Case Report

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Super-refractory status epilepticus in a 29-year-old pregnant female

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Abstract

Super-refractory status epilepticus is a rare medical and neurological emergency due to the high mortality and morbidity associated with this condition. Furthermore, there is very little data regarding its incidence, etiology, and management in the pregnant population with super-refractory status epilepticus. The treatment of super-refractory status epilepticus during pregnancy is specifically a major challenge as there are limited available therapeutic options due to the well-established teratogenicity of most antiepileptic drugs and the unknown safety profile of some of the anesthetics commonly used for seizure control. We report a case of successfully treated super-refractory status epilepticus in a 29-year-old, 26 weeks pregnant female who after an emergent delivery and prolonged exposure to multiple antiepileptic drugs recovered full neurological function.

Keywords

Epilepsy, status epilepsy, pregnancy, supra-refractory status epilepsy

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Introduction

Super-refractory status epilepticus (SRSE) is defined as status epilepticus (SE) that persists at least 24 h, despite the administration of intravenous anesthetic drugs (IVADs), including those cases where SE recurs after the reduction or withdrawal of anesthesia.[1] SRSE is seen in about 12% to 26% of SE cases in the general population.[2] The exact prevalence among pregnant patients remains unclear. Pregnancy is associated with variety of endocrine, physiological, and psychological changes, which might contribute to lowering the seizure threshold. SRSE carries high maternal mortality rate with increased rate of fetal complications.[3] In a Turkish population–based study, pulmonary embolism, cerebrovascular event, and cerebral vein thrombosis were attributed as the cause of death in maternal deaths that are accompanied by epilepsy.[4]

Medications used for the treatment of SRSE include benzodiazepines (BZDs), antiepileptic drugs (AEDs), and IVADs, often used simultaneously. There are no guidelines providing specific recommendations for the treatment of SRSE. Furthermore, the management of pregnant patients is even more challenging due to the teratogenicity of most first- and second-line AEDs and the lack of available literature studies regarding the safety of prolonged use of IVADs in this population.

Case report

A 29-year-old, 26 weeks pregnant patient presented with a past medical history of hypertension, traumatic brain injury (TBI), synthetic marijuana abuse, and generalized seizure disorder (diagnosed after TBI in 2014 and has not been compliant with taking her AEDs). She developed seizure activity while driving, leading to a motor vehicle accident. On arrival to the emergency department, she continued to experience generalized tonic-clonic seizures. Repeat doses of intravenous (IV) lorazepam were required to physically suppress the convulsions. IV magnesium was given as it was unknown at this point whether eclampsia was playing a role in her

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condition. Emergency medical services (EMS) reported that the patient had large amounts of synthetic marijuana in her possession at the scene.

On physical examination, she was somnolent with a Glasgow Coma Scale score of 6.[5] Vital signs were stable. She was noted to have a gestational uterus and a concave right cranial defect secondary to her prior TBI. She was intubated for airway protection due to declining neurological status and was taken to the medical intensive care unit.

Initial electroencephalography (EEG) showed periodic lateralized discharges in the right hemisphere. Head imaging were negative for acute findings. Laboratory results showed an elevated white blood count of 23.6 × 103/μL and a high random urine protein/creatinine ratio of 0.6. Cerebrospinal fluid analysis, blood and urine cultures, and liver function tests, among others, all of which were unremarkable.

She was started on IV levetiracetam and midazolam, but her seizure activity persisted. Midazolam was discontinued. Propofol 55 mcg/kg/min, fosphenytoin 100 mg IV three times per day, lacosamide 400 mg IV twice per day, ketamine 2 mg/kg/h, and pentobarbital 2 mg/kg/h were added to the regimen, given the persistent abnormal EEG findings. An EEG burst suppression pattern (seizure control) was finally achieved for the first time after 25 h of pharmacologic therapy at maximal doses. Propofol was eventually discontinued.

Weaning of pentobarbital was attempted after several days of non-epileptic EEG pattern, but bilateral cerebral hemisphere seizure activity quickly recurred, forcing continued use of pentobarbital at maximum doses. However, no improvement in the EEG tracing was obtained after increasing this medication and EEG seizure activity continued. Furthermore, fetal distress was noted on hospital day 6 requiring an emergent bedside cesarean section. After delivery, valproic acid and pyridoxine were added, and burst suppression pattern was again achieved on hospital day 10. The patient's neurological status slowly improved, allowing for liberation from mechanical ventilation. Finally, after 14 days of hospitalization, a normal EEG pattern was obtained, and the patient was transferred out of the intensive care unit. The patient's baby had a prolonged hospitalization, but was eventually discharged home.

Discussion

The incidence of SE ranges from approximately 5 to 40 per 100,000 with a recent meta-analysis reporting an annual incidence of 12.6 per 100,000.[2] SRSE is uncommon in any patient population, and even more so in the pregnant population. It is considered a medical emergency, as sustained seizure activity is associated with a risk of permanent brain damage, and significant morbidity and mortality. The mortality rate of SE in the general population ranges from 20% to 40%.[6] In addition, SRSE in pregnant patients can compromise placental flow, causing fetal hypoxia, potentially leading to severe neurodevelopmental delays.[3] Hence, it is imperative to promptly identify and treat the etiology of SRSE in order to suppress seizure activity as early as possible.

SE in pregnancy is caused by many things including TBI, strokes, cavernous angiomas, pyridoxine deficiency, eclampsia, noncompliance with AEDs, viral encephalitis, systemic lupus erythematosus, reversible cerebral vasoconstriction syndrome, subarachnoid hemorrhage, NMDA (N-methyl-D-aspartate) receptor antibody-mediated autoimmune encephalitis, and hormonal changes associated with pregnancy.[7] Eclampsia was considered as a contributor to SRSE in our patient, but after a thorough investigation by the obstetricians, this diagnosis was ruled out. This patient's SRSE was likely due to the combination of risk factors making her seizures so refractory to treatment.

When deciding on a treatment for SE in pregnancy, the control of seizure activity must be balanced against the potential risks of the AEDs for the developing fetus.[8] Regarding SE in general, BZDs continue to be the initial drug of choice for suppression of seizure activity. However, when they are unsuccessful at controlling seizure activity, AEDs should be added to the treatment regimen.[2] The choice of which AEDs to use was very difficult for this patient, given the safety profile for each medication in gravid patients. Levetiracetam was added first, but fosphenytoin, lacosamide, and valproic acid were eventually added secondary to the worsening clinical condition.

If the seizure activity continues for at least 24 h, despite the addition of IVADs, the diagnosis of SRSE is confirmed, as in this patient.[1] Unfortunately, IVADs are the last available pharmacological option for the treatment of SE and there is no general consensus regarding which specific drug should be used, especially in the pregnant population.

There are several proposed therapies for the management of SRSE in the general population, all of which include the use of three classes of medications: BZDs, AEDs, and IVADs. However, these recommendations are primarily based on clinical reports and have not been studied in pregnant patients. Furthermore, most of these medications have known teratogenic effects. Early identification and treatment of patients with epilepsy may help to decrease unfavorable outcome. This case illustrates the successful treatment of SRSE in a pregnant patient, without significant long-term adverse effects for the patient or her child.

Conclusion

The management of SRSE is extremely challenging, especially for pregnant patients, as evidence-based protocols for treatment are currently unavailable. The current pharmacological options are limited, and most of them have teratogenic effects, but if SRSE is left untreated, it may become life-threatening not only for the mother but also for their

offspring. Further studies are needed in order to determine the safest therapies for this patient population.

Author contribution

All authors contributed equally.

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Informed consent

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