

Rare Conduction Abnormality in a Four-year-old Child with Carbamazepine Acute Poisoning

Cristina Iolanda VIVISENCO^{a, b}, Coriolan Emil ULMEANU^{a, b}

^a„Grigore Alexandrescu” Emergency Children’s Hospital, Bucharest, Romania

^bPediatrics Department, „Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

Background: Cardiac conduction abnormalities are reported after ingestion of a toxic dose of carbamazepine.

Case presentation: We describe the case of a four-year-old child with carbamazepine acute poisoning who developed reversible synatrial block along with neurological toxic signs, despite a serum level of carbamazepine close to the upper limit of the therapeutic range.

Discussion: Although carbamazepine-induced sinoatrial block has been reported in the literature even at therapeutic doses in adult patients, our personal research has not identified any record of this cardiac conduction abnormality in acute carbamazepine poisoning at pediatric age.

Conclusion: The electrocardiogram is indispensable in the assessment and monitoring of pediatric cases with acute poisoning with carbamazepine.

Keywords: carbamazepine, poisoning, synatrial block, child.

BACKGROUND

Carbamazepine is a carbamylated derivative of iminostilbene, structurally similar to imipramine and other tricyclic antidepressants. It is used especially in the treatment of epilepsy, but also in other conditions such as neuropathic pain and bipolar disorder (1). Ingestion of a toxic dose causes adverse effects in the central nervous system, cardiovascular and respiratory systems. The most important manifestations are encephalopathy, coma, respiratory failure, seizures,

tachycardia, cardiac conduction disturbances (QRS complex widening) and hypotension (2). □

CASE PRESENTATION

A four-year-old male was sent to our hospital from another medical unit for heart rhythm disorder and drowsiness alternating with agitation, symptomatology that occurred two hours after the child was left unattended and ingested three or four tablets containing 200 mg carbamazepine, medicine belonging to another family member. The patient was drowsy, with periods of

Address for correspondence:

Cristina Iolanda Vivisenco

„Grigore Alexandrescu” Emergency Children’s Hospital, Iancu de Hunedoara Bd, 30-32, Sector 1, Bucharest, Romania

Tel: 0213169366

Email: iolanda.vivisenco@gmail.com

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agitation, ataxic, a score of 12 on Glasgow Coma Scale (GCS) and mydriatic pupils, and had the following vital parameters: 37.4 Celsius degrees, respiratory rate 26 bpm, oxygen saturation measured by pulse oximetry 97%, heart rate 65-100 bpm, blood pressure 95/60 mm Hg. Auscultation revealed irregular cardiac beats and frequent sinus pauses were recorded on the electrocardiogram (ECG) (Figure 1).

At admission – 4 hours after ingestion, the laboratory tests - acid-base balance, blood gases, glycemia, kidney and liver function tests, troponin Ic, creatine-kinase MB and brain natriuretic

peptide - were within normal ranges. The serum carbamazepine level was 10.6 mg/L (therapeutic level 8-10 mg/L). The ECG showed sinus pauses where the PP interval was measuring twice the length of the previous PP interval, a suggestive pattern for type II second degree sinoatrial block. QRS was normal (75 ms), but the QTc was slightly elongated (480 ms) (Figure 2). The patient was treated with crystalloid solutions in perfusion, with continuous cardiac monitoring. In the first 24 hours, he was drowsy with periods of agitation, with the sinoatrial block present on the cardiac monitor and ECG record. After 24 hours of

