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CASE REPORT
Coronary intervention

A case report describing myocardial ischaemia as a side effect of carbamazepine overdose

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Background Overdoses of carbamazepine may occur due to various reasons. The summary of product characteristics of carbamazepine includes information about the possibility of side effects after taking this drug. However, the symptoms described do not include coronary vasospasm, which occurred in the case described. Making such a diagnosis is a key element in therapeutic management, as it changes further clinical decisions.

Case summary A 46-year-old patient was admitted to the hospital for disorders of consciousness following an overdose of carbamazepine. On the second day, the patient exhibited respiratory distress. Subsequently, the patient was transferred to the intensive care unit, intubated, and placed on mechanical ventilation. On the same day, the patient experienced recurrent cardiac arrhythmias in the form of pulseless ventricular tachycardia and ventricular fibrillation; the patient was resuscitated and defibrillated eight times. Due to a rapid decline in cardiac output coupled with persistent electrocardiographic changes and haemodynamic instability, the patient underwent urgent coronary angiography. The procedure revealed a spasm in the initial segment of the circumflex branch of the left coronary artery, which subsequently resolved following nitroglycerin administration. Subsequent to the implementation of this therapeutic approach, a reduction in the demand for norepinephrine and dobutamine was achieved. In the following days, the patient's general condition improved. The patient was discharged home while maintaining full cognitive capacity and cardiovascular and respiratory fitness.

Discussion In the case described, the expeditious performance of a cardiological diagnostic evaluation played a pivotal role in achieving therapeutic success, enabling the prompt initiation of appropriate treatment.

Keywords Coronary artery spasm • Carbamazepine • Intoxication • Arrhythmia • Case report

ESC curriculum 3.4 Coronary angiography • 7.2 Post-cardiac arrest • 7.1 Haemodynamic instability

Learning points

- Carbamazepine overdose may cause coronary artery spasm and myocardial ischaemia.
- This case report highlights the importance of an interdisciplinary approach to the diagnosis and treatment of acute poisoning.

Introduction

Carbamazepine is widely used in both neurology and psychiatry. It is employed in the management of various medical conditions, including acute manic episodes, epilepsy, trigeminal neuralgia, bipolar affective disorder, and schizophrenia.[1] Therapeutic carbamazepine concentrations typically fall within the range of 4–12 mg/dL, while toxic symptoms typically occur at concentrations exceeding 40 mg/dL and can

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affect multiple organs.[2,3] Overdoses of carbamazepine may occur due to various reasons, including intentional ingestion as a suicide attempt, accidental consumption exceeding the recommended dosage, and misuse for its euphoric effects.[4] Carbamazepine shows a substantial volume of distribution and is predominantly bound to plasma proteins.[4] Carbamazepine's cardiotoxicity has been demonstrated both *in vitro* and in clinical practice.[3,5] The official product information for carbamazepine includes warnings regarding the possibility of cardiac conduction disturbances and exacerbation of coronary artery disease, among other potential adverse effects.[3]

Summary figure

Time	Events
On the day of a toxic dose of carbamazepine	The patient was circulatory and respiratory stable. The physical examination revealed no significant abnormalities; vesicular breath sounds were present, and the heartbeat was regular with clear heart tones. Disorders of consciousness occurred.
	Symptomatic management, gastric lavage, and activated charcoal administration were applied.
Day 2	Respiratory failure occurred: shallow, accelerated breathing, and a drop in oxygen saturation to 90%, despite the use of passive oxygen therapy.
	Transfer of the patient to the intensive care unit, intubation, and mechanical ventilation were applied.
	Recurrent cardiac arrhythmias occurred in the form of pulseless ventricular tachycardia and ventricular fibrillation; the patient was resuscitated and defibrillated eight times.
	The patient underwent urgent coronary angiography.
	Nitroglycerin infusion was included in the treatment. A reduction in the demand for norepinephrine and dobutamine was achieved.
Day 5	Infusion of catecholamines was excluded.
Day 7	Extubation of the patient.
	Patient in full logical communication
Day 12	End of hospitalization

