

A 31-Year-Old Woman Found Unresponsive with Tachycardia

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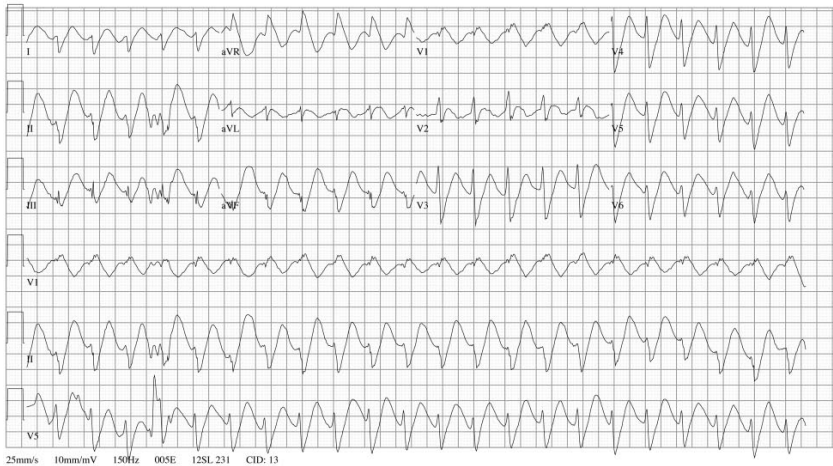


Figure 1. Initial electrocardiogram of the case patient demonstrating wide QRS complex tachycardia.

CASE PRESENTATION

A 31-year-old woman was brought to the emergency department by paramedics after the patient's husband found her unresponsive. He reported that he last saw her at baseline status approximately 1 hour prior to arrival in the emergency department. At that time, she complained of a headache and took an unknown medication to treat her symptoms; her behavior was otherwise normal. The paramedics reported that no drug paraphernalia or empty pill bottles were found at the scene. The patient's husband provided a medical history significant for headaches, but he was unclear about the patient's current medications or her drug allergies. There was no known history of illicit drug abuse.

Physical examination revealed a heart rate of 136 bpm, systolic blood pressure of 82 mm Hg, respiratory rate of 21 breaths/min, temperature of 96.9°F, and a pulse oximetry of 100% on a nonrebreather mask. Neurologic examination revealed 7-mm pupils with slow reactivity, poor gag reflex, no response to auditory stimuli, withdrawal from painful stimuli in all 4 extremities, 2+ reflexes, and a negative Babinski's sign. Cardiovascular examination demonstrated tachycardia, but the remainder of the physical examination was within normal limits.

The patient was placed on a cardiac monitor, intravenous access was established, blood was sent to the laboratory for analysis (complete blood count, renal panel, cardiac biomarkers, liver panel, lactate level, blood cultures, ammonia level, and serum drug screen), and a noncontrast head computed tomography (CT) scan was ordered. An electrocardiogram (ECG) was obtained (**Figure 1**). The patient was unstable for transport, and laboratory analysis was pending. A tentative diagnosis was made, and the patient was treated with 2 ampules of sodium bicarbonate. Repeat ECG was obtained after treatment, which confirmed the suspected diagnosis (**Figure 2**). The patient's hemodynamic profiles also improved with treatment. She was electively intubated for airway protection, underwent CT scan, and was admitted to the intensive care unit.

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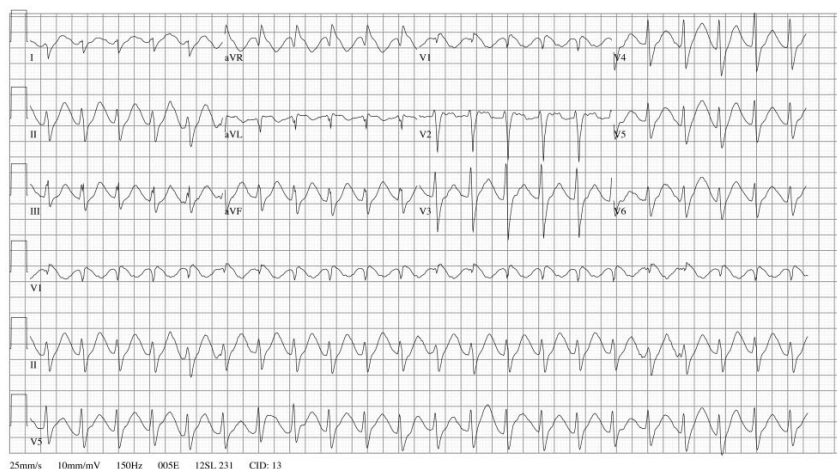


Figure 2. Repeat electrocardiogram of the case patient following treatment demonstrates narrowing of the QRS complex.

