UNILATERAL FOOT DROP FOLLOWING ACUTE CARBAMAZEPINE OVERDOSE: A CASE REPORT.

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ABSTRACT

Introduction: Carbamazepine is a commonly prescribed anticonvulsant and mood-stabilizing drug. While its toxicity profile is well-documented, rare complications are infrequently reported. This case report aims to highlight an unusual presentation of acute carbamazepine toxicity leading to foot drop. **Case presentation:** A 25-year-old female with a history of depression presented to the emergency department with confusion, ataxia, and generalized weakness after an intentional overdose of 40 grams of carbamazepine. Initial serum carbamazepine levels were significantly elevated at 70 mcg/mL (therapeutic range: 4-12 mcg/mL). Despite supportive care and administration of activated charcoal, the patient developed an acute unilateral foot drop on the seventh day of hospitalization. Neurological examination revealed decreased dorsiflexion strength and sensory deficits in the L4-L5 dermatomes. Electromyography confirmed peripheral neuropathy consistent with carbamazepine-induced neurotoxicity. **Conclusion:** This case underscores the importance of vigilance for atypical neurological complications in patients with carbamazepine toxicity. Clinicians should consider carbamazepine-induced peripheral neuropathy in the differential diagnosis of acute foot drop, particularly in the context of overdose.

Keywords: Acute poisoning; foot drop; Antidote; Carbamazepine toxicity; Peripheral neuropathy.

INTRODUCTION

Carbamazepine is a widely used anticonvulsant and mood-stabilizing drug, frequently prescribed for the management of epilepsy, bipolar disorder, and neuropathic pain **(Weihrich, 2021)**. While the therapeutic efficacy of carbamazepine is well-established, its overdose can result in a range of toxic effects, primarily involving the central nervous system and cardiovascular system. Common manifestations of carbamazepine toxicity include dizziness, ataxia, nystagmus, altered mental status, and in severe cases, seizures, and cardiac arrhythmias **(Dart, 2004).**

Peripheral neuropathy, and more specifically, foot drop, is a rare and underreported complication associated with carbamazepine toxicity. Foot drop is characterized by the weakness or paralysis of the muscles involved in lifting the front part of the foot, leading to difficulty in walking and an increased risk of falls. The underlying mechanisms of carbamazepine-induced foot drop are not well understood, but it is hypothesized to involve neurotoxic effects on the peripheral nerves **(Nori and Stretanski, 2024).**

In this report, we present a patient who developed an acute unilateral foot drop following an intentional overdose of carbamazepine. The case aims to highlight the importance of considering peripheral neuropathy as a potential complication in patients presenting with carbamazepine toxicity and to discuss the clinical approach to such presentations.

CASE REPORT

A 25-year-old married woman was discovered unconscious in her room, with empty carbamazepine blister packs nearby. When her family discovered this, they immediately brought her to the Poison Control Center at Alexandria Main University Hospital, Egypt, approximately eight hours post-ingestion. The family suspected a suicide attempt involving approximately 10 strips of carbamazepine (400mg), which had been recently prescribed to her. Upon obtaining a history from her family, it was revealed that the patient had been healthy until six months prior

when she began experiencing symptoms of depression. She had no other significant medical or surgical history.

Upon arrival at the emergency room, eight hours post-ingestion, the patient was deeply unconscious with a Glasgow Coma Scale (GCS) score of 5 (Eye-opening 1, Flexion response to pain 3, No sounds 1). Her pupils were dilated and sluggishly reactive to light bilaterally. Vital signs included blood pressure of 90/60 mmHg, heart rate of 120 bpm, respiratory rate of 12 breaths/min, and temperature of 37°C. Chest examination revealed diminished air entry bilaterally with crepitations. Arterial blood gas (ABG) analysis showed pH 7.30, PCO2 45 mmHg, PaO2 60 mmHg, HCO3 16 mEq/L, and O2 saturation 80%.

