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Refractory Hypoglycemia with Generalized Convulsive Status Epilepticus in Suspected Propranolol Overdose: Is Early Intubation the Key?

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Abstract

There are many ways to manage status epilepticus. The rationale for aggressive treatment of generalized convulsive status epilepticus lies solely on the premise that best outcomes rely upon rapid seizure control. Metabolic and toxic seizures can be particularly refractory to therapy, exposing a patient to the threat of aspiration, hyperkalemia, rhabdomyolysis, hyperthermia, myocardial infarction, and arrhythmias.[1]

The role of intubation is controversial. Neurologists tend to view intubation as a form of "treatment failure", reflecting inability to treat the seizure with traditional agents.[1] However, it is our opinion that intubation is often the key therapeutic intervention to not only control the seizure, but prevent its deadly complications.

In our case report, we highlight the emergent airway management of a 29-year-old pre-morbidly healthy female who was referred to us from a secondary care center with generalized convulsive status epilepticus and refractory hypoglycemia, following an alleged history of propranolol overdose.

Keywords: Intubation; Toxic Seizure; Hypoglycemia; Propranolol.

INTRODUCTION

Among the presentations seen in the Emergency Department, few command the same respect as status epilepticus. It is, in itself, both a diagnostic dilemma, and at times a therapeutic nightmare. There's a reason it's the very first domino to fall in the dreaded sequence of "seizure, coma, death". That being said, status epilepticus can be nuanced to manage.

Status epilepticus can be defined in two ways:

1. Continuous seizure lasting more than 5 minutes *or*
2. Two or more seizures within a 5 minutes period without return to neurological baseline in between.

Most seizures resolve spontaneously in 1–3 minutes. However, by the time the seizure is

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identified and strategies put into place to abort the episode, most actively seizing patients who have not already stopped seizing will be in status epilepticus.[2]

In our case, we highlight an amalgamation of multiple factors resulting in an extremely vulnerable patient. Our emphasis during the discussion is on early tracheal intubation not just as a means to an end, but rather the most vital component of therapy in successfully producing a good outcome in a case such as this one.

Case Presentation

A 29-year-old female was received in our Emergency Department (ED) from paramedics who had transported her from a secondary care center, with an in-transit history of generalized tonic convulsions in the ambulance; two episodes, each lasting for a few seconds, spaced 3 minutes apart, with no apparent response to 3 mg of intravenous midazolam.

The patient had been admitted to the secondary care center the night before with symptoms of paroxysmal dizziness and profound malaise; there was a documented episode of generalized tonic convulsions at the time of admission, lasting for approximately 10 minutes. Treatment records available at the time showed that she had received 2 mg of midazolam and 1000 mg of levetiracetam intravenously, which subsequently aborted the seizure, but the patient never returned to her neurological baseline after that episode. It was important to note that her random blood sugar on admission at the secondary care center was 22 mg/dl. There was also a record of bradycardia (sinusal, at 45/min) and persistent altered mental status. Despite attempts to correct her blood sugar with dextrose, the patient's levels never went above 65 mg/dl, finally prompting her transfer to a higher center.

Her medical background was healthy, except for a history of headaches and vertiginous symptoms a few days earlier, for which she had been prescribed propranolol 20 mg tablets by a general physician (the prescribed dose and duration of the course was unavailable to us). She had no known allergies, no addictions, and no surgical history of relevance. The patient had been married for six months, with no children; her last menstrual period was indiscernible.

On arrival to our ED, the patient was profoundly altered. She had an oropharyngeal airway in-situ, which was clamped down on, causing bleeding within the oral cavity. There was a 20 gauge peripheral line, which was patent, and an indwelling 14 Fr. Foley's catheter. Her Glasgow Coma Scale was E1V2M4. There was no nuchal rigidity, and pupils were reacting equally to light at 1.5 mm in size. Her heart rate was 120 beats per minute (regular), blood pressure 110/70 mm Hg, and respiratory rate 38 breaths per minute; axillary temperature 98.6 degrees Fahrenheit. Oxygen saturation was 95% on room air. The random blood sugar was 64 mg/dl.

The immediate next step in her management was the plan to perform a rapid sequence induction (RSI) and mechanical ventilation in view of poor protective reflexes. This was after attempting to correct her blood glucose using 25% dextrose. However, despite this measure, there was no improvement in her mental status. Thus, an RSI was completed with propofol and atracurium, following which a midazolam infusion was initiated (in order to prevent unmanageable hypotension caused by propofol). The patient's hemodynamics remained stable through out the procedure. An adjunct dose of 100 mg hydrocortisone was also administered after drawing her blood for testing, along with 1 mg of subcutaneous glucagon. Basic laboratory panel and metabolic profile didn't reveal any discrepancies. Her urine was clear for toxins, and her urine pregnancy test was negative. A magnetic resonance venogram (MRV) did not reveal cortical venous thrombosis.

