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CASE REPORT

Anesthetic considerations in Dravet syndrome

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Abstract

We describe a two-year-old boy with Dravet syndrome, a severe genetic epilepsy, who developed a generalized tonic-clonic seizure immediately following an intravenous bolus of lidocaine given for propofol pain amelioration during induction of anesthesia for emergency gastroscopy. Although lidocaine has not specifically been reported as potentiating seizures in Dravet syndrome, it is well-established that sodium channel blockers can worsen seizures in this population.

KEYWORDS

adverse events, complications, drugs, epilepsy, local anesthetics, neurological disease

INTRODUCTION

Dravet syndrome is one of the most common severe genetic epilepsies, occurring at an incidence of approximately 1/15000.¹ Children with Dravet syndrome typically present in the first year of life with prolonged tonic-clonic seizures triggered by febrile illness or vaccines. Afebrile seizures later develop and epilepsy remains treatment-resistant into adulthood. Approximately 90% of individuals with Dravet syndrome have a pathogenic variant in the *SCN1A* gene, with resultant loss of function in the neuronal sodium channel Nav1.1. Use of sodium channel blocking antiseizure medications can aggravate seizures in Dravet Syndrome.²

Lidocaine is a class 1b antiarrhythmic and local anesthetic drug that is frequently used during intravenous induction of anesthesia with propofol to reduce injection pain. Lidocaine is a sodium channel blocker and, although not described in the Dravet literature, presumably has the potential to exacerbate seizures.

We describe a child with Dravet syndrome, on multiple anti-seizure medications known to inhibit clearance of hepatically

metabolized drugs, who had a generalized tonic-clonic seizure immediately following intravenous administration of lidocaine. The patient's mother provided informed consent.

CASE SUMMARY

The child is a two-year-two-month-old 12.5 kg boy with Dravet syndrome, diagnosed aged 9 months, due to a pathogenic *SCN1A* variant. In the year prior, he had had four febrile tonic-clonic seizures, three being prolonged. He also had infrequent afebrile focal seizures. His regular antiseizure medications were cannabidiol, sodium valproate, clobazam, and stiripentol. Previously he had used topical EMLA cream without adverse event.

Following a croup-like illness 10 days prior, for which he was treated with 2 days of prednisolone and ibuprofen, he presented with hematemesis and melena. He was afebrile and, apart from mild rhinorrhea, had no symptoms of infection. His hemoglobin

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was 68 g/L (normal range: 110–160 g/L) and he received a red blood cell transfusion and intravenous pantoprazole prior to transfer to our hospital for gastroscopy. None of his usual antiseizure medications were omitted. Due to the history of hematemesis, an intravenous rather than inhalational induction of anesthesia was performed. Doses were determined based on actual body weight. Blood taken 10 min prior to anesthesia showed a hemoglobin of 113 g/L, normal hematocrit, electrolytes, and glucose. An injection of 1 ml of 1% lidocaine (0.8 mg/kg) was given intravenously for propofol pain amelioration into a peripheral vein with a brief proximal tourniquet, after which the child developed a tonic-clonic seizure. The seizure terminated with 0.1 mg/kg of intravenous midazolam followed by a rapid induction using propofol and remifentanyl. The remaining anesthesia was uneventful without signs of cardiac dysfunction.

Gastroscopy revealed gastric ulcers consistent with NSAID use. No further seizures occurred during the admission.

DISCUSSION

Most individuals with Dravet syndrome survive into adulthood and are likely to require multiple anesthesia, for example, during emergent management of status epilepticus, dental examination, and gastrostomy insertion. Intravenous lidocaine is used for a variety of indications including nerve blocks, perioperative pain management, and cardiac arrhythmias. Given that our patient's seizure occurred while he was afebrile, and unlike his usual seizures was brief and easily terminated with midazolam, it is plausible that it was precipitated by lidocaine use.

The *SCN1A* gene encodes the alpha protein subunit of the voltage-gated sodium channel Nav1.1, which is the major sodium channel on inhibitory (GABAergic) interneurons. *SCN1A* mutations impair channel and interneuron function, resulting in a hyperexcitable state. Sodium channel blockers further reduce GABAergic inhibition, increasing seizure propensity. Literature suggests that carbamazepine, oxcarbazepine, and lamotrigine should be avoided in Dravet syndrome due to exacerbation of seizures and poorer long-term cognitive outcomes.² Use of lidocaine for anesthesia therefore, might similarly increase seizure risk.

Multiple factors may have contributed to our patient's seizure following the lidocaine injection. Usually, lung uptake of lidocaine results in lower arterial versus venous plasma concentrations protecting against neurotoxicity following injection, including in patients with epilepsy.^{3,4} With tourniquet use the central bolus rate may have been augmented, resulting in a brief but significant elevation in arterial lidocaine concentration; however, even a slow injection mixed with propofol could potentially cause a seizure in Dravet syndrome. An increased free fraction of lidocaine due to changes in plasma protein content following the gastrointestinal bleed and transfusion may also have contributed, while the gastric ulcers themselves could reduce antiseizure medication absorption. Finally, drug error is a possibility to

consider, however both the strength and dose administered were carefully checked.

Anesthetic management in Dravet syndrome should consider potential drug interactions. Some drugs used in Dravet syndrome including stiripentol, cannabidiol, and fenfluramine result in inhibition of cytochrome P450 enzymes. Given the child's seizure occurred after a bolus of lidocaine, hepatic drug metabolism is unlikely to have contributed. However, in other circumstances, decreased clearance of hepatically metabolized drugs, for example, midazolam when used as an oral premedication, may result in excessive sedation or need for airway protection.

Intravenous lidocaine, particularly administered as a bolus, should be avoided in Dravet syndrome. Potential interactions of anesthetic drugs with antiseizure medications should be considered.

LEARNING POINTS

- Dravet syndrome is a common genetic epilepsy and remains treatment-resistant into adulthood.
- Lidocaine, and other sodium channel blockers, should be avoided in Dravet syndrome.
- Be cautious of reduced midazolam clearance in patients taking enzyme-inducing antiseizure medications.

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CONFLICT OF INTEREST

No authors have any conflicts of interest to disclosure.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICAL APPROVAL

The Royal Children's Hospital's Human Research Ethics Committee (HREC)'s policy is that case reports are exempt from HREC review.

INFORMED CONSENT

Informed written consent was given by the patient's parents who have read and approved of the case report.

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