Successful Emergency Treatment of Refractory Neuroleptic Malignant Syndrome With Electroconvulsive Therapy and a Novel Use of Dexmedetomidine

A Case Report From California in the Era of COVID-19

Rajani Rajan, MA, MD and Mary Sage, MD†*

Abstract: We describe the case of a patient, hospitalized in a California community medical ICU for over a month, with severe neuroleptic malignant syndrome (NMS), unresponsive to medical management, but responsive to electroconvulsive therapy (ECT). We discuss the medical, logistical, and legal challenges in providing ECT in this setting. We also describe a previously unpublished use of dexmedetomidine, which aided in the safe and rapid reduction of benzodiazepines and permitted a successful ECT course. The rapid delivery and efficacy of ECT were essential because of the burgeoning coronavirus pandemic. The patient's treatment required exemplary efforts by providers across multiple disciplines, ongoing medicolegal consultation with the county mental health medical director, as well as consultation with expert members of the International Society for ECT and Neurostimulation. We conclude with a discussion of the unique challenges of providing emergency ECT to patients in California, including during a serious pandemic, when courts are closed. This case illustrates the importance of cultivating and maintaining high-quality ECT expertise in community hospitals and keeping ECT services available even during pandemics. Also, this case demonstrates that ECT is not "merely an elective procedure" but a vital, life-saving treatment, even during the era of COVID-19. To our knowledge, this is the first such published case of emergency ECT performed in California.

Key Words: electroconvulsive therapy, neuroleptic malignant syndrome, dexmedetomidine, COVID-19, emergency services

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Neuroleptic malignant syndrome (NMS), existing on a continuum with malignant catatonia, is a potentially fatal complication of antipsychotic treatment, with a mortality rate of up to 40%.[1] Although stopping antipsychotic medications is often effective, some patients will not respond to additional supportive care and pharmacotherapy. In such refractory cases, electroconvulsive therapy (ECT) is a lifesaving emergency medical treatment.

Even in life-threatening situations, providing ECT presents unique challenges in the United States. Some states—California, Texas, and New York, in particular—have been described as particularly "stringent" in permitting emergency ECT.[2]

The current COVID-19 epidemic presents additional challenges. Rapid treatment of hospitalized patients is essential to protect patients and staff from nosocomial spread of this life-threatening infection.

Appropriate use of limited personal protective equipment (PPE) must be addressed.

From the *Department of Psychiatry, Kaiser Permanente, Santa Clara; and †Department of Psychiatry, Kaiser Permanente, Walnut Creek, CA.
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Reprints: Rajani Rajan, MA, MD, Department of Psychiatry, Kaiser Permanente, 710 Lawrence Expressway, Santa Clara, CA 95051 (e-mail: rajani.s.rajan@kp.org).
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Dexmedetomidine, a selective α-2-adrenergic receptor agonist with sedative and anxiolytic properties and lacking respiratory depression, is frequently used in anesthesiology and critical care. Dexmedetomidine in conjunction with benzodiazepines has also been used off-label to successfully treat alcohol withdrawal.[3] In ECT, dexmedetomidine has been used to manage postictal delirium and attenuate the hyperdynamic response, with literature indicating a generally neutral effect on seizure duration. In the case described, we hypothesized that dexmedetomidine might facilitate the safe reduction of a high benzodiazepine dose and permit successful ECT.

CASE PRESENTATION

The patient was a 60+-year-old married White woman, with a history of an anxiety disorder, who, after a life stressor and subsequent orthopedic fracture, developed delusional somatic anxiety associated with depression and suicidal ideation. The patient was psychiatrically hospitalized and treated successfully with haloperidol 5 mg twice daily, mirtazapine, fluvoxamine, and lorazepam. Her mood and psychosis appeared to improve, and she was discharged home.

Over the next 4 weeks, the patient physically slowed, progressing from being ambulatory to requiring a cane, walker, then finally a wheelchair. Mirtazepine was stopped, and haloperidol tapered off over 2 weeks and stopped 3 days before medical hospitalization. Stiffness progressed, and the patient became unable to open her eyes or speak. She was referred to the emergency department. There, she was found to have symptoms of autonomic instability including hyperthermia (101°F) and tachycardia, marked rigidity, and elevated creatine kinase of 650. She was diagnosed with NMS and admitted to the ICU. Creatine kinase peaked at 918 3 days after admission.

Over the following weeks, the ICU team sought consultations from toxicology, psychiatry, and neurology. The patient received multiple medications used to treat NMS. Lorazepam intravenously and via nasogastric tube produced mild improvement in autonomic parameters, but without significant improvement in her ability to move or communicate. Maximum lorazepam dosing was 11 mg/d, limited by hypotension. Dantrolene was started at 2 mg/kg every 6 hours. However, shortly after initiation, the patient's mental status worsened, stiffness persisted, breathing worsened, patient aspirated, and was intubated. Bromocriptine was added and later titrated. Dantrolene was also increased, later abandoned because of inefficacy. Carbidopa/levodopa and amantadine were tried and ineffective, with carbidopa/levodopa discontinued after a week.

Electroconvulsive therapy was considered. However, coincident with patient's decline, COVID-19 was rapidly spreading in the United States. Several counties ordered "shelter in place" as the serious nature of viral spread became apparent. Hospitals worked to prepare their facilities for a surge of contagious patients.

Additionally, PPE was in short supply. An accepting facility that could provide both critical care and ECT services could not be found — multiple programs had temporarily closed or restricted ECT services. The few facilities that could meet the patient's requirements were unable to accept transfers because of local demand during the anticipated surge. The patient could not be weaned from the ventilator because of the ongoing autonomic instability, leading to tracheostomy placement.