Case presentation

A 46-year-old patient was admitted to the hospital due to altered consciousness following a suicide attempt by ingesting several dozen carbamazepine tablets, each containing 200 mg. The patient had no history of chronic illness and was professionally active, working in manual labour. Symptoms began 2 h before hospitalization and gradually worsened, with the patient becoming increasingly confused. Approximately 4 h after admission, logical communication was no longer possible. Toxicological examination confirmed carbamazepine intoxication (*Table 1*). Initially, the patient was circulatory and respiratory stable (blood pressure 138/95 mmHg, heart rate 95/min, and oxygen saturation 96–98%). The physical examination revealed no significant abnormalities; vesicular breath sounds were present, and the heartbeat was regular with clear heart tones.

Initial treatment on the first day of hospitalization consisted of symptomatic management, gastric lavage, and activated charcoal administration, although the patient's condition did not improve. On the second day, the patient exhibited respiratory distress characterized by shallow, accelerated breathing and a drop in oxygen saturation to 90%, despite receiving passive oxygen therapy. Subsequently, the patient was transferred to the intensive care unit, intubated, and placed on mechanical ventilation. On the same day, the patient experienced recurrent cardiac arrhythmias in the form of pulseless ventricular tachycardia and ventricular fibrillation; the patient was resuscitated and defibrillated eight times (*Figures 1* and *2*). Laboratory tests ruled out electrolyte disturbances as the cause of the heart rhythm abnormalities and cardiac arrest.

Laboratory assessments indicated significantly elevated troponin levels but normal creatine kinase concentrations (*Table 1*). Due to a rapid decline in cardiac output as observed through haemodynamic monitoring and confirmed by bedside echocardiography, coupled with persistent electrocardiographic changes and haemodynamic instability, the patient underwent urgent coronary angiography. The procedure ruled out the presence of parietal changes in the coronary vessels, but it revealed a spasm in the initial segment of the circumflex branch of the left coronary artery (Cx), which subsequently resolved following nitroglycerin administration. Nitroglycerin infusion was included in the treatment, despite high doses of catecholamines. Subsequent to the implementation of this therapeutic approach, a reduction in the demand for norepinephrine and dobutamine was achieved. Life-threatening cardiac rhythm disturbances were no longer observed in the electrocardiographic recordings (*Figure 3*). On the fifth day of hospitalization, the patient no longer required the administration of catecholamines. On the seventh day, the patient was extubated. Following a comprehensive diagnostic assessment and psychiatric consultation, the patient was discharged home on the 12th day while maintaining full cognitive capacity and cardiovascular and respiratory fitness, with a recommendation for continued treatment in an outpatient setting. The patient was scheduled for further planned cardiological diagnostics but did not attend the appointment. In the described case, the most likely cause of the arrhythmia was isolated coronary artery spasm, since after pharmacological coronary vasodilation, the arrhythmia resolved and cardiac systolic function improved (*Table 2*).

Discussion

The summary of product characteristics of carbamazepine includes information about the possibility of side effects after taking this drug. The most common symptoms of overdose include dizziness, drowsiness, ataxia, nausea, fluid retention, weight gain, skin changes, and fatigue.

Among those that may occur in the cardiovascular system are cardiac arrhythmias, bradycardia, arrhythmia, atrioventricular block, congestive heart failure, or, eventually, increased symptoms of coronary artery disease. However, the symptoms described do not strictly include coronary vasospasm, which occurred in the case described. Making such a diagnosis is a key element in therapeutic management, as it changes

Table 1 The values of the measured parameters on each day of hospitalization

Day of hospitalization	1	2	3	4	5	6	7	8	9
Carbamazepine[a], mg/L	69.9	30.8		27.4	22.5	10.7	10.7		
Troponin[b], ng/L	1015	304					25.9		
Creatine kinase[c], mg/dL	108	172			131				54

[a]Norm: <12.
[b]Norm:0–0.5.
[c]Norm: 39–308.

