

# Super-refractory status epilepticus in a pregnant woman with schizencephaly

Soo-Hyun Park<sup>1</sup>, Tae Jung Kim<sup>2,3</sup>, Sang-Bae Ko<sup>2,3</sup>

<sup>1</sup>Department of Neurology and Department of Critical Care Medicine, Inha University Hospital, Incheon, Republic of Korea

<sup>2</sup>Department of Neurology and Department of Critical Care Medicine, Seoul National University Hospital, Seoul, Republic of Korea

<sup>3</sup>Department of Neurology, Seoul National University College of Medicine, Seoul, Republic of Korea

Received November 5, 2020;  
Accepted January 4, 2020

Schizencephaly is an uncommon congenital malformation caused by defective cell migration during the early prenatal period [1]. Schizencephaly usually presents with developmental delays, motor weakness, or recurrent seizures during childhood [2]. Rarely, it may present with super-refractory status epilepticus (SRSE) [3]. Herein, we report a case of SRSE in a pregnant woman with schizencephaly. Given that SRSE is potentially life-threatening to the mother as well as to the foetus, emergency delivery of the foetus might play a beneficial role in its management [4].

A 33-year-old pregnant woman, at 35 weeks of gestation, had been presenting with continuous generalized tonic-clonic seizures for the past three hours. On arrival at the emergency room, she was experiencing convulsive movements involving the left upper extremity and face. She was born by normal full-term delivery and denied any prenatal history of trauma, infection, or exposure to toxins including smoking, alcohol, or drugs. She had intellectual disability (mini-mental status examination score of 20) with congenital hemiparesis on the left side. She had been diagnosed with perimenstrual catamenial epilepsy at the age of 18. The seizures were initially motionless with repetitive lip-smacking which progressed to generalized convulsions. The total duration of seizures was usually one or two minutes. The patient usually experienced seizures two or three days before her menstrual cycle, which were well controlled with sodium valproate (900 mg/day). This was her first pregnancy and

she did not have any miscarriages or abortions before. On neurological examination, the patient was comatose (Glasgow Coma Scale, E2V2M3) with sluggish light reflex and brisk deep tendon reflexes on the left. Blood pressure was 115/80 mmHg, respiratory rate was 18 breaths per minute, temperature was 38.5 °C, and oxygen saturation was 98% while the patient was breathing ambient air. There were no signs of generalized oedema suggesting eclampsia.

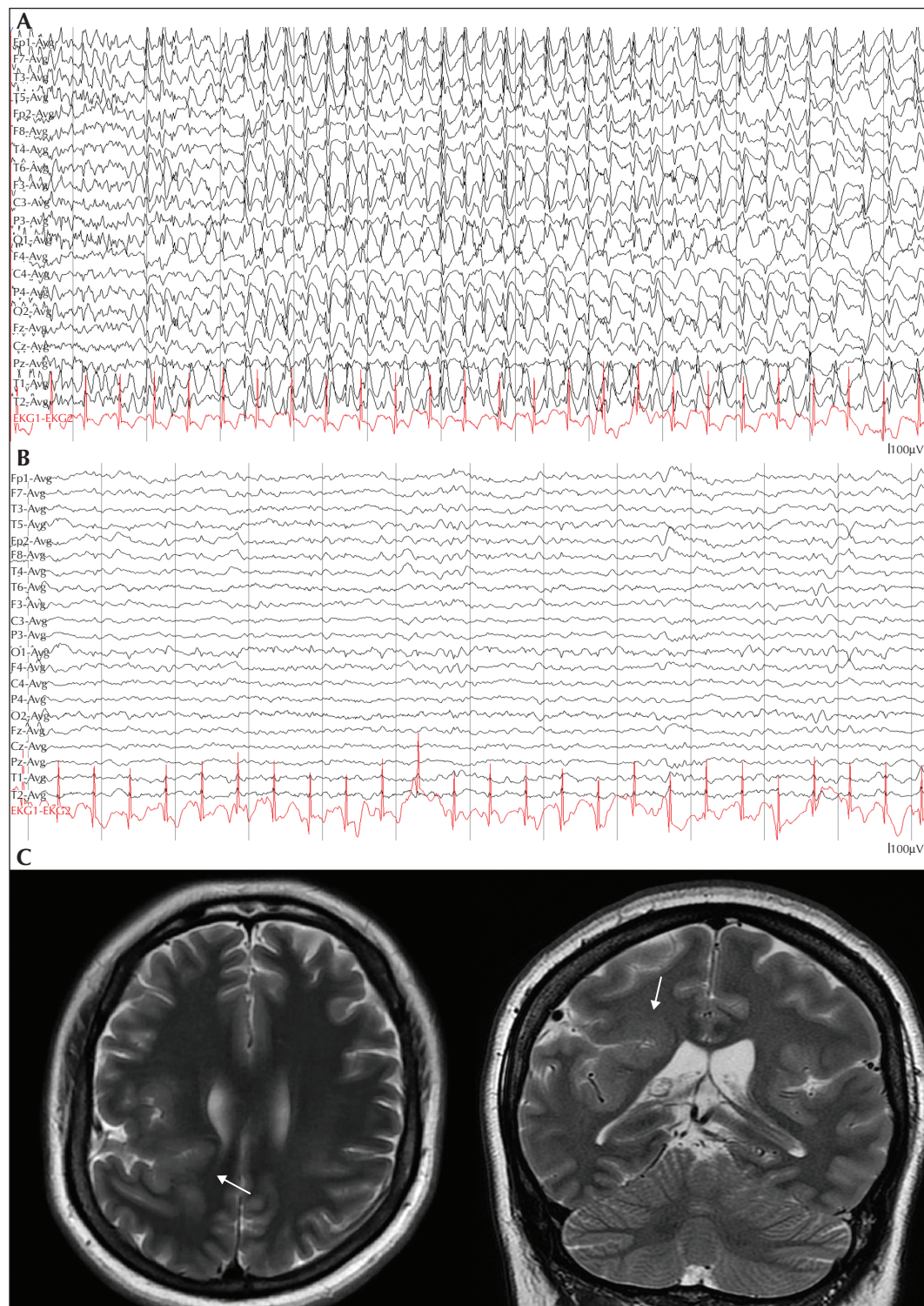
Laboratory test results were unremarkable except for a low drug concentration of valproic acid (27 mcg/mL). An intravenous injection of lorazepam (4 mg) temporarily stopped the seizures. When the patient was transferred to the emergency intensive care unit, generalized-tonic clonic seizures appeared and a loading dose of levetiracetam (1,500 mg) was administered. However, generalized tonic-clonic seizures persisted and the patient underwent an emergency Caesarean section for rapid termination of the pregnancy.