In the Intensive Care Unit (ICU), the patient was continued on an infusion of 50% dextrose, which was gradually tapered. Further testing for insulin, pro-insulin, acetone and C-peptide levels turned out to be normal. Her course in the ICU remained progressively positive; the 25% dextrose infusion was switched to Dextrose Normal Saline (DNS) on Day 2, and she was successfully extubated on Day 3, holding blood sugars at 100-110 mg/dl. She was transferred to the ward on Day 5, with the DNS infusion stopping on Day 6. The patient was discharged from the hospital on Day 7. Her blood sugars at the time of discharge were at 110-125 mg/dl. She was kept on oral levetiracetam, with a planned follow-up after one week with her neurologist and an endocrinologist (both of whom were involved in her care at the time of admission).

DISCUSSION

Acute symptomatic seizures occur in close temporal relationship with an acute central nervous system insult that may be metabolic, toxic, structural, infectious, or inflammatory in nature.[3]

The prognosis after unprovoked seizures and symptomatic seizures differ with regard to risk of seizure recurrence and mortality; therefore, it is also essential to define metabolic conditions when acute symptomatic seizures might occur.[4] In our case, the nature of insult seemed pretty obvious as prolonged refractory hypoglycemia, albeit at the time, the etiology of the hypoglycemia was under question. An acute neuroglycopenic symptom is a direct result of brain glucose deprivation and includes cognitive impairment, behavioral changes, psychomotor abnormalities, seizures, and coma.[5]

Our patient had recently been prescribed prophylactic propranolol for her episodic headaches, although there was no record of this prescription. Persistent interrogation of the family revealed strips of the beta blocker with unaccounted tablets, which made us suspect the possibility of an overdose. In normal individuals without evidence of impaired glucose metabolism, propranolol can account for blockade of epinephrine induced hepatic glucose production by effects of its beta-adrenergic antagonism, resulting in hypoglycemia. Non-selective beta blockers have also shown to directly inhibit pancreatic glucagon release. Additionally, since the counter regulation of adrenaline is diminished, sympathetic induced glycogenolysis and gluconeogenesis are reduced, thus inhibiting glucose disposal by insulin dependent tissues.[6,7]

Propranolol is one of the most lipophilic of beta-blockers, which means that it may easily cross the blood brain barrier, directly resulting in seizures in overdose situations.[8]

When it comes to aggressive treatment of generalized status epilepticus, best outcomes rely upon rapid seizure control. The longer the seizure continues, the more refractory it becomes to therapy. The duration of status epilepticus which may cause permanent brain damage is unknown, with experts currently suggesting thirty minutes.[9]

The rationale for propofol as a second line anti-epileptic has been explored before; however, most patients who fail benzodiazepines will require intubation eventually. Delaying intubation to allow for a trial of anti-epileptics risks prolonging the seizure and increasing associated complications.[1] Our patient's generalized seizures were resistant to benzodiazepines, and levetiracetam had failed to prevent recurrence.

Patients who are intubated early usually have good neurologic outcomes allowing extubation a day or two later. Alternatively, patients who are intubated after long periods of uncontrolled seizures are at increased risk for super-refractory status epilepticus, poor neurologic outcomes, aspiration pneumonia, and longer time on the ventilator.[1]

CONCLUSION

We have reported a case of refractory hypoglycemia presenting with generalized convulsive status epilepticus. It is our opinion that when faced with the possibility of metabolic or toxic (symptomatic) status epilepticus, early invasive ventilation is a key therapeutic intervention in the management of the seizure. Rapid control of the seizure followed by prevention of its complications are added benefits of early intubation.

We believe that the novelty of this case lies in a combination of factors:

1. A clinical possibility of propranolol overdose in a case of refractory hypoglycemia and seizures - we advise the emergency physician to indulge in comprehensive interrogation, corroborate the physiologic findings, and keep a high index of suspicion.
2. Early intubation in toxic or metabolic generalized convulsive status epilepticus – easy to wean off sedation, potentially early extubation (as against infective seizures), may prevent deadly complications of prolonged epileptic activity.

The following observation is our personal opinion based on the positive outcome noted. We suggest that the benefit of early intubation in such cases be studied more comprehensively in order to generate a higher class of recommendation.

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