Case Report

Carbamazepine Toxicity Masquerading as Complex Febrile Seizures in a Pediatric Patient

Richard J Chen, Muhammad Ershad, Maricel Dela Cruz, and Ahmed Mamdouh Taha Mostafa

Drexel University College of Medicine, Department of Emergency Medicine, Division of Medical Toxicology, Philadelphia, PA, USA

Correspondence should be addressed to Richard J Chen; chenrich@einstein.edu

Received 24 October 2019; Accepted 25 February 2020; Published 16 March 2020

Academic Editor: Vasileios Papadopoulos

Copyright © 2020 Richard J Chen et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Carbamazepine is an antiepileptic drug that can cause seizures in overdose. In certain patient populations, this may be misdiagnosed as a seizure disorder. We describe a case of a 20-month-old female who presented with fever and seizure-like activity who was initially thought to have complex febrile seizures. Further historical information prompted carbamazepine level to be checked, which was found to be 29 mcg/ml (therapeutic range of 4–12 mcg/ml). Her carbamazepine levels downtrended with multidose activated charcoal. Her condition improved, and she was discharged without evidence of permanent neurologic sequelae. This case illustrates that xenobiotic exposure should often be considered, even if historical clues are not present, as they can often present as other conditions leading to misdiagnosis and delayed treatment.

1. Introduction

Carbamazepine (CBZ), known by the brand name Tegretol, is an iminostilbene compound. It is used in the management of seizure disorders, trigeminal neuralgia, and psychiatric illness, such as bipolar disorder and pain syndromes [1, 2]. Because of its pharmacologic properties, carbamazepine has the potential to be life threatening in overdose.

Carbamazepine functions by inhibition of sodium channels and interference with glutamate metabolism. As a result of this, CBZ has cardiotoxic properties and has significant effects on the CNS. In the pediatric population, where accidental ingestion and inability to verbalize events can cloud clinical diagnosis, it is especially dangerous because of its lower threshold of toxicity [3]. We present here a case of a 20-month-old presenting with status epilepticus due to carbamazepine toxicity.

2. Case

A 20-month-old previously healthy female was brought into the emergency department because of acute onset of altered mental status. The mother had noted that the patient also had episodes of flexion and extension of her upper extremities. The patient was then observed in emergency department to have tonic clonic seizure activity, which was responsive to lorazepam.

The patient was febrile at 104.5° F and tachycardic at 160 bpm and had a blood pressure of 111/76 and breathing 25 breaths/minute with an oxygen saturation of 100% on RA. The patient was noted to be lethargic, with pupils that were 2 mm in size, sluggishly reactive, bilaterally. Neurologically, the patient was observed to have decreased tone, midline gaze, and no facial asymmetry. She was not responsive to noxious stimuli. Deep tendon reflexes were noted to be 3+ bilaterally in the upper and lower extremities. Patient initial blood work was notable for hypokalemia (2.6 meq/L), metabolic acidosis, and elevated lactate of 6 mmol/L. The patient continued to have focal seizures not controlled by lorazepam.

The patient was subsequently admitted to the pediatric intensive care unit (PICU). An extensive workup was undertaken. The patient was empirically treated for severe infection. Her workup was notable for negative blood
3. Discussion

This was a case of accidental poisoning with carbamazepine in a 20-month-old that resulted in status epilepticus that was initially misdiagnosed as complex febrile seizures. Unintentional/accidental nonfood poisoning in children <5 years old is best described by the term exploratory ingestion. This arises from the increased curiosity and sense of independence a child begins to gain as they grow older. There is usually an environmental component to increasing risk of ingestion, such as poor storage with easy access. Often, an underestimation of a child’s physical ability plays a large part in poor storage practices [4].

Ingestion of >10 mg/kg of CBZ generally results in supratherapeutic levels. In overdose, carbamazepine primarily affects the central nervous system. At lower serum levels, patients will initially present with nystagmus, mydriasis, and tachycardia. At higher levels, patients can develop myoclonus and hyperthermia, become significantly more lethargic, and develop seizures, with progression to coma and respiratory arrest [5,6]. Although the correlation between clinical symptoms and serum levels is poor, typical toxic serum concentrations are >20 mg/L, with cardiotoxicity more common at >40 mg/L, but in children, lower serum concentrations can result in serious toxicity [3, 5, 7].