After successful delivery of the foetus (APGAR score of 5, 1 minute; APGAR score of 6, 5 minutes), phenobarbital (loading dose of 1,500 mg with a maintenance dose of 300 mg/day) was administered without clinical improvement. A 24-hour video-EEG showed continuous generalized polyspike-and-wave discharges (figure 1A) requiring continuous infusion of midazolam (0.4 mg/kg/h). During midazolam treatment, breakthrough seizures were controlled with an intermittent bolus injection of thiopental sodium (100 mg, three times/day). On post-delivery Day 2, the EEG

## • Correspondence:

Sang-Bae Ko  
Department of Neurology,  
Department of Critical Care  
Medicine,  
Seoul National University  
Hospital, Seoul National  
University College of Medicine  
101 Daehak-ro, Jongro-gu,  
Seoul, 03080, Korea  
<sangbai1378@gmail.com>

doi:10.1684/epd.2021.1286



■ **Figure 1.** Continuous video-EEG and brain MRI of the patient. (A) Video-EEG shows continuous generalized polyspike-and-wave discharges, more prominent on the left hemisphere. (B) A follow-up EEG shows diffuse theta slowing. (C) T2-weighted brain MRI showed unilateral “closed lips”, lined by the cortical grey matter in the right parietal area (white arrows).

improved and showed diffuse theta slowing without epileptiform discharges. Therefore, midazolam was tapered off on post-delivery Day 3 while lacosamide (200mg/day) was added to existing medications (levetiracetam [1,500 mg/day] and phenobarbital [300 mg/day]) (figure 1B). Brain magnetic resonance imaging revealed a schizencephalic cleft on the right parietal lobe (figure 1C). Despite prenatal exposure to valproic acid and SE, the baby boy did not have any congenital malformations or developmental delays and she recovered to her baseline neurological status.

This is a rare case of SRSE in a pregnant woman with undiagnosed schizencephaly, and an emergency Caesarean delivery was helpful in the management of SRSE. The common causes of seizures or SE in the third trimester are eclampsia, posterior reversible encephalopathy syndrome, encephalitis, or autoimmune encephalopathy [5, 6]. However, she did not have any clinical evidence of any of these. She had been diagnosed with perimenstrual catamenial epilepsy at the age of 18 years, which was well controlled. Given that patients with perimenstrual catamenial epilepsy tend to have a reduced seizure frequency throughout the pregnancy, this patient also did not have any seizures before this presentation [7]. One of the reasons for worsening seizures during the third trimester is a reduction in plasma concentration of antiepileptic drugs (AEDs). Expansion of plasma volume, an increase in hepatic metabolism, or augmentation of renal clearance were suggested as one of the mechanisms [2]. The plasma concentration of valproic acid was 58 mcg/mL before pregnancy and was measured at 27 mcg/mL on presentation, which was below therapeutic levels. Moreover, elevated plasma oestrogen levels during the late phase of pregnancy also contributed to the aggravation of seizures [8]. The clinical expression of schizencephaly depends on its size, location, and accompanying abnormalities such as agenesis of the corpus callosum, polymicrogyria, heterotopias, or optic nerve hypoplasia, which the patient, in this case, did not have [1, 2]. Unilateral schizencephaly may present with hemiparesis or recurrent seizures, as in our case. However, the patient had not received any medical attention, which could have delayed the diagnosis. Given that the clonic movements were on the left, we believe that a decrease in drug concentration in late pregnancy could provoke the occurrence of seizures from the right schizencephaly.