WHAT IS YOUR DIAGNOSIS?

- (A) Hyperkalemia
- (B) Hypothermia
- (C) Subarachnoid hemorrhage with myocardial stunning
- (D) Tricyclic antidepressant overdose
- (E) Ventricular tachycardia from acute myocardial infarction

ANSWER

The correct answer is (D), tricyclic antidepressant (TCA) overdose.

DISCUSSION

The initial ECG obtained was significant for a wide-complex tachycardia and a large terminal R wave in the aVR lead. The response to treatment with sodium bicarbonate reveals a significant narrowing of the QRS complex. Hyperkalemia is associated with a wide-complex rhythm that may respond to sodium bicarbonate, but the clinical situation of acute ingestion and mental status change is not compatible with that diagnosis. Subarachnoid hemorrhage (SAH) often presents with a headache followed by rapid neurologic decline. However, the neurologic examination typically reveals more focal signs than were seen in this patient. SAH can cause myocardial stunning with resultant hypotension and ECG changes, although the ECG changes most associated with SAH are elevation or depression of the ST segment, very deep T waves, lengthening of the QT interval, and the presence of U waves.¹ Ventricular tachycardia resulting from acute myocardial infarction is unlikely in this patient's age group. Finally, hypothermia is not an etiology for this patient's presentation, given that her temperature was 96.9°F. In addition, the classic ECG changes associated

with hypothermia (eg, Osborne waves) were not present on her initial ECG. The patient's clinical picture, ECG, and response to treatment are all consistent with TCA overdose.

TRICYCLIC ANTIDEPRESSANT TOXICITY

TCA medications are prescribed for the treatment of psychiatric conditions including major depression, panic and phobia disorders, obsessive-compulsive disorders, and eating disorders as well as for migraine prophylaxis and chronic pain syndromes.² The incidence of poisonings from these medications has decreased in recent years due to the development of safer alternative medications. Despite this trend, TCAs were still responsible for toxicology-related morbidity and mortality in 2007.³ Familiarity with the clinical features of TCA overdose is necessary to expedite diagnosis and initiate the appropriate therapy.

Pathophysiology

The therapeutic mechanisms of TCAs have been attributed to inhibition of the presynaptic reuptake of norepinephrine and serotonin.² The side effects and toxicity of these medications are related to a variety of other interactions. TCAs inhibit histamine receptors, which creates sedation and contributes to coma found in overdoses. Inhibition of α -adrenergic receptors also creates sedation and may contribute to the hypotension often present in overdoses. Seizures are commonly encountered, most likely due to γ -aminobutyric acid receptor blockade. Anticholinergic activity produces various symptoms in overdose, including tachycardia, delirium, hyperthermia, and urinary retention.² Cardiotoxicity resulting from sodium channel blockade is the major cause of morbidity in TCA overdoses. This blockade in Purkinje cells of the heart results in conduction

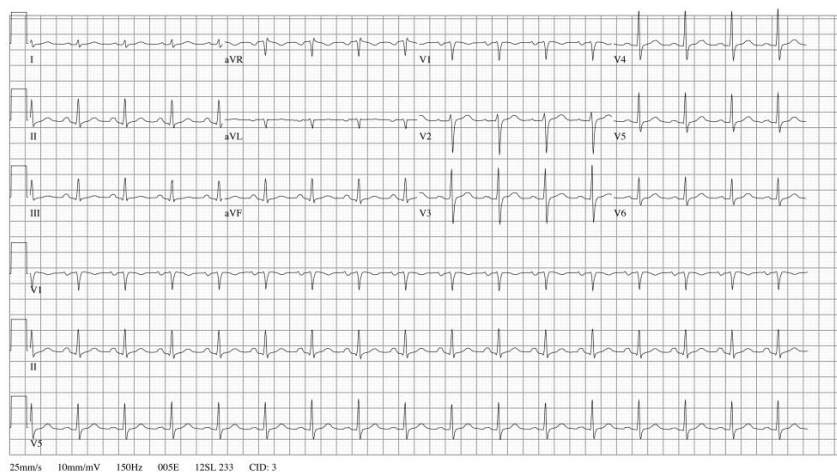


Figure 3. Electrocardiogram of the case patient at hospital day 3 demonstrates resolution of tricyclic antidepressant toxicity.

abnormalities that can be appreciated on an ECG. Sodium channel blockade also affects contractility of the heart, which results in hypotension. TCAs may inhibit potassium channels and leads to prolonged QT intervals. These changes predispose the patient to ventricular dysrhythmias and death.^{2,4,5}