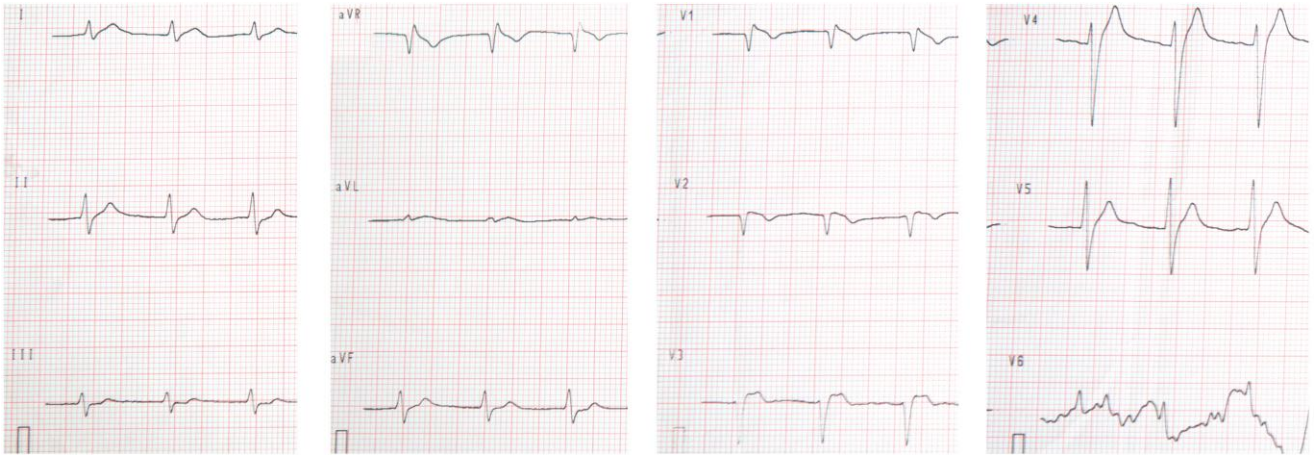

Figure 1 Electrocardiogram performed before sudden cardiac arrest occurred.