Given the patient's severe, refractory symptoms, the hospital's psychiatry consultation-liaison service consulted with ECT providers at 2 affiliated hospitals. As the patient lacked capacity to consent for ECT, legal and county mental health consultations were sought. Legal counsel initially pursued the typical court order of incapacity and delegation of consent to the surrogate decision-maker — in this case, the patient's husband.

However, because of COVID-19, courts were closed, and the case was unable to be heard. The county mental health medical director and involved providers agreed that the patient was in an emergency medical situation, which could not wait for courts to reopen. In California, Business and Professions Code Section 2397(c)(2) and (3) and Probate Code Section 3210(b) permit treatment in patients lacking capacity during a medical emergency.[4] The county mental health medical director and legal consultants advised that ECT could be provided as an emergency medical treatment under this statute. The patient's husband and surrogate decision maker fully supported the pursuit of ECT. He provided informed consent for each treatment and was actively involved throughout the treatment course.

To rapidly facilitate ECT, lorazepam was lowered from 10 to 9 mg/d over approximately 4 days, whereas bromocriptine and amantadine were continued. It was hoped that the benzodiazepine could be reduced further and held the night before ECT. However, rigidity and autonomic instability (tachycardia, hypertension, overbreathing ventilator) prompted the ICU nurse to administer an additional lorazepam 1 mg dose about 2 hours before the first ECT treatment.

Per consultation with national and local experts, daily bilateral ECT commenced, using a MECTA ECT device (SpECTrum 5000Q; MECTA Corporation, Tualatin, OR). A local ICU nurse was instructed about post-anesthesia care for ECT patients. To preserve PPE, the patient was tested for COVID-19 and found negative before ECT start.

On ECT day 1, the patient was rigid and unable to communicate. Etomidate was chosen because of its relative seizure-permitting effects. Rocuronium was chosen to reduce possible dangerous hyperkalemia. One milligram of flumazenil was given before induction. Cuff method was used to determine motor seizure duration, whereas EEG tracing was used for seizure duration. The patient received a bitemporal treatment using a 0.5-ms pulse width with frequency of 90 Hz, duration of 8 seconds, current of 800 mA and with a maximal charge output of 576 mC. No motor or EEG seizure resulted.

Given the concerns about the high benzodiazepine dose needed to stabilize vital signs, before ECT day 2, dexmedetomidine drip was initiated after the patient's bedtime lorazepam dose. Dexmedetomidine at 0.4 to 1.4 μg/kg/h was titrated by ICU nurse using a Richmond Agitation Sedation Scale Score of −1 to −3 and continued for several days. Flumazenil was increased to 2 mg before ECT. Pt was then treated with 1 ms bilateral ECT with 2.0-second duration stimulus, at a frequency of 60 Hz, and with an 800 mA, corresponding to 192 mC charge delivered. An adequate motor seizure of 52 seconds was achieved; no additional benzodiazepine was needed.

Over the next several treatments, autonomic symptoms stabilized. Before treatment number 4, the patient was able to thank the treating team, and mouth "what happened to my voice?" By this time, lorazepam was safely lowered from 9 to 4.5 mg. On that same day, dexmedetomidine was tapered off. Lorazepam was eventually tapered down to a daily dose of 3 mg daily while maintaining autonomic stability. Patient had no breakthrough seizures between treatments.

Electroconvulsive therapy frequency was decreased from 5 days/week during the first week, to 4 days/week during the second week, to 3 days/week during the third week. The patient received 12 ECT treatments in total.

At this point, the patient was able to speak, eat, and stand with support, and stably transfer out of the ICU. Electroconvulsive therapy was no longer deemed clinically necessary as emergent medical treatment for NMS. The psychiatry consultation team petitioned the court for involuntary ECT, in the event of relapse to NMS and the future need for ongoing ECT. As writing of this article, no relapse to NMS had occurred. The patient discharged from acute medical hospital to an acute rehabilitation facility, then returned home, without psychiatric symptoms except for short-term memory deficits, and physically significantly recovered, even able to walk up and down 15 stairs. Outpatient, the patient was prescribed no psychiatric medications, except for gradual oral lorazepam taper.

DISCUSSION

NMS is a life-threatening medical emergency that does not always respond to withdrawal of offending agent and use of dopaminergic and muscle relaxing agents. In such cases, ECT should be considered. Patients with refractory NMS may require high benzodiazepine doses, making effective ECT more difficult. The ECT provider must not only circumvent the anticonvulsant effects of benzodiazepines but also avoid additional dysautonomia when lowering benzodiazepines. Here, the brief off-label use of dexmedetomidine to stabilize autonomic symptoms, while quickly tapering down lorazepam, promoted successful ECT treatment of NMS. Dexmedetomidine may also have reduced postictal agitation.

Legally, this case is similar to a Texas case, where statutes pertaining to emergency treatment in medical situations permitted ECT where it may have otherwise proven more challenging.[5] Although court closures due to COVID-19 undoubtedly complicate ECT for needy patients without immediate medical risk, court closures combined with immediate medical risk may actually have permitted this patient to receive ECT more quickly.

The family and multisite team were gratified by the patient's rapid improvement, a bright spot during the otherwise grim COVID-19 pandemic.

This case demonstrates the importance of ECT as a life-saving medical treatment in refractory NMS, with unique challenges in the context of a pandemic. It also demonstrates a novel approach to treating NMS patients, and potentially other patients on high doses of benzodiazepines, who require rapidly effective ECT. Approaches to ECT that are safe, rapid, and effective are particularly important in the uncertain era of COVID-19.

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