CASE REPORT

Rapid diagnosis and treatment of severe tricyclic antidepressant toxicity

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SUMMARY

A woman in her mid-50s contacted her social worker and expressed intent to commit suicide by ingesting prescription medications. On arrival of emergency responders, the patient was found unconscious with an empty bottle of amitriptyline. Time of ingestion was estimated using the social worker's contact with local authorities. The patient's presentation at the emergency department (ED) exemplified tricyclic antidepressant toxidrome with a poor prognosis, based on measurable criteria and physical findings. Respiratory and cardiovascular collapse was managed emergently. Haemodynamic status and EKG findings responded in a stepwise fashion with therapy in the ED and intensive care unit. Full clinical recovery took 7 days, and the patient was subsequently transferred to an in-patient psychiatric facility for further evaluation. Eight days later, she was discharged home with no neurological sequelae.

BACKGROUND

Reported tricyclic antidepressant (TCA) use in recent years has decreased with the introduction of selective serotonin reuptake inhibitors (SSRIs)¹; however, these drugs still play a role in the treatment of major depressive disorders and other off-label conditions such as chronic pain syndromes. Up to 8.9% of fibromyalgia patients are treated with TCAs.² Rates of chronic pain syndromes continue to increase, with fibromyalgia reportedly affecting 2% of the general population.³ Ilgen *et al*⁴ report that individuals with chronic pain are at higher risk of suicidality. Therefore, physicians can expect to continue to manage large numbers of antidepressant overdoses. In the USA, TCA overdoses result in a higher rate of both hospitalisation and fatality than SSRI overdose.⁵

We report a case in which severe toxicity was overcome with rapid implementation of supportive measures, and adherence to basic treatment principles (ie, Guidelines in Emergency Medicine Network (GEMNet) guidelines).⁶ This case is of specific value because the time of ingestion was well established. This established timeframe allowed us to evaluate the timing of characteristic signs and symptoms of TCA overdose to include the evolution of EKG changes with respect to the inciting event.

CASE PRESENTATION

A 56-year-old woman reported to her social worker that she had intentionally ingested a large amount of medication recently prescribed by her family doctor for a chronic pain syndrome. When

emergency medical services arrived at the patient's home, she was found unconscious with an empty bottle of amitriptyline near her body. She was transferred to the emergency department (ED). Time between the patient's call to the social worker and presentation to the ED was approximately 45 min. On initial assessment in the ED, the patient's Glasgow Coma Scale (GCS) was 3, and she began seizing. Intranasal midazolam was administered, and she was emergently intubated. Initial blood pressure was 47/36 and EKG indicated a wide complex bradycardia with prolonged PR and QT intervals.

INVESTIGATIONS

The patient's initial EKG ([figure 1](#)) at time of presentation, approximately 45 min after ingestion, indicated sinus bradycardia with bigeminal premature ventricular contractions, first degree atrioventricular (AV) block, a widened QRS (184 ms) and a prolonged QTc (555 ms). A deep, slurred S wave appeared in leads I and augmented vector left (aVL), and a slurred, terminal R wave was seen in augmented vector right (aVR) with an R/S ratio of around 1.67. Approximately 1 h post-ingestion ([figure 2](#)), the patient was administered two ampules of sodium bicarbonate and 1 mg of atropine, and the following EKG changes were noted: QRS duration of 148 ms and QTc interval of 577 ms. A sodium bicarbonate drip was initiated and the following improvements were noted at approximately 105 min post TCA ingestion ([figure 3](#)): QRS of 136 ms and QTc interval of 508 ms. A rhythm strip from the intensive care unit (ICU) at approximately 7 h post-ingestion demonstrated narrowing of the QRS interval <100 ms ([figure 4](#)). An EKG performed approximately 65 h after ingestion demonstrated normal QRS duration <100 ms and no QTc prolongation (464 ms) ([figure 5](#)).