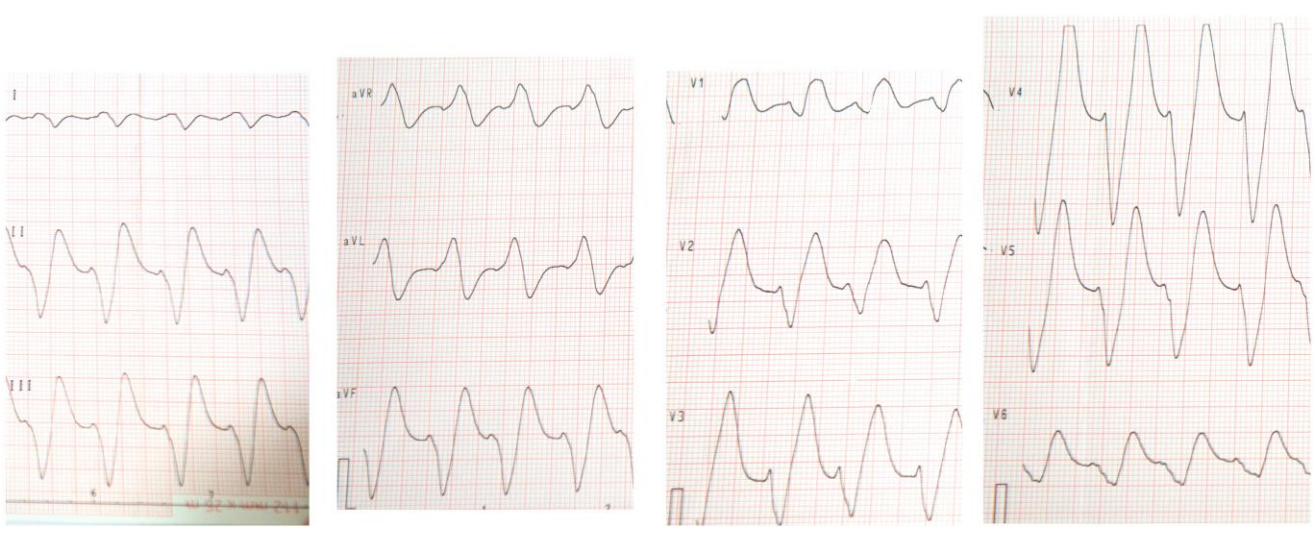

Figure 2 Electrocardiogram performed immediately after return of spontaneous circulation, before coronary angiography.

further clinical decisions. In the case described, after coronary artery spasm was diagnosed by coronary angiography, despite the need for high doses of catecholamines, the drug nitroglycerin was included in the treatment. This proceeding can cause a significant reduction in blood pressure through its action on blood vessels. However, it also has a strong effect on the coronary vessels, causing them to dilate. Consequently, despite the use of nitroglycerin, a decrease in the demand for catecholamines was observed.

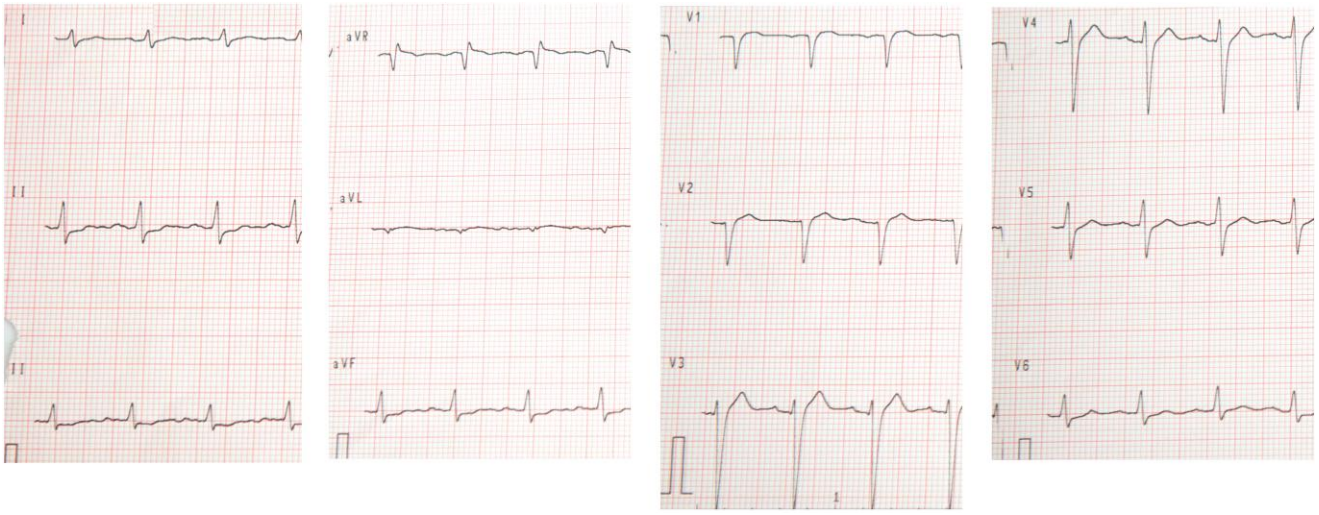

Figure 3 Electrocardiogram performed the day after coronary angiography. The patient received intravenous nitroglycerin by continuous infusion.

