CASE REPORT

Severe carbamazepine-induced cardiotoxicity with multisystem involvement: early recognition and advanced therapeutic approach

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ABSTRACT

Carbamazepine (CBZ) toxicity is a medical emergency due to severe neurological and cardiovascular risks. Management is challenging due to CBZ's prolonged elimination, enterohepatic recirculation, and active metabolites. We report a severe CBZ intoxication in a 23-year-old male who ingested 24 g in a suicide attempt. He presented in profound coma (Glasgow Coma Scale 3) with respiratory failure, requiring orotracheal intubation and mechanical ventilation. ECG showed sinus tachycardia and slightly widened QRS complexes. Echocardiography revealed myocardial depression with a left ventricular ejection fraction of 40%. His CBZ plasma level was critically high (44 mcg/mL). Treatment included multiple-dose activated charcoal, intravenous lipid emulsion, and continuous venovenous hemodiafiltration, leading to rapid CBZ clearance, cardiotoxicity reversal, and neurological recovery. He was extubated on day three and discharged in stable condition. This case highlights severe CBZ-induced cardiotoxicity and emphasizes early recognition and advanced therapies for improved outcomes.

KEYWORDS: Carbamazepine toxicity; cardiotoxicity; hemodiafiltration; lipid emulsion therapy

INTRODUCTION

Carbamazepine (CBZ) is a first-line anticonvulsant for epilepsy, also used for neuropathic pain and psychiatric disorders [1,2]. It blocks presynaptic voltage-gated sodium channels in the CNS, reducing neurotransmitter release, particularly glutamate [3,4]. However, its narrow therapeutic index makes overdoses, often intentional, highly toxic [5].

CBZ undergoes hepatic metabolism via cytochrome P450, producing active metabolites like carbamazepine-10,11-epoxide. Its lipophilicity, enterohepatic recirculation, and prolonged elimination complicate management [6,7]. Toxicity occurs at plasma levels above 12 mcg/mL, with severe cases exceeding 30 mcg/mL [8]. The active metabolite further increases toxicity [1,9].

CBZ poisoning is a medical emergency, affecting the CNS, cardiovascular, and respiratory systems. Symptoms range from dizziness and ataxia to seizures, arrhythmias, and cardiac arrest. Respiratory depression and aspiration risk further complicate treatment [1,10,11].

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Management is challenging, especially with extended-release (ER) formulations. Supportive care includes airway protection, seizure control, and cardiovascular stabilization, as no antidote exists [9,12]. Activated charcoal reduces absorption, with multiple doses proving more effective [13]. In severe cases, hemodialysis (HD) or hemodiafiltration (HDF) enhances CBZ clearance [8]. Intravenous lipid emulsion therapy (ILE) is a promising adjunct due to its ability to sequester lipophilic drugs [14].

This article presents a severe CBZ intoxication case, highlighting acute toxic effects and cardiotoxicity, and the role of advanced therapies like lipid emulsion and extracorporeal treatments.

CASE PRESENTATION

A 23-year-old male was admitted to the Emergency Department (ED) in a comatose state after ingesting approximately 80 ER CBZ 300 mg tablets, taken from his grandparents. The ingestion occurred 2–3 hours prior, in a suicide attempt linked to reactive depression after a breakup. His family also reported a recent, unreported morphine ingestion attempt.

On arrival, he was in profound coma (Glasgow Coma Scale 3), requiring orotracheal intubation and mechanical

ventilation. His vitals showed a blood pressure of 138/80 mmHg and heart rate 120 bpm. Physical examination revealed bilateral periorbital edema, left-sided ecchymosis, facial abrasions, and self-inflicted thigh injuries, without significant chest or abdominal trauma.

