Super-refractory status epilepticus (SRSE) is defined as status epilepticus (SE) that persists at least 24 h, despite the administration of intravenous anesthetic drugs (IV ADs), 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 IV ADs, 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 6.³ 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 intu-
bated 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, keta-
mide 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 24 h of pharma-
ologic 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 contin-
ued use of pentobarbital at maximum doses. However, no
improvement in the EEG tracing was obtained after increas-
ing this medication and EEG seizure activity continued.
Furthermore, fetal distress was noted on hospital day 6
requiring an emergent bedside cesarean section. After deliv-
ery, valproic acid and pyridoxine were added, and burst sup-
pression 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 even-
tually discharged home.

Discussion

The incidence of SE ranges from approximately 5 to 40 per
100,000 with a recent meta-analysis reporting an annual inci-
dence 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 addi-
tion, SRSE in pregnant patients can compromise placental
flow, causing fetal hypoxia, potentially leading to severe neu-
rodevelopmental delays.³ Hence, it is imperative to promptly
detect 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, eclamp-
sia, noncompliance with AEDs, viral encephalitis, systemic
lupus erythematosus, reversible cerebral vasoconstriction
syndrome, subarachnoid hemorrhage, NMBA (N-methyl-D-
aspartate) receptor antibody-mediated autoimmune encepha-
litis, 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 obstetri-
cians, this diagnosis was ruled out. This patient’s SRSE was
likely due to the combination of risk factors making her sei-
zures 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 sec-
ondary 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 availa-
able 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 preg-
nant 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, espe-
cially for pregnant patients, as evidence-based protocols for
treatment are currently unavailable. The current pharma-
co logical options are limited, and most of them have terato-
genic 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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