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Refractory Arrhythmias in a Young Patient Poisoned by Imipramine

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Abstract
Tricyclic antidepressants are used to treat a variety of mental disorders, and are considered a common cause of fatal drug poisoning. This study reports a young woman with no history of cardiac diseases who presented to the emergency department with heart palpitation, weakness, and lethargy. After a short period of time, she became unconscious and experienced hypotension and refractory arrhythmia, finally being diagnosed with imipramine poisoning. Accurate history taking and the possible causes of these complications including cardio-toxic drug poisoning should be considered in such patients.

Keywords Refractory arrhythmias · Poisoning · Cardio-toxic drug · Tricyclic antidepressant · Case report

Introduction

Tricyclic antidepressants are used to treat a variety of mental disorders, including depression, anxiety, and chronic pain. Since these drugs are easily available, they are sometimes used to attempt suicide and are considered a common cause of fatal drug poisoning because they have more toxic effects compared to other antidepressants [1, 2]. The American Association of Poison Control Centers has enumerated tricyclic antidepressant (TCA) drugs as the third most common cause of poisoning [1]. Tricyclic antidepressant poisoning is also one of the most common types of toxicity with high mortality in developing countries [3–6]. Death from TCAs is mainly due to cardiac arrhythmias and hypotension [7], and half of those who die from TCA poisoning show some few signs of toxicity on presentation, although in following hours, this turns into a severe toxicity [1]. By the development of acidosis, TCA poisoning becomes more refractory. Hence, rapid diagnosis and aggressive treatment are essential steps in reviving the patients [7]. This study reports a young woman who referred to us without a history of cardiac diseases, but with palpitation, weakness, lethargy, and refractory arrhythmia.

Case Presentation

A 19-year-old female referred to our emergency department with the major complaints of heart palpitation, weakness, and lethargy. Reportedly, she had had two to three episodes of palpitation within the last 2 weeks before presentation. She did not mention any history of cardiac disease or medication consumption. On admission to the emergency department, the patient became unconscious and experienced a drop attack. She immediately underwent cardiopulmonary monitoring, and an electrocardiogram (ECG) was performed which showed regular wide complex tachycardia (Fig. 1). Her blood pressure was 100/80. Eventually, the patient was diagnosed with PSVT and was given 6 mg of adenosine which established the sinus rhythm. However, she returned to her previous state mandating another 6 mg of adenosine although she did not recover with this medication, anymore.

Because of the hemodynamic instability, the patient was given a 100-J biphasic shock, after which a VF heart rhythm ensued (Fig. 2). Therefore, the patient received a 200-J shock with 300 mg of amiodarone and 2 mg of

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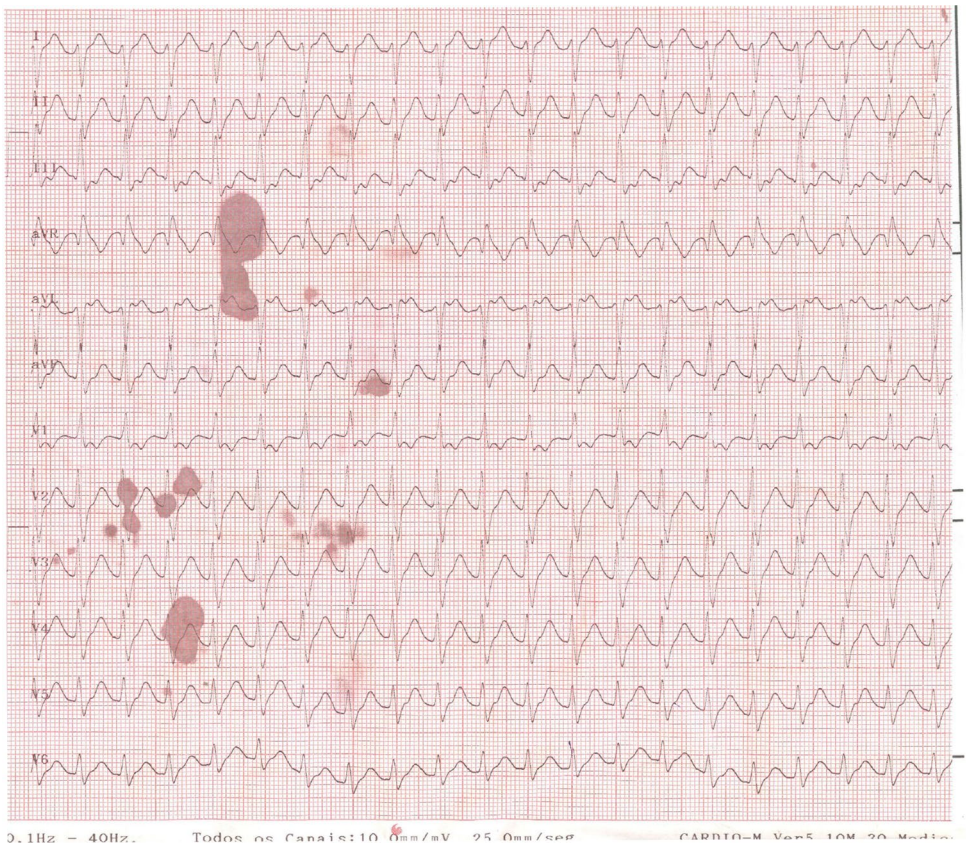