ECG showed sinus tachycardia, tall positive T waves in anterior leads and slightly widened QRS complexes. High-voltage QRS complexes were noted in inferior and precordial leads (Figure 1). Activated charcoal (1 g/kg) was administered via a nasogastric tube, followed by continuous doses every four hours for 12 hours. Laboratory results indicated leukocytosis, elevated muscle enzymes Creatine Kinase (CK) (5,477 IU/L), CK-MB (162 IU/L), and high-sensitivity cardiac troponin I (189 ng/L). Urine toxicology was positive for tricyclic antidepressants (TCAs). ILE therapy was given as a bolus, followed by continuous infusion for one hour.

A cranio-cerebral CT scan showed right temporo-parietal cerebral edema, a right fronto-parieto-temporal epicranial hematoma (12 mm), and a left palpebral hematoma, without skull fractures (Figure 2). Neurosurgical evaluation recommended anti-edematous treatment and monitoring. Ophthalmologic examination was normal.

Due to ECG changes and elevated cardiac biomarkers, cardiology consultation was recommended. Echocardiography showed interventricular septal hypokinesia and a reduced left ventricular ejection fraction (LVEF) of 40%, consistent with CBZ cardiotoxicity. Rhabdomyolysis was confirmed due to elevated CK levels, likely caused by seizures and a traumatic fall.

Three hours after admission, the patient was transferred to the Toxicology ICU. CBZ serum levels were critically high (44.03 mcg/mL; therapeutic range: 4–12 mcg/mL). The active metabolite, CBZ-10,11-epoxide, was detected.

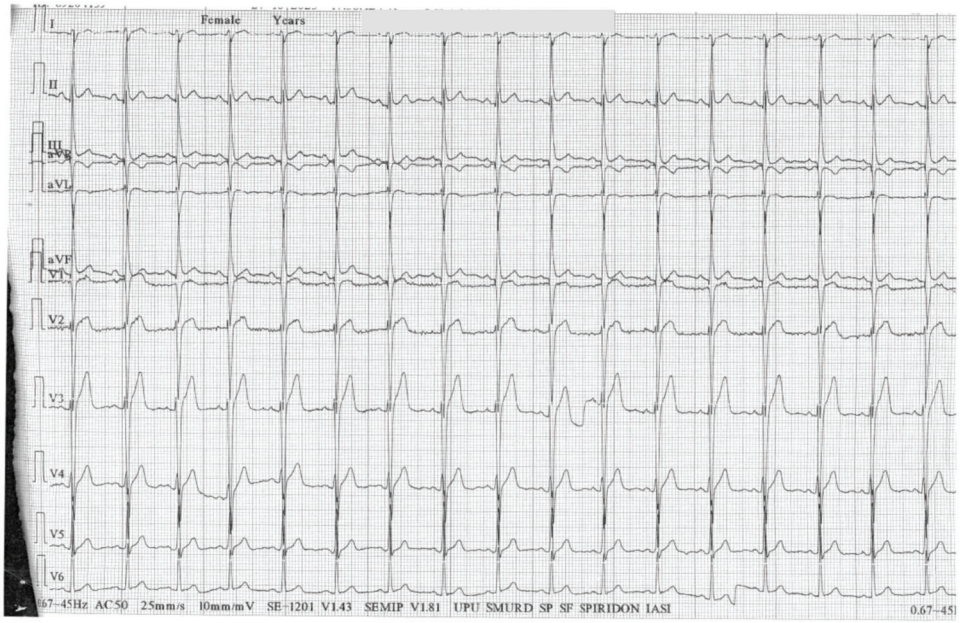

Fig. 1. Initial ECG: sinus tachycardia, slightly widened QRS complexes (0.10 sec); high-voltage QRS complexes in inferior (II, III, aVF) and precordial leads.

