Brain Stimulation 17 (2024) 676–677

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.journals.elsevier.com/brain-stimulation

Electroconvulsive therapy in new onset refractory status epilepticus (NORSE) in a pediatric patient

Dear Editor,

New onset refractory status epilepticus (NORSE) is a diagnosis of exclusion for patients with refractory status epilepticus (RSE) without known epilepsy or identifiable seizure etiology. Patients fail to respond to conventional treatments, with seizures persisting for weeks or even months. When first line antiseizure medications (ASMs) fail, alternatives are pursued, including immunotherapy, cannabidiol, and ketogenic diet [1,2]. Electroconvulsive therapy (ECT) has been occasionally used for treatment of RSE, but rarely in children [3,4]. We report a previously healthy 8-year-old girl with NORSE whose epileptic burden improved with escalating therapies, including ECT and subsequent vagal nerve stimulator (VNS) placement.

Our patient presented with one week of headache, fever, and new-onset seizures. Within 24 hours, she developed multiple seizures that rapidly evolved into RSE and was intubated in the intensive care unit for airway protection. Extensive infectious, autoimmune, rheumatologic, metabolic, neoplastic, and genetic work up was unrevealing. Repeat brain MRIs were normal. Aggressive ASM management with maximum doses of intravenous levetiracetam, fosphenytoin, phenobarbital, valproic acid, and lacosamide failed to abort seizures. She was simultaneously treated with 5 days of pulse-dose steroids and intravenous immunoglobulin (IVIG) without improvement. Ketogenic diet was initiated on day 8 of hospitalization, cannabidiol on day 11, and 1st high-dose rituximab on day 12.

Despite these aggressive measures, she remained in RSE, so ECT was initiated on hospital day 12. She continued on high dose ASM infusions in/out of pentobarbital coma, along with maintenance ASMs. ECT was performed daily for seven days with two stimulations per session, using a Thymatron device with bitemporal electrode placement. Propofol was paused 1 hour before ECT sessions, with boluses of ketamine, fentanyl, and rocuronium used to ensure the patient was appropriately sedated prior to each ECT session. Flumazenil was administered 2 minutes prior to stimulation to temporarily mitigate anticonvulsive effects of ASMs. After the second ECT seizure each day, a bolus dose of midazolam was given and propofol resumed. ECT achieved seizures lasting between 7 and 19 seconds in all treatments, with median post-ictal suppression of 70.5%, indicating good seizure quality (Table 1 summarizes parameters and outcomes of each session) [5].

After the 1st ECT session, she achieved 24 hours of seizure freedom without significant change in EEG background. By the 3rd treatment, the pentobarbital infusion had been weaned with subsequent increase in subclinical seizures, but with gradual improvement in EEG background activity. She had clusters of seizures when propofol was paused for ECT sessions, as well as frequent seizures overnight, so phenobarbital was maximized to supra-therapeutic levels. Clobazam was added after ECT session day 5 to help manage overnight breakthrough seizures. By day 7 of treatment, propofol infusion had been discontinued and she was experiencing an average of 3 brief (<1 minute), discrete electrographic seizures in 24 hours, with much-improved EEG background, less frequent periodic discharges, and return of sleep spindles.

She was weaned off all ASM infusions one day post-ECT completion and extubated shortly thereafter. She received her 2nd high-dose rituximab hospital day 26, with VNS placement day 29, and transferred to inpatient rehabilitation day 33. Ketogenic diet was discontinued due to intolerance. She remained completely seizure-free and stable on maintenance ASMs one month after hospital discharge.

Nine months after presentation, the patient remains in school relatively high-functioning. She has on average 1 brief (<1 minute) seizure per month. She remains on an ASM regimen of oral clobazam, phenobarbital, and cannabidiol, with cenobamate added 8 months post-discharge. VNS settings are 1.5mA current, 1.625s auto-stim, and 1.75mA magnet. She has no motor impairment and was discharged from physical therapy after six months. She still has ongoing disinhibited behaviors with increased irritability, affective instability, and defiance; for this, she is being treated with a selective-serotonin reuptake inhibitor. Phenobarbital is also being weaned, as there is concern this may be contributing to her behaviors.

In summary, we present an 8-year-old, previously healthy girl with NORSE who responded to ECT initiated on day 12 of hospitalization, following the failure of numerous ASMs and immunomodulatory therapies. There is considerable experience using ECT safely for the treatment of resistant depression and catatonia in adolescents in psychiatry [5,6]; however, there have been limited reports of its use for RSE. Nath *et al.* (2021) compiled data on 6 published cases of ECT for treatment of RSE in children ages 3-16-years between 1997 and 2021 [3]. RSE etiologies included, focal cortical dysplasia, polymicrogyria with cerebral palsy, epilepsia partialis continua, and febrile infection-related epilepsy syndrome (FIRES). Outcomes described included termination of non-convulsive RSE after ECT treatments, seizure freedom within one month to one year, severe cognitive and motor impairment, or no response at all with patients eventually dying [3]. Zeiler *et al.* reports treating 19 individuals with ECT; 4 were children ages 7–13 years [4]. In this study, seizure reduction was reported in 58% of patients: 4 demonstrated partial electrographic improvement and 7 achieved greater than 24-hour seizure cessation [4]. Frequency and number of treatments of ECT varied for each reported case, so there is no established protocol in the literature to date.