The management of schizencephaly is usually conservative. However, the patient had SRSE with recurrent breakthrough seizures while on appropriate anaesthetic treatment, which could be potentially toxic to the foetus. Moreover, repetitive uncontrolled seizures pose a risk of hypoxemia, which might lead to foetal hypoxemia and a poor outcome. Therefore, we decided to stop the pregnancy and deliver the foetus. Considering that the patient was in SRSE, we do

not believe that cessation of the SRSE over the two days was due merely to midazolam. It is reported that an emergency termination of pregnancy could be an effective treatment option for refractory status epilepticus in a pregnant woman [8, 9]. The suggested mechanisms are a reversal of pregnancy-related neuronal excitability and hormonal imbalances [9]. Moreover, we could use potentially teratogenic AEDs, such as a high dose of phenobarbital, without a worry of adverse outcomes in the foetus. Taken together, we believe that the emergency delivery contributed to the successful treatment of SRSE in this patient.

In conclusion, our case demonstrates that schizencephaly may present with SRSE in a pregnant woman. Moreover, an emergency Caesarean section might be considered as one of the treatment options for SRSE when a patient is in the third trimester of pregnancy. ■

#### Supplementary material.

Summary slides accompanying the manuscript are available at [www.epilepticdisorders.com](http://www.epilepticdisorders.com).

#### Disclosures.

None of the authors have any conflicts of interest to declare.

#### References

1. Lopes CF, Cendes F, Piovesana AM, SG, Torres F, Lopes-Cendes I, Montenegro MA, et al. Epileptic features of patients with unilateral and bilateral schizencephaly. *J Child Neurol* 2006; 21: 757-60.
2. Jbili N, Mounir K, Kechna H, Bibiche L, Laoutid J, Dai A, et al. A rare case of super-refractory epileptic status in pregnant woman: Schizencephaly. *Anaesth Crit Care Pain Med* 2019; 38: 195-8.
3. Hirsch LJ, Gaspard N, Baalen AV, Nabbout R, Demeret S, Loddenkemper T, et al. Proposed consensus definitions for new-onset refractory status epilepticus (NORSE), febrile infection-related epilepsy syndrome (FIRES), and related conditions. *Epilepsia* 2018; 59: 739-44.
4. Lu YT, Hsu CW, Tsai WC, Cheng MY, Shih FY, Fu TY, et al. Status epilepticus associated with pregnancy: A cohort study. *Epilepsy Behav* 2016; 59: 92-7.
5. Licht EA, Sankar R. Status epilepticus during pregnancy. A case report. *J Reprod Med* 1999; 44: 370-2.
6. Rajiv KR, Radhakrishnan A. Status epilepticus in pregnancy: Etiology, management, and clinical outcomes. *Epilepsy Behav* 2017; 76: 114-9.
7. Cagnetti C, Lattanzi S, Foschi N, Provinciali L, Silvestrini M. Seizure course during pregnancy in catamenial epilepsy. *Neurology* 2014; 83: 339-44.
8. Pack AM. Having catamenial epilepsy equals fewer seizures in pregnancy. *Epilepsy Curr* 2015; 15: 124-5.
9. Alibas H, Demir N, Agan K, Buyukbayrak EE, Yildizhan B, Midi I. Refractory status epilepticus during pregnancy resolved by cesarian section. *Seizure* 2019; 65: 109-10.

## TEST YOURSELF

**(1) Which of the following statements about families with schizencephaly is correct?**

- A. Schizencephaly is associated with congenital malformation caused by defective cell migration;
- B. Schizencephaly is always associated with super-refractory status epilepticus in a pregnant woman;
- C. The clinical expression of schizencephaly is not associated with its size, location, or accompanying abnormalities.

**(2) Which of the following statements during the third trimester is correct?**

- A. Worsening seizures are associated with a reduction in plasma concentration of anti-epileptic drugs.
- B. Worsening seizures are associated with decreased plasma oestrogen levels during the late phase of pregnancy
- C. Worsening seizures are not associated with an expansion of plasma volume, an increase in hepatic metabolism, or augmentation of renal clearance.

**(3) Was the emergency Caesarean section helpful in the management of super-refractory status epilepticus in this study?**

- A. Yes. The emergency Caesarean section was effective.
- B. No. The emergency Caesarean section was harmful.
- C. Neither of the above.

---

*Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, [www.epilepticdisorders.com](http://www.epilepticdisorders.com), under the section "The EpiCentre".*

---