Fig. 1 12-Lead ECG with a regular wide QRS complex tachycardia in a patient with TCA poisoning at admission

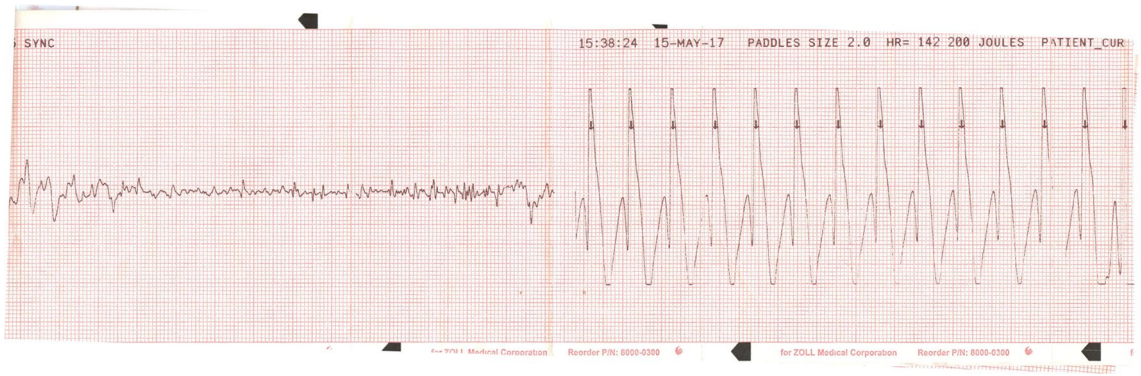

Fig. 2 Rhythm strip with an VF in a TCA-poisoned patient

magnesium sulfate, but she still had a VF heart rhythm and no pulse. A 200-J shock was applied twice, after which ECG showed a wide complex tachycardia with a heart rate of 140 beats per minute, and the blood pressure was 100/50 mmHg. Given the patient's ECG pattern (Fig. 3), (wide QRS complex, morphology of right bundle branch block, terminal 40-msec right axis deviation on the frontal plane in the form of a terminal R-wave on lead aVR, and the deep indented S wave in the lead I derivation), refractory arrhythmia, the patient's young age, and absence of cardiac diseases and medication history, she was suspected to be drug-poisoned. Accordingly, a drug screening urine test was performed.