Our 8-year-old with NORSE responded well to a 7-day course of ECT with subsequent VNS implantation. Multiple ASMs and immunomodulatory therapies failed to improve the overall epileptic burden. The therapeutic effect of ECT is supported by the timing of response in each seizure produced. However, interpretation of its efficacy is confounded by close succession of other treatments including phenobarbital, rituximab, cannabidiol, ketosis, and VNS implantation. As such, it is difficult

https://doi.org/10.1016/j.brs.2024.05.006
Received 1 May 2024; Accepted 13 May 2024
Available online 18 May 2024

Table 1
ECT Sessions with Thymatron device with bitemporal electrode placement and effects on epileptic burden.

Session (Day)	Stim (mC)	Motor Sz (sec)	EEG Sz (sec)	Post-Ictal Suppression	Sz burden 24 hours post-ECT	Infusions (mg/kg/hr)/ASMs
1 (12)	508.5	6	10	66.8 %	No seizures x 24 hours	Pentobarbital 2, propofol 80, midazolam 0.4,
	508.5	2	9	–		phenobarbital, lacosamide, cannabidiol, Keto (TPN)
2 (13)	509.5	4	10	71 %	6 hours sz free, then had 8 brief (20sec) szs after	Pentobarbital 1, propofol 80, midazolam
	510.1	2	7	–		0.35phenobarbital, lacosamide, cannabidiol, Keto (TPN)
3 (14)	509.9	7	15	<10 %	Propofol paused prior to procedure and had 12 szs. Then 1	Off pentobarbital, propofol 80, midazolam
	511.1	6	13	60.2 %	sz immediately after ECT, followed by 15 hours sz freedom, then 1 brief sz.	0.4phenobarbital, lacosamide, cannabidiol, Keto (TPN)
4 (15)	509	10	17	74 %	12 hours sz free, then had 6 brief szs before next session	Propofol 80, midazolam 0.2 phenobarbital
	509	6	10	70 %		increased, lacosamide, cannabidiol, Keto (TPN)
5 (16)	509.2	5	10	19 %	5 hours sz free, then had brief 15 szs (all <1 minute)	Propofol 80, midazolam 0.2 phenobarbital,
	510.4	4	8	27 %		lacosamide, clobazam started, cannabidiol, Keto
6 (17)	508.1	11	19	77 %	5 hours sz free, the had 7 szs that evening (all brief)	Propofol 30, midazolam 0.2 phenobarb,
	508.3	0	12	74 %		lacosamide,clobazam increased, cannabidiol, Keto
7 (18)	507.8	10	17	86.3 %	1 hour sz free, 3 brief szs in the afternoon	Off propofol, midazolam 0.2 phenobarb,
	507.6	8	10	91.4 %		lacosamide,clobazam, cannabidiol, Keto

Table 1. ECT achieved seizures lasting between 7 and 19 seconds in all treatments with median post-ictal suppression of 70.5 %, indicating good seizure quality. All ASM infusions were weaned one day post-ECT completion with EEG showed decreased epileptic burden.

to make generalizable conclusions regarding ECT efficacy, specifically in RSE. Instead, we present a case where ECT contributed greatly to reducing seizure burden, allowing for VNS implantation and eventual near-complete seizure control. ECT merits consideration in treatment of NORSE patients when other measures are exhausted as it was safe and effective for our pediatric patient.

CRediT authorship contribution statement

Florence Sun: Writing – original draft, Writing – review & editing. **Spencer Eberhard:** Writing – review & editing. **Amy E. Hanson:** Writing – review & editing. **Laurence Walsh:** Supervision, Writing – review & editing. **Christopher T. Jackman:** Supervision, Writing – review & editing. **Danielle Maue:** Supervision, Writing – review & editing. **Susan K. Conroy:** Supervision, Writing – review & editing.

Declaration of competing interest

The autparahors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Wickstrom R, Taraschenko O, Dilena R, Payne ET, Specchio N, Nabbout R, Koh S, Gaspard N, Hirsch LJ, International NORSE Consensus Group. International consensus recommendations for management of new onset refractory status epilepticus (NORSE) including febrile infection-related epilepsy syndrome (FIRES): summary and clinical tools. Epilepsia 2022 Aug 11;63(11):2827–39. https://doi.org/10.1111/epi.17391. Epub ahead of print. PMID: 35951466; PMCID: PMC9826478.

[2] Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline committee of the American epilepsy society. Epilepsy Curr 2016;16:48–61.

[3] Nath M, Shah Y, Theroux L, Petrides G, Karkare S, Sanghani S, Kothare S. A role for electroconvulsive therapy in the management of new onset refractory status epilepticus (NORSE) in a young child. Neurol India 2021;69(5):1374–9.

[4] Zeiler FA, Matuszczak M, Teitelbaum J, Gillman LM, Kazina CJ. Electroconvulsive therapy for refractory status epilepticus: a systematic review. Seizure 2016;35:23–32.

[5] Eser Daniela, Nothdurfter Caroline, Schüle Cornelius, Damm Julia, Steng Yvonne, Möller Hans-Jürgen, Rupprecht Rainer, Baghai Thomas. The influence of anaesthetic medication on safety, tolerability and clinical effectiveness of electroconvulsive therapy. World J Biol Psychiatr: the official journal of the World Federation of Societies of Biological Psychiatry 2009;11:447–56. https://doi.org/10.1080/15622970902960897.

[6] Ghaziuddin N, Laughrin D, Giordani B. Cognitive side effects of electroconvulsive therapy in adolescents. J Child Adolesc Psychopharmacol 2000;10:269–76.

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