characterized by partial seizures. Considering the classification of epileptic seizures, propofol was determined to be appropriate. There are many reports on the effects of anesthetics during surgery on patients with epilepsy. However, there are no reports mentioning the postoperative effects. In this case, seizures did not worsen after discharge from the hospital. Propofol may be used safely intraoperatively and postoperatively in patients with progressive refractory epilepsy. Benzodiazepines can also be safely used in patients with epilepsy; however, antagonism with flumazenil may be necessary

to awaken the patient from anesthesia. In patients with refractory epilepsy, an oral midazolam solution is often administered to stop epileptic seizures. If an epileptic seizure occurs immediately after flumazenil administration, midazolam may be ineffective in stopping the seizure owing to its antagonistic effect.

Epileptic seizures are difficult to detect during general anesthesia. In this case, the patient was monitored using BIS to maintain appropriate anesthetic depth. The BIS is calculated using the EEG obtained from four electrodes placed on the patient's forehead. It is not clear whether BIS monitoring is useful in detecting seizures; however, Chinzei et al. [11] reported that BIS detected abnormal EEG changes in a patient with postencephalitic epilepsy under general anesthesia. Therefore, careful EEG observation may be useful in cases of sudden changes in BIS or decreases in the signal quality index.

Propofol infusion syndrome (PRIS) should be recognized while taking propofol. In particular, children require more propofol and have a higher incidence of PRIS [12] compared to adults. The dosage and duration of administration should be limited (≤4 $mg \cdot kg^{-1} \cdot h^{-1}$ for 48 h or less) to mitigate the PRIS risk [13]. Concomitant use of catecholamines and other agents that impact mitochondrial metabolism should be avoided, and vigilant monitoring should be conducted throughout the administration [12]. According to reports, propofol requirement is significantly reduced in patients who are concurrently taking three or more antiepileptic drugs [14]; therefore, overdosage during anesthesia should also be considered.

Immunosuppressive therapy has been attempted based on the hypothesis that RE is an immune-mediated process. Immunosuppressive therapy improves outcomes in terms of seizures, cognitive function, and motor function [2]. Immunosuppressive therapy regimens include periodic methylprednisolone pulse (MP) therapy and tacrolimus. For patients receiving >20 $mg \cdot day^{-1}$ prednisolone for a duration exceeding 3 weeks or those displaying symptoms of Cushing's syndrome secondary to MP treatment, the perioperative administration of supplementary glucocorticoids should be considered based on the extent of surgical intervention [15].

Conclusion

Herein, we reported a case in which general anesthesia was safely performed in a patient with RE. The most important aspect in the perioperative management of RE is the prevention of epileptic seizures. In this case, antiepileptic drugs and prednisolone were administered continuously before and after surgery. In addition, general anesthesia was performed with propofol, which has antiepileptic properties. The impact of anesthesia on progressive epilepsy remains uncertain. However, in this specific case, the patient did not experience a deterioration in epileptic seizures postoperatively. In the anesthetic management of patients with RE, the appropriate drug should be selected based on the patient's oral medications and the frequency and type of epileptic seizures. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. maetrial, see https://doi.org/10.1159/000534754).

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Statement of Ethics

Written informed consent was obtained from the patient's family for the publication of this case report. Ethical approval is not required for this study in accordance with local guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M. Akazawa, G. Yan, and R. Hirai were responsible for the anesthetic management of the patient. M. Akazawa and G. Yan wrote the manuscript. H. Kitagawa helped to draft the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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