

Causal Inference in Traumatic Brain Injury: A Case of Head Trauma and Mismatched Symptoms

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We present a case of a 14-month-old female presenting to the emergency department with head trauma. When her symptoms deviated from those associated with typical head trauma, the emergency department pharmacy team recognized a vital clue that directed the medical team toward the actual mechanism of injury and appropriate treatment of the child.

ABBREVIATIONS ECG, electrocardiogram; ED, emergency department; EMS, emergency medical services; TBI, traumatic brain injury

KEYWORDS clinical pharmacist; drug toxicity; health care team; pediatric emergency medicine; traumatic brain injury

J Pediatr Pharmacol Ther 2023;28(4):365–367

DOI: 10.5863/1551-6776-28.4.365

Introduction

Traumatic brain injury (TBI) is a common and ever increasing diagnosis of injury in pediatric emergency departments. Data from the US Centers for Disease Control and Prevention report for the year 2019 more than 16,000 children were hospitalized with TBI, and in 2020 there were 2774 TBI-related deaths.¹ Implementation of the Brain Trauma Foundation pediatric TBI guidelines² gives providers evidence-based treatment options and expectedly improved patient outcomes. However, in clinical practice there are often instances of overlapping conditions, and this case describes how the medical team used guidelines and clinical experience to treat such a scenario.

Case

A previously healthy 14-month-old female presented to the emergency department (ED) following head injury and was subsequently assigned level 3 trauma status. Per emergency medical services (EMS) report, the mother of the patient called EMS after witnessing the patient toddle on a carpeted surface, lose her balance, and strike the side of her forehead on a bed frame. Upon EMS arrival the patient had normal vital signs, yet she was unable to stand and was experiencing altered mentation. Mother of patient did not observe any loss of consciousness, seizure activity, or vomiting prior to EMS arrival.

Upon arrival to the ED, the patient was fitted with a cervical collar and an intravenous line was placed. Presenting vital signs were still unremarkable and within normal range. A point of care blood gas and blood electrolytes were obtained and the results were within normal limits. During the initial trauma assessment,

examination of the head revealed a left frontal contusion but was otherwise atraumatic. The child's pupils were equally round and reactive to light. She was graded a Pediatric Glasgow Coma Scale score³ of 13, (eye 4, verbal 4, motor 5). The patient appeared quite altered in a dissociative-like state, unable to track gaze and exhibiting whimper cries. The only other finding of note on exam was a diaper rash with broken skin. Because of her altered mental status, the patient was given a 10 mg/kg dose of levetiracetam for seizure prophylaxis per the pediatric TBI guidelines.² A computerized tomography scan of her head and chest and cervical spine x-rays were performed and all were reported as normal.

During the trauma assessment, the team began to question the etiology of this child's mental status changes. The patient's cry was "fussy" instead of painful. She appeared lethargic, somnolent, dazed, and notably was experiencing nystagmus. The pharmacist suggested possible toxin ingestion as a more likely cause for the patient's symptoms. The physician decided to investigate this possibility further through discussion with the child's mother. The mother denied any opportunity for ingestion as the child was supervised, and there were no drugs in the home of the grandmother where the event occurred. However, the mother did disclose that 15 minutes prior to the fall, she had changed the child's diaper and had used the grandmother's neck pain cream to treat the child's diaper rash. The mother had the patient's grandmother send the team a picture of the label for the neck pain cream for review. The cream had been compounded by a local pharmacy, and labeled as: KETA/BAC/DIC/GABA/TETR 10/2/3/6/2% CREAM.

The physician assigned the ED pharmacist the task of ingredient identification. The pharmacist and pharmacy

student concluded baclofen, diclofenac, gabapentin, and tetracaine were likely the latter 4 ingredients. However, KETA was less obvious. The team was unable to contact the local pharmacy because of the belated hour. The pharmacy student suggested that ketamine was a possibility. The pharmacist then asked the bedside nurses if the nystagmus and dissociated state reminded them of a patient receiving ketamine for sedation, which the nurse affirmed with a look of recognition and a resolute yes. The pharmacy team presented these conclusions to the physician, who agreed. The residual diaper cream was removed immediately. The patient's grandmother arrived later with the cream, and we confirmed that it contained ketamine.

Poison control was contacted and recommended obtaining an electrocardiogram (ECG), basic metabolic panel, and a blood methemoglobin concentration. Blood gases were also obtained, as is standard with presumed toxin exposure. Urine and serum toxicology tests were negative. Of note, ketamine is not included on our standard toxicology screen. Initial ECG noted sinus tachycardia. The nurse was alerted to watch for the following symptoms: central nervous system depression, lethargy, confusion, hypotension, bradycardia, respiratory depression, and nausea or vomiting. Initial and subsequent basic metabolic panels and blood gases were unremarkable and revealed no evidence of kidney injury from the probable diclofenac exposure. Methemoglobin was 0.2%, well below the normal limit of 1%, eliminating concern for methemoglobinemia secondary to tetracaine exposure.⁴ This result minimized our concern for potential seizures or arrhythmias.