Electrocardiogram (ECG) revealed sinus tachycardia at a rate of 120 bpm, PR interval of 0.12 seconds, QRS duration of 0.08 seconds, normal ST, and flat T waves **Fig. 1**.

The patient experienced tonic-clonic seizures in the resuscitation room and was treated with diazepam (10 mg). She was then intubated, and a nasogastric tube was inserted to administer multiple doses of activated charcoal (MDAC) (50 grams). Continuous cardiac monitoring and crystalloid hydration (500 cc) were initiated before transferring her to the intensive care unit (ICU) on mechanical ventilation.

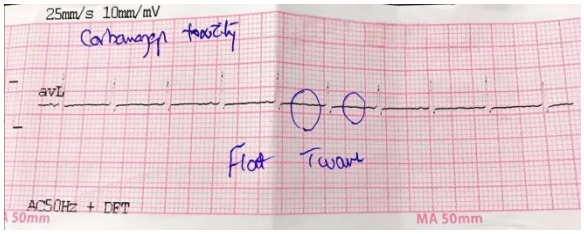

Figure (1): ECG showing flat T wave

In the ICU, her pulse rate was 125 bpm, and her blood pressure was 110/80 mmHg. Follow-up ABG showed pH 7.59, PaO2 126 mmHg, PCO2 19 mmHg, HCO3 18 mEq/L, and O2 saturation 99.7%. Initial laboratory workup, as shown in **Table (1)**, included a total serum carbamazepine concentration of 70 ng/mL, that confirmed acute carbamazepine toxicity. The sodium level was 140 mmol/L. Chest X-ray revealed bilateral consolidations **Fig. 2**.

On the second day, the patient developed severe respiratory distress, with a respiratory rate of 40 breaths/min and noticeable intercostal and subcostal retractions. Acute respiratory distress syndrome (ARDS) was diagnosed based on clinical and radiographic findings. Management included mechanical ventilation adjusted to low tidal volume to minimize lung injury, sedation with propofol and midazolam, and paralysis with atracurium to optimize ventilation and reduce oxygen consumption. A conservative fluid strategy was employed to prevent fluid overload and reduce pulmonary oedema, while empirical antibiotics were initiated with meropenem and amikacin to manage suspected secondary infections. Later, teicoplanin was added to cover potentially resistant organisms. Additionally, prophylactic anticoagulation with heparin was administered to prevent thromboembolic events due to prolonged immobility. On the third day of admission, the patient was found to be hypokalemic with a potassium level of 2.5 mmol/L and received 5 ampoules of potassium supplementation, the sodium level was 136 mmol/l. Additionally, liver enzymes began to rise. On the fifth day post-admission, the sodium level was 138 mmol/l and on the seventh day post-admission, the patient's consciousness began to improve as sedation was reduced, and her chest condition also started to improve.

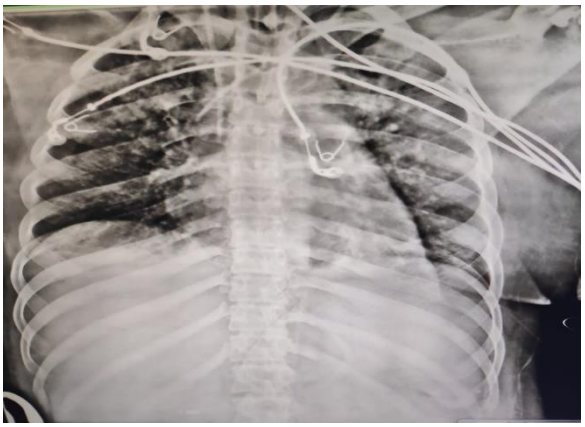

Figure (2): Chest X-ray revealed bilateral consolidations

Table (1): Laboratory workup of the patient at the ICU.

