New-onset refractory status epilepticus in pregnancy: a case report and review of the literature surrounding management

Wilson E[1], Teasdale S[2], Janssens S[1], Dionisio S[3]

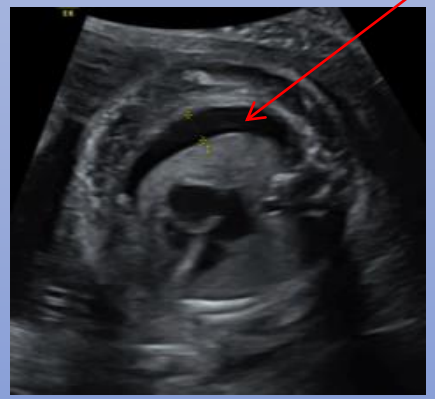
[1]Department of Obstetrics & Gynaecology, Mater Mothers' Hospital, Stanley Street, South Brisbane, Queensland 4101, Australia
[2]Department of Obstetric Medicine, Mater Mothers' Hospital, Stanley Street, South Brisbane, Queensland 4101, Australia
[3]Department of Neurology, Mater Hospital, Stanley Street, South Brisbane, Queensland 4101, Australia
Case published with patient consent. Contact: em3wilson@gmail.com

2021 RANZCOG Virtual Annual Scientific Meeting 15–18 February

Background:

- The incidence of status epilepticus (SE) in pregnancy ranges between 0.6-1.8% of all pregnancies in women with epilepsy (WWE)[1,2]
- Fetal hypoxia may occur as a result of maternal hypoxia, decreased placental blood flow or postictal apnoea
- The EURAP study reviewed 3784 WWE throughout pregnancy.[3] Status epilepticus (SE) was reported in 21 (0.6%) of these. Seizure control was improved during pregnancy in the catamenial group (44.1% experienced a reduction in seizures of ≥ 50%)[2]
- This is possibly attributable to the absence of cyclical hormone variations and increased progesterone and allopregnanolone levels in pregnancy (which have anti-seizure properties)

Incidental finding of hydrops fetalis at 25 weeks with ascites seen



Case:

- 23-year-old primip with a history of genetic general catamenial epilepsy & left temporal lobe epilepsy
- Increased focal seizure frequency from 19 weeks
- 25 weeks: patient was transferred to ICU with **cryptogenic new-onset super refractory status epilepticus (NORSE)**
- At K25 antenatal **steroid** loading occurred due to concerns regarding increased uterine activity and maternal sepsis 2nd to ventilator-acquired pneumonia
- Cervical length USS to establish preterm birth risk at K25+6 identified **fetoplacental hydrops**. The middle cerebral artery peak systolic velocity of <1.5MoM suggested that the fetus was not anaemic. The hydrops was likely related to fetal hypoxia: a secondary effect of altered uteroplacental blood flow in the setting of status epilepticus, pneumonia-induced respiratory compromise, mechanical ventilation and sepsis
- Delivery was planned due to concerns about: **1) development of maternal Mirror Syndrome secondary to hydrops and 2) ongoing status epilepticus** exacerbated by the pregnant state causing further maternal and fetal compromise
- Delivery occurred at K26 weeks. Birth weight: 1140g
- Paired cord blood gases were within normal limits. Apgar scores were 2 @1 min and 4 @5 mins
- EEG monitoring showed no ongoing status epilepticus day 2 postpartum. **Pregnancy was the most likely cause of the patient's NORSE episode.** Four days postpartum, all anti-epileptic infusions were ceased.
- Lactation suppression was suggested in the setting of multiple AED use
- A progesterone-based contraceptive was recommended

Discussion:

- All investigations into seizure aetiology were unremarkable. Our patient's extreme refractory status episode suggests that not all catamenial seizure patterns = favourable prognosis in pregnancy
- There are **no established guidelines** for management of SE in pregnancy: treatment should involve benzodiazepine use followed by first line AEDs: phenytoin, phenobarbitone and levetiracetam. Intubation and general anaesthesia with propofol, midazolam or thiopentone should be commenced for refractory status [4]
- Other therapies considered for refractory status were found in the literature including:
  - **Plasma exchange** [5]
  - **Anakinra** targeting IL-1 in presumed autoimmune encephalitides. Data published on the use of anakinra in the perinatal period for other rheumatological conditions appears to be generally reassuring.[6]
  - **Ketogenic diet** was also given consideration. However, there were concerns about the resulting metabolic acidosis, hypoglycaemia and ketone effects on the baby with implementation of this regime[7]
  - **Electroconvulsive therapy (ECT)** to terminate the status episode.[3,7] Risks reported include: preterm delivery, caesarean section, deep vein thrombosis, intrauterine growth retardation, neonatal respiratory distress, neonatal death, mental retardation, optic nerve atrophy, abortion, congenital cardiac disease and intrauterine death.[8,9,]

Conclusion:

- No clear aetiology was identified in this case of NORSE
- **Termination of the pregnancy for maternal and fetal indications was ultimately therapeutic**, likely altering neuronal excitability, hormonal balance and immunity
- Large multicentre prospective controlled studies are required to better determine optimal evaluation and treatment of SE in pregnancy.

References:

1) Battino D, Tomson T, Bonizzoni E, et al. Seizure control and treatment changes in pregnancy: observations from the EURAP epilepsy pregnancy registry. *Epilepsia*. Sep 2013;54(9):1621-1627.
2) Group ES. Seizure control and treatment in pregnancy: observations from the EURAP epilepsy pregnancy registry. *Neurology*. Feb 14 2006;66(3):354-360.
3) Tomson T, Battino D, Bonizzoni E, et al. Antiepileptic drugs and intrauterine death: A prospective observational study from EURAP. *Neurology*. Aug 18 2015;85(7):580-588.
4) Jones L, Kilos J. Algorithm for the treatment of status epilepticus: an Australian perspective. *Intern Med J*. Apr 2016;46(4):500-503.
5) Gofton TE, Gaspard N, Hocker SE, Loddenkemper T, Hirsch LJ. New onset refractory status epilepticus research: What is on the horizon? *Neurology*. Apr 23 2019;92(17):802-810.
6) Youngstein T, Hoffmann P, Gul A, et al. International multi-centre study of pregnancy outcomes with interleukin-1 inhibitors. *Rheumatology (Oxford)*. Dec 1 2017;56(12):2102-2108.
7) an der Louw EJ, Williams TJ, Henry-Barron BJ, et al. Ketogenic diet therapy for epilepsy during pregnancy: A case series. *Seizure*. Feb 2017;45:198-201.
8) Zeiler FA, Jurkiewicz M, Teitelbaum J, Gillman LM, Kazina CJ. Electroconvulsive therapy for refractory status epilepticus: A systematic review. *Seizure*. Feb 2016;35:23-32.
9) Sinha P, Goyal P, Andrade C. A Meta-review of the Safety of Electroconvulsive Therapy in Pregnancy. *J ECT*. Jun 2017;33(2):81-88.