The patient experienced 2 to 3 episodes of emesis while in the ED and remained somnolent until transfer to the pediatric intensive care unit for overnight observation. In the pediatric intensive care unit, the patient continued to be fatigued and dazed. A follow-up ECG showed normal sinus rhythm. All labs remained unremarkable. In the morning she was discharged home, having recovered to her normal baseline, being alert, interactive, ambulatory, and tolerating oral nutrition.

Discussion

This case is a prime example of a "red herring" in medicine. The mechanism of injury, although reported and confirmed on physical examination as head trauma, was actually discovered to be an intoxication due to topical exposure of a potentially harmful extemporaneously formulated cream not intended for use on our patient. A case like this reinforces the necessity for a detailed history to assess for any and all possible/probable compound exposures present within the child's environment combined with continual evaluation of the patient's clinical status to better refine one's differential diagnosis. The drug history component of the complete history and physical exam should include all medications (prescribed, over-the-counter, natural products,

etc) within the pediatric patient's environs, which may extend to other caregivers' and relatives' homes.

The topical cream responsible for the symptoms experienced by our patient was prescribed for treatment of her grandmother's neck pain. This cream was used incorrectly and without medical consultation on a pediatric patient for pain secondary to diaper rash, which is similar to the case reported by Sullivan et al.⁵ It has been almost a decade since the publication of the case by Sullivan et al, who reported a case of an 18-month-old male who required endotracheal intubation following toxic exposure to a medicated pain ointment prescribed to the father of the child. Similarly to our case the caregiver applied the cream to relieve diaper rash, despite having received no medical direction to do so. The components of the pain medications in both cases were similar, containing a non-steroidal anti-inflammatory drug, gabapentin, and ketamine. However, the 18-month-old was also exposed to clonidine, as opposed to baclofen, which may have been the difference between necessity of respiratory support in this patient. In our case we portend that the collaborative nature of our ED team may have accelerated the discovery of the exposure and prevented unnecessary procedures (imaging, lab draws, etc). Because few "red-herring" cases are reported, we submit our case to remind and admonish health care providers of the importance of education surrounding prescribing and dispensing of compounded topical creams. Additionally, we hope to reeducate ED teams to consider topical intoxication as a potential cause or complicating factor in altered mental status, respiratory dysfunction, or cardiac arrest.

A detailed discussion of mechanisms of action/toxicity and indications for all 5 active ingredients included in the compounded cream are outside the scope of this brief report. However, we will opine on the effect these medications had on our patient and her observed symptoms. Ketamine, a medication used for its analgesic and sedative properties, was suspected to be the most probable cause of sedation, confusion, dreamlike state, tachycardia, nausea, and nystagmus.⁶ Baclofen and gabapentin may have contributed to the dizziness, drowsiness, nausea, and vomiting experienced by our patient.^{7,8} The exposure to the other agents (diclofenac and tetracaine) did not appear to be associated with any appreciable toxicity.^{9,10}

Our case demonstrates the potential for harm when using prescription medications in those patients for whom it was not originally prescribed. Although adverse effects resulting from systemic absorption of topical medications is uncommon, there are properties that may predispose certain individuals to harm.¹¹ In this case, systemic absorption was likely intensified by at least 3 possible mechanisms, including occlusion from the patient's diaper, a compromised epidermis/dermis (broken skin) from her diaper rash and age-related differences in skin barrier function relative to adults.^{11,12} This case serves as a great reminder for prescribers and pharmacists to boldly

advise against sharing of medications/compounds that are not specifically prescribed by a qualified healthcare provider for the child; and to provide counseling about the potential for increased absorption if a heating pad or occlusive bandage (i.e. diaper) is applied over the medicated area, or if the topical agent is applied to any area with thin or broken skin.

This case exemplifies the value of a team-based approach to patient care. We would like to highlight the importance and value of the ED pharmacist,¹³ who through clinical questioning/investigation led to the identification of a medication exposure being the most likely cause of the patient's symptoms. Also, the pharmacy student's helpful role in the clinical discovery should encourage pharmacists to precept whenever possible. This case further underscores the importance of having a multidisciplinary team consisting of professionals with different areas of expertise available within the ED to optimize patient care.

Article Information

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Disclosure. The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all patient information in this report and take responsibility for the integrity and accuracy of the report.

Ethical Approval and Informed Consent. The authors received Intermountain Healthcare Research Institutional Review Board approval and written consent from the patient's caregiver was provided

Acknowledgment. The authors would like to thank the medical team of the emergency department of Primary Children's Hospital.

Submitted. December 9, 2021

Accepted. July 27, 2022

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