Clinical Features

Mild or early overdose may present with features of an anticholinergic toxidrome, which may include sinus tachycardia, delirium, hyperthermia, dry skin, and/or urinary retention. The hallmarks of a moderate to severe TCA overdose include sedation/coma, cardiotoxicity, and seizures. Sedation can be mild and may be associated with slurred speech and confusion. In cases of severe sedation, patients can present in a coma state with minimal neurologic activity. The cardiotoxicity includes both rhythm abnormalities and hypotension. Interventricular conduction delays and prolongation of the QT interval can lead to ventricular tachycardia or ventricular fibrillation. The spectrum of seizure activity ranges from single, brief, self-resolving seizures to status epilepticus. Seizure activity compounds the toxicity by contributing to confusion and by creating acidosis that can worsen the cardiotoxicity.²

ECGs of patients with TCA overdose often demonstrate prolongation of the QRS interval (> 100 msec). The morphology of the QRS complex is often similar to a right bundle branch complex, but nonspecific intraventricular conduction delays are possible. The most specific ECG sign is right axis deviation of the terminal 40 msec vector of the QRS complex in the frontal plane (terminal R wave in aVR and a deep slurred S wave in lead I).⁶ Prolongation of the PR and QT interval may also be appreciated. Finally, ST-segment and T-wave abnormalities can be present and may mimic

the Brugada pattern (downsloping ST-segment elevation in V₁–V₃ with a right bundle branch block).⁶

Diagnosis

The clinical diagnosis of a TCA overdose relies heavily on a thorough history and a physical examination. Family members, friends, and prehospital providers are critical to making a prompt diagnosis as the patient may be comatose. Often prehospital providers make the diagnosis by bringing empty pill bottles found at the medical scene to the hospital with the patient. An ECG with the previously described features in the setting of a suspected overdose, coma, or reported seizure is sufficient to make a tentative diagnosis and begin treatment. Further work-up such as laboratory testing and radiographic imaging can be performed to confirm the diagnosis and exclude alternative diagnoses after therapy has been initiated. If the patient arrives in the emergency department clinically normal but a TCA overdose is reported or suspected, observation is required to exclude delayed onset of symptoms.²

Treatment

Treatment of TCA toxicity should focus on the cardiovascular status of patients, since the leading causes of mortality in TCA overdoses are dysrhythmias and hypotension.^{2,6} Sodium bicarbonate is the treatment of choice for both abnormalities. Its efficacy has been attributed to both serum alkalinization and sodium loading, thus counteracting the sodium channel blockade.⁷ A starting dose of 1 to 2 mEq/kg is appropriate if there are ECG abnormalities. A standard ampule of sodium bicarbonate, used routinely in code situations, is 50 mEq. Therefore, 1 to 2 ampules delivered by intravenous push is an appropriate starting point. Afterwards, additional boluses can be given until a sodium bicarbonate

drip can be administered, with the endpoint goals of QRS interval narrowing to less than 100 msec, pH no greater than 7.50, and resolution of hypotension. A drip can be prepared by adding 3 ampules of sodium bicarbonate to 1 L of 5% dextrose in water. This solution will be an isotonic infusion and should be started at a typical maintenance fluid rate.^{2,6,7}

Initiation of sodium bicarbonate therapy should be undertaken parallel to routine care of any critically ill patient. Priority should be given to airway, breathing, and circulation. Endotracheal intubation should be considered early in TCA overdoses as seizure activity and coma can predispose the patient to morbidity from aspiration pneumonia.² Intubation also allows for the safe performance of gastric lavage and charcoal administration. Although significant controversy surrounds the exact role of these therapies, they are generally indicated for life-threatening overdoses, especially when presenting early after ingestion.² Persistent hypotension should be treated with either additional sodium bicarbonate boluses or increases in the rate of infusion.^{2,6} If the patient remains hypotensive despite this intervention, then norepinephrine should be started. Norepinephrine is preferred over dopamine because its mechanism allows for direct competition with TCAs at the α -adrenergic receptor.⁸ The dose is 1 μ g/min titrated to effect up to 30 μ g/min. Benzodiazepine agents are first-line treatment for seizures. If seizures prove refractory, barbiturates and/or propofol can be started.²

CLINICAL COURSE OF THE PATIENT

The patient's potassium level was slightly low at

3.2 mEq/L, and a urine toxicology screen was positive for TCAs. The CT scan was normal, thus ruling out SAH. Poison control was consulted and recommended a continuous infusion of sodium bicarbonate. The patient's mental status slowly improved, and she was extubated on hospital day 2. A final ECG obtained on hospital day 3 revealed resolution of admission abnormalities (**Figure 3**). The patient reported that she ingested amitriptyline, prescribed for migraine prophylaxis. She admitted to suicidal ideation triggered by the severity of her migraines and was transferred to the psychiatric service. **HP**

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