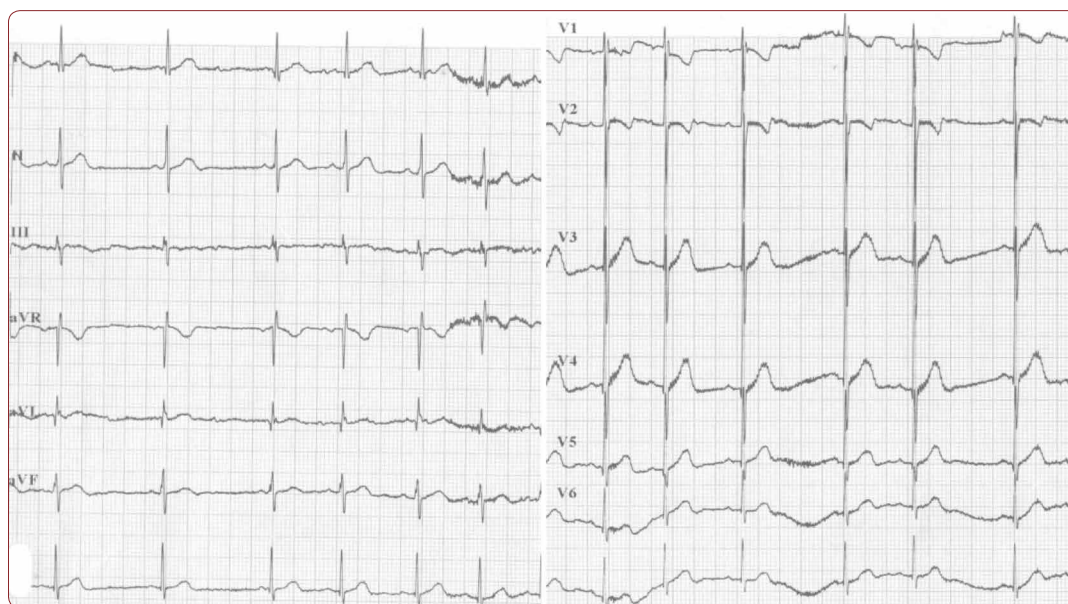


FIGURE 1. Sinus rhythm with frequent sinus pauses

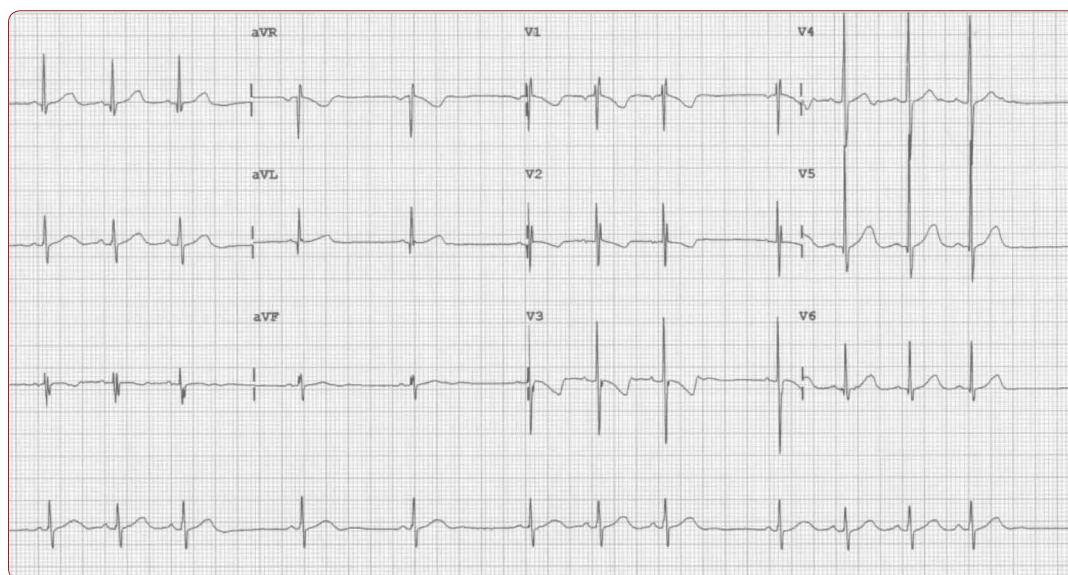


FIGURE 2. Type II second-degree sinoatrial block. Long QT

admission, the outcome was favorable with the disappearance of drowsiness and normalization of the ECG record. The patient was discharged from the hospital on day 5 in good condition. □

DISCUSSION

The main mechanism of action of carbamazepine is the inhibitory effect on voltage-gated sodium channels with neural membrane-stabilizing effect and suppression of excitatory pulse propagation. The drug exerts weak anticholinergic effects, more obvious at toxic doses, and a paradoxical effect on adenosine receptors. In therapeutic doses, the drug inhibits presynaptic reuptakes of adenosine, with modulatory and inhibitory effects on excitatory neurotransmitters (glutamate). In toxic doses, carbamazepine antagonizes adenosine receptors, which explains the proconvulsive activity observed in acute poisoning (1, 3).

Dosage of serum level of carbamazepine should be performed in all cases with known or suspected exposure (2). The published data on the correlation between the serum level and the severity of the clinical features in acute poisoning with carbamazepine are contradictory. Spiller and colleagues conducted a prospective study on 25 children aged under six and 10 adolescents with toxic exposure to carbamazepine, demonstrating a poor correlation between serum levels and serious clinical manifestations: coma, seizures and respiratory failure requiring mechanical ventilation. Intracardiac conduction disorders were rare in the studied group (one case of Mobitz type II second-degree atrioventricular block), while the anticholinergic manifestations (decreased intestinal motility and sinus tachycardia) were more common (4). Tibballs reviewed 82 pediatric cases of acute poisoning with carbamazepine, finding a statistically significant correlation between serum level and coma stage, occurrence of seizures, hypotension or need for assisted ventilation (5). Potter and Donnelly identified a subgroup of patients who developed signs of acute poisoning despite normal carbamazepine serum levels. This phenomenon was due to the presence of a significant concentration of the active metabolite carbamazepine 10,11-epoxide, with a decrease in the carbamazepine/epoxide ratio (6). However, subsequent studies have not established the clinical utility of

dosing the serum level of the metabolite (7). In our case, clinical signs were significant, despite a serum level close to the upper limit of the therapeutic range.

Although carbamazepine is structurally related to tricyclic antidepressants, exerting similar effects on myocardial sodium channels and on action potential phase 0, serious cardiotoxic manifestations are rarely reported in carbamazepine poisoning compared to tricyclic antidepressants (2). However, carbamazepine exposures complicated with severe arrhythmias and cardiogenic shock have been reported (8, 9). Bradycardia and heart block have been described even at therapeutic doses (10, 11). In a study by Doyon and Zorc in pediatric patients, QRS widening was reported in 35% of cases (12). In Tibballs' study, a subgroup of patients with deep coma (GCS 3-4) and mean serum carbamazepine of 213 $\mu\text{mol/L}$ (50.4 mg/L) experienced hypotension due to myocardial depression and conduction disturbances. These patients required high dose of inotropic support. There was one case of death due to heart failure and cardiogenic shock (5).

In our case, the clinical manifestations of acute poisoning consisted in neurological signs (drowsiness, ataxia), anticholinergic signs (agitation, midriasis) and cardiovascular signs (type II second-degree sinoatrial block, QTc prolongation). Prolongation of the QTc interval is associated with acute carbamazepine poisoning, separate studies by Apfelbaum and Ciszowski assessing a 50% and 53% prevalence of this ECG finding in the studied groups (13, 14). Carbamazepine-induced sinoatrial block has been reported in the literature even at therapeutic doses in adult patients treated for epilepsy (15). Personal research of the literature has not identified any record of this cardiac conduction disorder in acute carbamazepine poisoning at pediatric age. □

CONCLUSION

Electrocardiogram is an indispensable tool in evaluating and monitoring cases of acute poisoning with drugs that may affect the cardiac conduction system, such as carbamazepine. □

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