Based on the results of this test along with a more accurate history of the patient taken from her family, it was revealed that she had had access to her mother's imipramine pills and might had ingested imipramine as a non-supervised action. Sodium bicarbonate (15 cc twice) and calcium gluconate were administered. Despite the administration of amiodarone, the patient still had arrhythmia and, given the patient's better reaction to lidocaine, amiodarone was substituted with lidocaine. The patient received a bolus dose

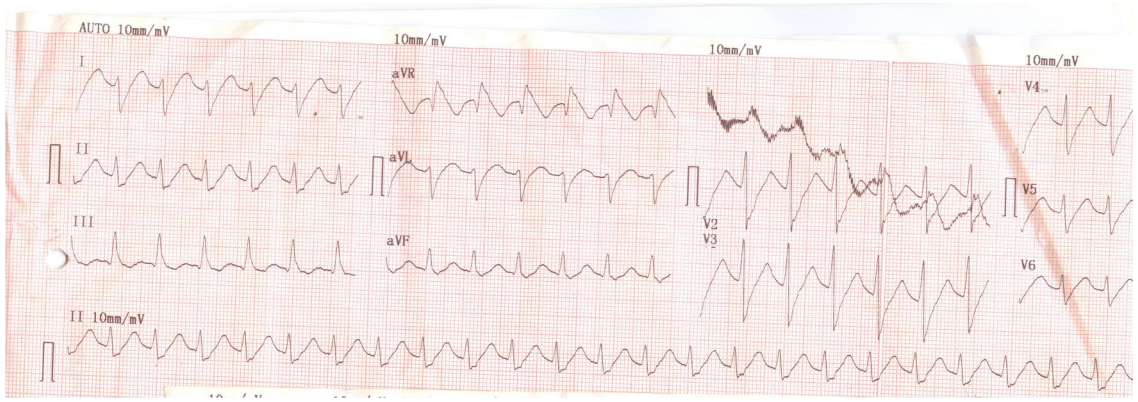

Fig. 3 12-Lead ECG in the patient with TCA poisoning

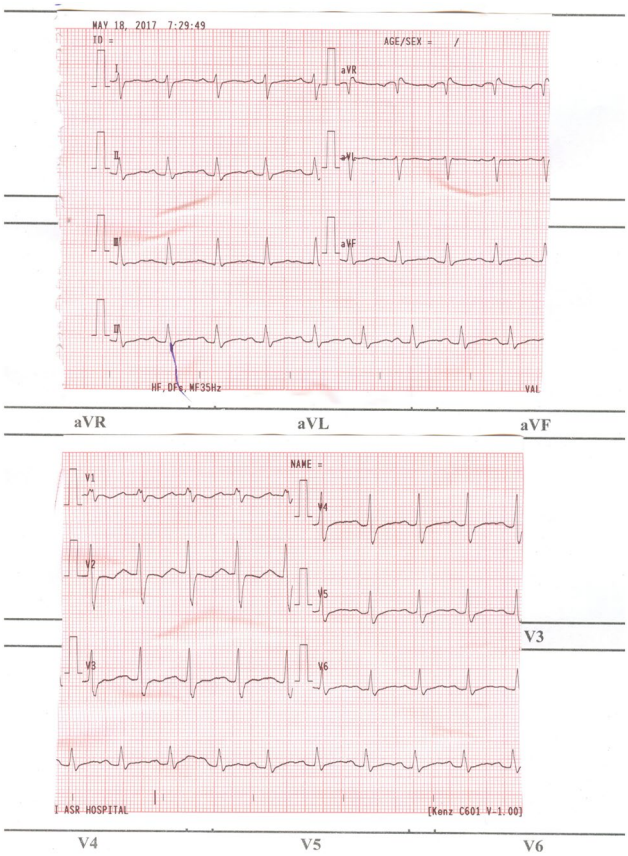

Fig. 4 The narrowed QRS complex after admission in the CCU

of 60 mg of lidocaine and a 4-mg/min infusion of it was also initiated which controlled the arrhythmia, decreased the heart rate to 80 bpm, and stabilized the hemodynamic. Eventually, the patient was intubated and transferred to the ICU ward. Infusion of lidocaine and sodium bicarbonate and gastric decontamination were continued in the ICU, and the QRS complex narrowed in the ECG (Fig. 4). After 12 h in ICU, the patient was extubated and transferred to the CCU while she was completely alert. The patient's laboratory test results in the course of hospitalization are reported in Table 1. She gave her informed consent for her case to be published.