Laboratory Investigation	Day 1	Day 3	Day 5	Day 10	Reference range
Random Blood Sugar	170 mg/dl	140 mg/dl	145 mg/dl	135mg/dl	110-140 mg/dl
Arterial Blood Gases	pH:7.30 PaCO2:45 PaO2:50 HCO3:16 SO2:80%	pH:7.59 PaCO2:19 PaO2:126 HCO3:18 SO2:99.7%	pH:7.40 PaCO2:35 PaO2:90 HCO3:22 SO2:95%	pH:7.38 PaCO2:40 PaO2:95 HCO3:24 SO2:98%	pH=7.35-7.45 PCO2=35-45 mmHg PaO2=70-100 mmHg HCO3=22-26 S02= >95%
Haemoglobin	11.7 g/dl	10.1 g/dl	10 g/dl	9.3 g/dl	11-14 g/dl
Total leukocyte count	7.8 cell $x10^3/mm^3$	20.43 cell $x10^3/mm^3$	16 cell$x10^3/mm^3$	12.11 cell $x10^3/mm^3$	5000-15000 cell $x10^3/mm^3$
platelets	342 cell $x10^3/mm^3$	227 Cell$x10^3/mm^3$	252 cell$x10^3/mm^3$	392 cell $x10^3/mm^3$	150,000–450,000 cell $x10^3/mm^3$
Serum Sodium	140 mmol/l	136 mmol/l	138 mmol/l	140 mmol/l	136–145 mmol/L
Serum Potassium	4.2 mmol/l	2.5 mmol/l	3.3 mmol/l	4.1 mmol/l	3.5-5.1 mmol/l
Alanine transaminase (ALT)	34 U/l	194 U/l	286 U/l	48 U/l	10-49 U/L
Aspartate transaminase (AST)	39 U/l	99 U/l	328 U/l	36 U/l	15-37 U/L
Serum Urea	19 mg/dl	19 mg/dl	20 mg/dl	20 mg/dl	19–42 mg/dl
Serum Creatinine	0.6 mg/dl	0.6 mg/dl	0.5 mg/dl	0.5 mg/dl	0.55–1.1 mg/dl
Serum Carbamazepine concentration	70 mcg/ml	-	-	-	4-12 mcg/ml

On the other hand, despite supportive care, she developed acute unilateral foot drop. Neurological examination showed decreased dorsiflexion strength and sensory deficits in the L4-L5 dermatomes **Fig. 3**. Electromyography confirmed peripheral neuropathy consistent with carbamazepine-induced neurotoxicity.

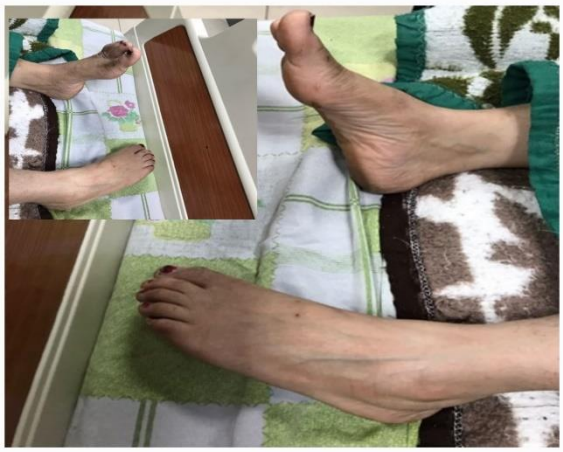

Figure (3): Unilateral foot drop

The patient was weaned from mechanical ventilation after 10 days when her GCS was 14 (Eye-opening 4, Obey commands 6,

Disoriented 3) and a sodium level of 140 mmol/l. Due to elevated liver enzymes, consultation with a hepatologist was done and drug-induced liver injury was diagnosed. Liver support measures were given in the form of acetylcysteine and silymarin. Follow-up liver enzyme levels showed gradual improvement **(Table 1)**

The patient was discharged after 20 days of hospitalization including 11 days in the ICU and 9 days in the Poison Control Center. While she overall recovered well, the unilateral foot drop persisted as a neurological sequela.