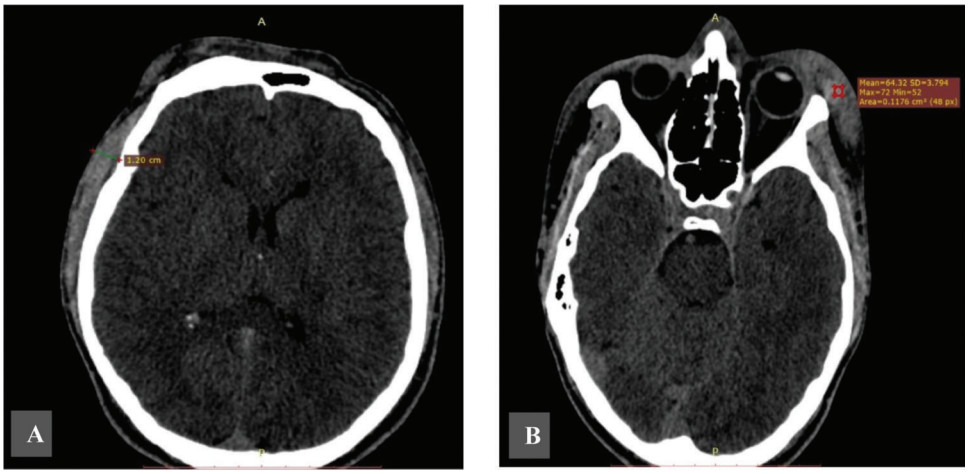

Fig. 2. Cranio-cerebral CT scan: right fronto-parieto-temporal epicranial hematoma (12 mm thickness) (A); left palpebral hematoma (B).

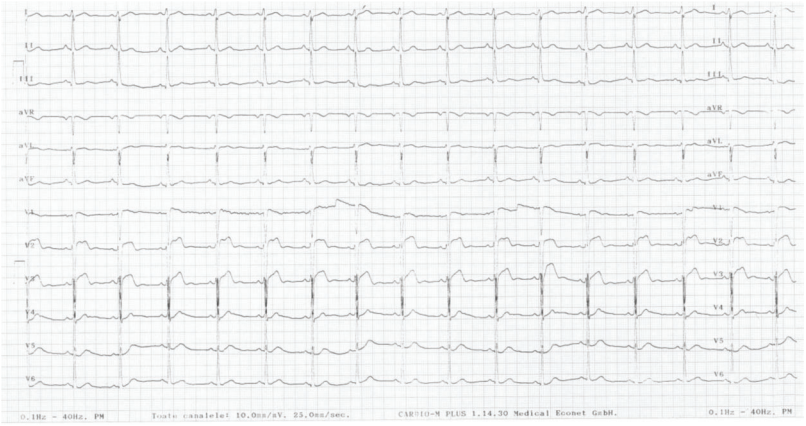

Fig. 3. ECG after specific treatments: sinus rhythm 75 beats/min; normalization of QRS complexes and T waves.

Continuous venovenous hemodiafiltration (CVVHDF) was initiated, alongside intravenous hydration, mannitol, and furosemide for cerebral edema. After 36 hours of CVVHDF, CBZ levels dropped to 8.5 mcg/mL, ECG normalized (Figure 3), and myocardial function recovered.

On day three, he was extubated and transferred to the Internal Medicine Toxicology Unit. Follow-up CT showed reduced cerebral edema and hematomas. After six days, he was discharged in a significantly improved condition.

DISCUSSION

Acute CBZ poisoning primarily presents with neurological manifestations, but severe cases can cause significant cardiovascular toxicity [6,8]. This case report describes a young patient who developed life-threatening CBZ toxicity, emphasizing the importance of early diagnosis and advanced therapeutic interventions. CBZ toxicity usually manifests within 1–3 hours post-ingestion, though plasma levels fluctuate due to enterohepatic recirculation, gradual dissolution of ER tablets, and CBZ-induced bowel hypomotility induced by its anticholinergic effects [2]. Our patient was found in a profound coma (GCS 3) approximately 2–3 hours after ingestion.