Table 1 Laboratory findings of the patient in the course of hospitalization in intensive care unit

Laboratory findings	First day	Second day	Third day
K (mEq/L)	3.5	–	–
Na (mEq/L)	141	–	–
Ca (mg/dL)	7.7	–	–
P(mg/dL)	2.6	–	–
FBS (mg/dL)	88	–	–
WBC (10×3/μL)	7.2	16	12.7
PMN (%)	74	87	90
PH	7.6	7.44	7.5
PaO_2 (mmHg)	202	189	
PCO_2 (mmHg)	31	25	27
HCO_3 (mEq/L)	20	25	21

K potassium, *Na* sodium, *Ca* calcium, *P* phosphorus, *FBS* fasting blood sugar, *WBC* white blood cell, *PMN* polymorphonuclear leukocytes, PaO_2 partial pressure of arterial oxygen, PCO_2 partial pressure of carbon dioxide, Hco_3: serum bicarbonate

Discussion and Conclusion

Patients referring with TCA poisoning encounter various clinical problems and require cardiac care. These patients show some few signs of toxicity at the time of admission. Certain physical reactions, such as fatigue, weakness, and lethargy can typically occur [1], and our reported case had weakness, lethargy, and heart palpitation. In the next stage, hypotension and arrhythmia may occur, which indicate cardiovascular toxicity in this type of poisoning [2].

Hypotension is probably due to decreased myocardial contractility and decreased systemic vascular resistance due to alpha-adrenergic block [2].

These drugs have antidepressant effects through the inhibition of noradrenaline and serotonin reuptake; their toxic effects in overdose involve inhibition of noradrenaline reuptake in nerve endings, direct blockage of the alpha-adrenergic receptors and of the sodium channels in nerve endings as well as some anticholinergic effects [1, 2, 7]. Blocking the ion channels, including sodium channels, by TCAs has antiarrhythmic effects in therapeutic doses but proarrythmic effects in overdose [1, 8]. The entry of sodium into the heart cells initiates the zero phase of depolarization in the Purkinje fibers and the heart muscle, leading to cardiac muscle contraction (systole). This phase can be measured by QRS wave duration in ECG; widened QRS and increased heart rate are prognostic factors for arrhythmia in patients poisoned with such drugs [1]. Generally, cardiovascular toxicity due to TCA poisoning occurs at doses above 10–20 mg/kg, and consuming 1 g or more is often considered fatal [3, 7]. The effect of such drugs on prolonged QRS duration has a direct relationship with plasma concentration, so that plasma concentration of 1 µg/mL can prolong the wave up to 100 milliseconds [9].

Numerous studies have reported the effects of TCA drugs on prolonged QT and incidence of arrhythmia [1, 10, 11]. Sanaei-Zadeh and Toussi reported wide complex tachycardia in a 25-year-old patient poisoned with 20–25 Nortriptyline tablets [12]. Sabah et al. reported wide complex tachycardia in a 25-year-old patient poisoned with 2500 mg of amitriptyline [13]. Additionally, in a cohort study on 793,460 patients consuming tricyclic antidepressants, Wu and associates revealed the increased risk of ventricular arrhythmias (VA) and sudden cardiac death (SCD) associated with the use of these drugs [14]. Amiri et al. also reported an acute TCA poisoning case with status epilepticus, hypotension, and refractory QRS complex widening whose refractory arrhythmia was controlled by high doses of sodium bicarbonate (53 vials) [3].

The tricyclic antidepressants bind to albumin in PH-sensitive conditions and would have greater binding to albumin when serum PH increases, and thus they are less exposed to myocardial cells, leading to their reduced damage. Therefore, alkalizing the serum minimizes the drug distribution and eliminates its effects. The use of sodium bicarbonate in these patients narrows the QRS complex and reduces cardiac arrhythmias [7]. Our patient was also treated with sodium bicarbonate for the same purpose.

The unique aspect about our case is the fact that the patient did not mention history of drug ingestion or heart diseases. She had experienced loss of consciousness, drop attack, and arrhythmia that did not respond to conventional treatments. In such cases, although no clear history of poisoning is present, complete detailed history taking and confirmatory lab tests should be performed to rule out TCA poisoning. Early diagnosis and appropriate treatment are necessary in reviving the patient and any physician confronting a young patient with refractory arrhythmias with no history of cardiac disease should think about cardio-toxic medications, of the most important of which are TCAs.

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