Table 2 The demand for catecholamines, left ventricular ejection fraction, and indexed cardiac output during the relevant period of hospitalization

	1 h before cardiac arrest	1 h after coronary angiography and nitroglycerin infusion	24 h after coronary angiography	5 days after coronary angiography
Noradrenaline	0.5 mcg/kg/min	0.2 mcg/kg/min	0.12 mcg/kg/min	0
Dobutamine	18 mcg/kg/min	10 mcg/kg/min	4 mcg/kg/min	0
Left ventricular ejection fraction (LVEF)	~20% Segmental contractility disorders of the left ventricle—akinesia of the apex and the apical segment of the interventricular septum	20–25%	30–35%	45%
CI-indexed cardiac output	1.7	2.3	2.7–2.9	3.1

In the case described, the direct cause of the episodes of cardiac arrest in the form of recurrent episodes of pulseless ventricular tachycardia and ventricular fibrillation was coronary vasospasm. Focusing the treatment on reversing the cause of the haemodynamic instability resulted in stabilization and, ultimately, an improvement in the overall condition. Carbamazepine-induced Brugada-type electrocardiographic recording can be also considered on the basis of the electroencephalography (ECG).[6] In Brugada syndrome, heart rhythm disturbances caused by polymorphic ventricular tachycardia can lead to cardiac arrest.

Cardiotoxic effects of carbamazepine have been revealed, including disturbances in ventricular repolarization, the occurrence of premature ventricular contractions, tachycardia, and hypotension.[7] Carbamazepine's cardiotoxic effects have been confirmed in an animal model.[5] Combining carbamazepine with other medications, such as antipsychotics like quetiapine, can be particularly dangerous. In such cases, even therapeutic doses, through drug interactions, can cause cardiac arrhythmias and conduction disturbances.[8] Although there are recommendations for the management of acute carbamazepine poisoning, they do not cover complications such as coronary vasospasm. Despite clinical signs of myocardial infarction (ECG changes and apical akinesia), coronary angiography excluded the presence of atherosclerotic lesions, while transient coronary vasospasm was confirmed in the nitroglycerin test.

It is noteworthy that the life-threatening cardiac arrhythmia occurred on the second day of hospitalization. Given that not all hospitals have access to a haemodynamic laboratory and the ability to perform coronary angiography, it would be appropriate to take as standard the need to treat carbamazepine-poisoned patients in higher referral centres with 24-h access to a haemodynamic laboratory.

For many acute poisoning, including carbamazepine poisoning, optimal care can be provided in intensive care units, in hospitals with access to 24-h specialist consultations, and with in-depth imaging, laboratory, or functional diagnostics. The initially stable general condition of a patient with acute poisoning can quickly deteriorate. This, in turn, can pose a real threat of limiting the possibility of transporting the patient to centres with adequate diagnostic and treatment facilities and affect the deterioration of further prognosis.

For most acute poisoning, there are no specific antidotes. Recommendations for managing carbamazepine poisoning mainly involve supportive and symptomatic treatment.

In situations where there is no close availability of centres with experience in treating patients with acute poisoning, preliminary care should be provided on-site or at the nearest medical facility (such as gastric lavage, administration of activated charcoal, and securing basic life functions), and then the case should be promptly consulted with the appropriate center and, if necessary, the patient should be directed there for further treatment. This case report highlights the importance of an interdisciplinary approach to the diagnosis and treatment of acute poisoning.

Lead author biography

Małgorzata M. Skiba, PhD, is a specialist in intensive care and anaesthesiology. She completed her medical school training at the Medical University of Lublin in Poland, graduating in 2012. She works in the Intensive Care Unit at Stefan Cardinal Wyszyński District Specialist Hospital in Lublin, Poland.

Consent: The authors confirm that written consent for submission and publication of these case reports including images and associated text has been obtained from the patients in accordance with the COPE guidelines (patients signed written informed consent).

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Data availability

The data underlying this article cannot be shared publicly due to privacy of patient. The data will be shared on reasonable request to the corresponding author.

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