The patient exhibited significant cardiac abnormalities, including sinus tachycardia, widened QRS complexes, and LV hypokinesia, despite no preexisting cardiac pathology. The severity of intoxication correlates with CBZ plasma concentration, with mild form occurring above 10 mcg/ml, moderate form above 20 mcg/ml, and severe form above 30 mcg/ml [8]. The patient's plasma CBZ level was 44 mcg/mL, indicating severe toxicity. The presence of CBZ-10,11-epoxide further increased toxicity risk [1]. Cardiac dysfunction required differentiation from acute coronary syndromes and toxic myocarditis. However, the patient's young age, absence of prior cardiac disease, ECG aspect and rapid cardiac function normalization following CBZ elimination excluded these conditions. CBZ-induced LV dysfunction is complex, involving direct myocardial toxicity. Structurally similar to TCAs, CBZ can impair phase 2 depolarization, leading to widespread ventricular depression and a higher risk of reduced contractility [6,9]. In our patient, septal LV hypokinesia was a particular finding requiring differentiation from other causes, as discussed above.

Although uncommon, CBZ cardiotoxicity is clinically significant. A cohort study of 427 CBZ-intoxicated patients reported a 13% mortality rate, with lethal cases averaging a CBZ intake of 23.6 g [14]. Our patient ingested 24 g, highlighting the risks of his overdose.

Cranio-cerebral imaging performed due to coma and facial trauma revealed right temporo-parietal cerebral edema and epicranial hematomas, likely due to a traumatic fall. Rhabdomyolysis was attributed to seizures induced by CBZ toxicity and muscle trauma. An additional noteworthy finding was a positive urine toxicology screen for TCAs. Though CBZ is not a TCA, its tricyclic structure [1,8] may cause cross-reactivity in toxicology assays, necessitating careful clinical interpretation.

The therapeutic approach included airway protection, supportive care, and enhanced CBZ elimination. Multiple-dose activated charcoal was administered, according to specific guidelines, to reduce gastrointestinal absorption and interrupt enterohepatic recirculation, improving outcomes in severe CBZ intoxication [1,9]. ILE therapy was used as an adjunctive treatment, it creates a "lipid sink," sequestering lipophilic drugs and reducing systemic toxicity [1,15]. While primarily used in lipophilic drug overdoses like beta-blockers and calcium channel blockers, ILE has limited reported use in CBZ toxicity [1,15]. However, its potential to improve cardiac function has been suggested [16,17], which may have contributed to our patient's improvement.

Given the critical CBZ plasma level and severity of toxicity, CVVHDF was initiated, reducing serum CBZ concentration from 44 mcg/mL to 8.5 mcg/mL over 36 hours. HDF is superior to standard HD for CBZ elimination, due to its combined diffusion and convection mechanisms, effectively clearing CBZ and its active metabolite, CBZ-10,11-epoxide [1,8,18]. CBZ's high lipophilicity and protein binding (70–80%) render standard HD inefficient, whereas HDF enables faster and more complete clearance. Additionally, CBZ's enterohepatic recirculation prolongs its toxicity, whereas HDF accelerates elimination, facilitating faster recovery. Therefore, in severe CBZ poisoning with high plasma levels, HDF is preferred over HD [1,4].

The patient showed significant improvement following CVVHDF and ILE therapy. He was extubated on day three and discharged in stable condition. However, due to the intentional nature of the overdose, psychiatric evaluation and long-term psychological support were recommended.

CONCLUSION

This case highlights severe CBZ-induced cardiotoxicity in a young patient without previous heart disease, demonstrating significant myocardial depression and conduction abnormalities. The successful use of CVVHDF and ILE underscores their efficacy in severe CBZ poisoning. Early recognition and timely extracorporeal elimination are crucial for improving outcomes in life-threatening intoxications.

Conflicts of interest

The authors declare that they have no competing interests.

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Nothing to declare.

Informed consent

Written informed consent was obtained from the patient, whom the authors thank for permission to publish this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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