Due to its structural similarity to tricyclic antidepressants, CBZ has significant cardiotoxic properties of sodium channel blockade and potassium channel blockade as well as anticholinergic effects. It can cause QRS widening and QTc prolongation as manifest on the EKG, predisposing to fatal dysrhythmias. Case reports note that QRS widening is often transient and may not result in clinical consequence [5, 7]. Cardiac monitoring is advised in patients presenting with severe toxicity.

Metabolism of CBZ mainly occurs by CYP3A4, creating the active metabolite carbamazepine-10,11-epoxide. This active metabolite has a longer half-life and is thought to contribute to toxicity. This fact potentially explains the lack of correlation between CBZ levels and clinical symptoms [8].

In chronic use, CBZ has been associated with bone marrow suppression, hepatitis, cardiomyopathy, renal disease, and increased risk for Stevens–Johnson syndrome [1, 5]. The adverse effects are more commonly reported in chronic use, with time of onset within 6 months of therapy [9]. In acute toxicity, patients present with central nervous system toxicity, cardiotoxicity, and anticholinergic effects.

Treatment of CBZ toxicity is mainly supportive. Airway and breathing should be addressed as required, including intubation if needed. Intravenous fluids and vasopressors should be given early in the setting of hypotension. Decontamination should be considered in the acute setting, and multidose activated charcoal is effective in preventing enterohepatic recirculation of CBZ. This can help reduce the elimination half-life, effectively speeding up the time it takes for a patient’s burden of CBZ to decrease. Therefore, it is often recommended if there are no contraindications [5, 10].

4. Conclusions

In children, accidental ingestion of xenobiotics should always be considered. In pediatric patients who present with new onset status epilepticus, a detailed history including medications available at home should be obtained. In young children, even in the absence of a history suggesting xenobiotic exposure, accidental poisoning should remain on the differential. Failure to do so can lead to misdiagnosis and delayed treatment. Carbamazepine overdose can result in potentially life-threatening toxicity, secondary to cardiotoxicity and CNS toxicity, which may masquerade as complex febrile seizures, as in the patient presented here. Early identification prompts rapid intervention and treatment and will lead to improved patient outcomes.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] R. S. Hoffman, L. S. Nelson, M. A. Howland, N. A. Lewin, L. R. Goldfrank, and S. W. Smith, “Antiepileptics,” in Goldfrank’s Toxicologic Emergencies, pp. 719–731, McGraw-Hill Education, New York, NY, USA, 11th edition, 2019.
[2] H. A. Nasrallah, T. A. Ketter, and A. H. Kalali, “Carbamazepine and valproate for the treatment of bipolar disorder: a review of the literature,” Journal of Affective Disorders, vol. 95, no. 1–3, pp. 69–78, 2006.
[3] M. Liftshitz, V. Gavrilov, and S. Sofer, “Signs and symptoms of carbamazepine overdose in young children,” Pediatric Emergency Care, vol. 16, no. 1, pp. 26–27, 2000.
[4] V. R. Lee, M. Connolly, and D. P. Calello, “Pediatric poisoning by ingestion: developmental overview and synopsis of national trends,” Pediatric Annals, vol. 46, no. 12, pp. e443–e448, 2017.
[5] K. R. Olson, Poisoning and Drug Overdose, pp. 178–181, McGraw Hill Education, New York, NY, USA, 2018.
[6] S. Schmidt and M. Schmitz-Buhl, “Signs and symptoms of carbamazepine overdose,” Journal of Neurology, vol. 242, no. 3, pp. 169–173, 1995.
[7] A. Perez and J. F. Wiley, “Pediatric carbamazepine suspension overdose-clinical manifestations and toxicokinetics,” Pediatric Emergency Care, vol. 21, no. 4, pp. 252–254, 2005.
[8] R. I. Winnicki, B. Lopancinski, W. M. Szymczak, and B. Szymańska, “Carbamazepine poisoning: elimination kinetics and quantitative relationship with carbamazepine...
10,11-epoxide,” *Journal of Toxicology: Clinical Toxicology*, vol. 40, no. 6, pp. 759–765, 2002.

[9] S. Ganesh, L. Shukla, A. Kandasamy, and V. Benegal, “A case of carbamazepine-induced severe cholestatic hepatitis: case report and review of literature,” *Indian Journal of Psychological Medicine*, vol. 39, no. 5, pp. 688–690, 2017.

[10] AAMT and EAPCCT, “Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning,” *Journal of Toxicology: Clinical Toxicology*, vol. 37, no. 6, pp. 731–751, 1999.