DISCUSSION

Carbamazepine is a prevalent antiepileptic drug, also prescribed for conditions such as bipolar disorder and neuropathic pain. While effective within therapeutic ranges, carbamazepine overdose can lead to significant morbidity **(Behnoush et al., 2009)**. This case report shows a rare and serious complication of carbamazepine toxicity: acute unilateral foot drop, which underscores the broad spectrum of potential toxic effects of this drug.

Pathophysiology and Clinical Presentation.

The neurotoxic effects of carbamazepine are primarily due to its action on sodium channels, which can disrupt normal neuronal function and lead to various central and peripheral neurological symptoms in therapeutic doses, carbamazepine stabilizes hyperexcited nerve membranes, inhibits repetitive neuronal firing, and reduces synaptic propagation of excitatory impulses **(Catterall, 2014)**. However, in overdose, these stabilizing effects are exaggerated, resulting in central nervous system depression, seizures, and in this case, peripheral neuropathy **(Isik et al., 2013)**

Upon presentation, the patient exhibited signs of severe CNS depression, evidenced by a GCS of five, along with autonomic instability and respiratory distress. These symptoms are typical in carbamazepine overdose and necessitate prompt and aggressive management. The initial management included stabilization of vital signs, seizure control, and decontamination with activated charcoal, the standard protocols in such cases **(Spiller, 2001)**. Nasogastric lavage was not indicated for this patient as she presented eight hours post-ingestion. Gastric lavage is generally most effective provided it is performed within one to two hours of ingestion **(Benson et al., 2013).** Additionally, the patient was hemodynamically unstable, exhibiting hypotension and ARDS, which contraindicated extracorporeal treatments like hemodialysis. Hemodialysis is typically considered when the patient is stable enough to tolerate the procedure, which was not the case here **(Trainor et al., 2011).**

Peripheral Neuropathy and Foot Drop

The development of acute unilateral foot drop is an unusual complication of carbamazepine overdose. Carbamazepine toxicity can lead to foot drop through several mechanisms. Firstly, carbamazepine is known to cause peripheral neuropathy through direct toxic effects on peripheral nerves, which can result in motor deficits such as foot drop, additionally, carbamazepine's neurotoxic effects, primarily through its action on sodium channels, can disrupt normal neuronal function, stabilizing hyperexcited nerve membranes at therapeutic doses but causing exaggerated central nervous system depression and peripheral neuropathy in overdose cases (**Catterall, 2014; Isik et al., 2013**). Secondly, high doses of carbamazepine can lead to central nervous system depression, potentially affecting the motor neurons controlling the lower extremities. Finally, metabolic disturbances induced by carbamazepine toxicity, such as vitamin B_{12} deficiency, can also contribute to neurological deficits, including foot drop. It may also involve mitochondrial dysfunction, oxidative stress, or direct membrane destabilization **(Jayakumar and Mathaiyan, 2019)**. The exact mechanism by which carbamazepine induces peripheral neuropathy remains unclear, **(Green and Holton, 2016).**

In this patient, the diagnosis was confirmed through clinical examination and electromyography, which indicated peripheral neuropathy consistent with carbamazepine neurotoxicity. The persistent nature of the foot drop despite the overall recovery suggests potentially irreversible damage to the affected peripheral nerves.

Management and Outcomes

The management of this case followed the established protocols for carbamazepine toxicity, including respiratory support, seizure control with benzodiazepines, and gastrointestinal decontamination **(Al Khalili et al., 2023).** The patient's prolonged ICU stay and the need for mechanical ventilation underline the severity of her condition. The subsequent development of ARDS and secondary infections are common complications in severe

poisonings, requiring comprehensive ICU care **(Olson et al., 2022).**

Empirical antibiotic therapy was initiated to manage suspected secondary infections, which is a critical step in preventing further complications. Sedation and neuromuscular blockade were necessary to manage the patient's respiratory distress and facilitate mechanical ventilation. Prophylactic anticoagulation was also administered to prevent thromboembolic events, a common concern in critically ill, immobilized patients **(Hyzy, 2020).**

Neurological and Hepatic Considerations

The improvement in the patient's consciousness level and respiratory function over time was encouraging; however, the persistent foot drop presents a significant morbidity. Similar neurological sequelae necessitate ongoing rehabilitation and may require interventions such as physiotherapy, orthotic devices, and in some cases, surgical consultation **(Waseem et al., 2023)**.

The elevated liver enzymes observed during treatment were managed conservatively. Drug-induced liver injury, while reversible in this case, highlights the importance of regular monitoring and supportive care in managing the multi-system effects of carbamazepine toxicity **(Au and Pockros, 2013).**

CONCLUSION

This case underscores the complexity and potential severity of carbamazepine overdose, particularly concerning its neurotoxic effects. Acute foot drop as a manifestation of peripheral neuropathy in the context of carbamazepine toxicity is rare but significant, emphasizing the need for thorough neurological assessment and long-term follow-up in affected patients. Early recognition, aggressive supportive care, and interdisciplinary management are essential to improving outcomes in severe cases of carbamazepine poisoning.

Continued vigilance and research into the mechanisms and management of carbamazepine-induced neurotoxicity are warranted to understand better and mitigate these rare but serious complications.

Ethical approval and patient consent: The study was conducted in accordance with the World Medical Association Declaration of Helsinki, after approval of the Ethics Committee of the Faculty of Medicine, Alexandria University (IRB number: 00012098, approval serial number: 0201577). Written informed consent was obtained from the patient, including consent for publication and photography, ensuring respect for participants' rights and privacy.

Conflicts of interest: The author declares that there are NO conflicts of interest.

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الملخص العربي

هبوط ظاهر القدم نتيجة للتسمم الحاد من جرعة كاربامازيبين زائدة: تقرير حالة

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خلفية البحث: الكاربامازيبين هو دواء شائع الوصف كمضاد للتشنج ومثبت للمزاج. في حين أن ملف السمية الخاص به موثق، إلا أنه نادرًا ما يتم الإبلاغ عن مضاعفات نادرة. يهدف تقرير هذه الحالة إلى تسليط الضوء على عرض غير معتاد لسمية الكاربامازيبين الحادة ألا وهو هبوط القدم.

عرض الحالة: قدمت أنثى تبلغ من العمر 25 عامًا ولديها تاريخ من الاكتئاب إلى قسم الطوارئ في حالة من الارتباك والترنح والضعف العام بعد أن تناولت متعمدةً جرعة زائدة (40 جرامًا) من الكاربامازيبين. ارتفعت المستويات الأولية للكاربامازيبين في الدم بشكل ملحوظ إلى 70 ميكروغرام/مل (الجرعة الدوائية: 4-12 ميكروغرام/مل). وعلى الرغم من تقديم الرعاية الداعمة وإعطاء الفحم المنشط، أصيبت المريضة بهبوط مفاجئ في ظاهر القدم في اليوم السابع من دخولها المستشفى. أسفر كشف الفحص العصبي عن انخفاض قوة الانثناء الظهري وعجز حسي في المناطق الجلدية التي تغذيها الأعصاب المرتبطة بالفقرتين القطنيتين الرابعة والخامسة. أكد التصوير الكهربائي اعتلال الأعصاب المحيطي بما يتفق مع السمية العصبية التي يسببها الكاربامازيبين.

الاستنتاج: تؤكد هذه الحالة على أهمية الانتباه للمضاعفات العصبية غير النمطية لدى المرضى الذين يعانون من سمية الكاربامازيبين. يجب على الأطباء التفكير في الاعتلال العصبي الطرفي الناجم عن الكاربامازيبين في تشخيص هبوط القدم الحاد، لا سيما في سياق الجرعة الزائدة.