TREATMENT

The patient presented with signs and symptoms consistent with a TCA overdose. Therapy was initiated and managed in accordance with the GEMNet guidelines for management of TCA overdose.

Per GEMNet guidelines,⁶ initial pharmacological intervention was intranasal versed, which resulted in near-immediate termination of seizures. Intravenous phenytoin was not used because of the narrow therapeutic window and its known interaction with TCAs, possibly causing higher than anticipated plasma levels. The patient was unresponsive (GCS=3), requiring immediate intubation for airway protection. Time of ingestion was

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Figure 1 EKG at approximately 45 min postingestion shows a sinus bradycardia with bigeminal PVCs, first degree AV block, a widened QRS and a prolonged QTc. Note the deep, slurred S wave in leads I and aVL, and the slurred, terminal R wave in aVR. Also note that the R/S ratio in aVR is approximately 1.67. AV, atrioventricular; PVCs, premature ventricular contractions.

approximately 45 min based on the social worker's conversation with the patient, indicating likely therapeutic benefit of gastric decontamination. An orogastric tube was placed and 50 g of activated charcoal was administered. First-line therapy of patient's hypotension and bradycardia was initiated with a bolus of intravenous fluids and one-time dose of 1 mg atropine intravenous. She responded to fluid resuscitation but remained hypotensive. Persistent hypotension and increased risk of arrhythmia indicated a 100 mL of 8.4% sodium bicarbonate intravenous push, followed by another 50 mL of 8.4% sodium bicarbonate intravenous push until a sodium bicarbonate intravenous drip could be established. The patient was transferred to the ICU in critical, but stable, condition for further evaluation and treatment. During the ICU stay, treatments included norepinephrine

drip via femoral venous access for refractory hypotension, continuous propofol drip and intermittent lorazepam for sedation.

OUTCOME AND FOLLOW-UP

The patient was medically cleared for admission to a psychiatric facility for treatment of her major depressive disorder, requiring 8 days of in-patient therapy. The patient was discharged home without any neurological or cardiac sequelae, and advised to follow-up with her primary care physician in 4 weeks.

DISCUSSION

We present a case of severe amitriptyline overdose. Presentation with cardiac arrhythmias, seizures and respiratory depression due to TCA overdose is relatively rare in adult patients but is

Figure 2 EKG at 1 h postingestion was recorded after two amps of sodium bicarbonate as well as initiation of a sodium bicarbonate drip. Here we see improvement in the QRS, QTc and aVR-R/S ratio (now below 0.7).

Figure 3 A sodium bicarbonate drip was initiated and the following were noted at approximately 105 min postingestion: QRS narrowing (136 ms) and improvement in the QTc interval (508 ms).

indicative of poor prognosis.⁷ In this case, a timeline was well established, allowing us to depict cardiac presentation and response to treatment after severe amitriptyline overdose.

Limited availability of laboratory testing makes the inexpensive, swift bedside ECG a preferred diagnostic test for ED physicians. For this reason, it is essential for the emergency physician to know what findings indicate severe cardiotoxicity. One important initial finding in severe TCA overdose is a prolonged QRS duration. Initial QRS duration in our patient at approximately 45 min postingestion was 184 ms. A QRS duration greater than 100 ms has a sensitivity and specificity for fatal outcome of 0.81 and 0.62, respectively.⁸ Also important is the finding of a prolonged QTc interval, which has shown to increase the likelihood of death by 50%⁸; in our patient, initial QTc interval was 555 ms. An additional finding that makes the likelihood of subsequent arrhythmia (defined here as supraventricular tachycardia, ventricular tachycardia or cardiac arrest) likely is an R/S ratio of >0.7 in lead aVR; in our patient, it was 1.67.⁹ Lastly, TCA overdose has been shown to cause a rightward shift in the terminal 40 ms frontal plane QRS vector.¹⁰ This shift occurs because of an intraventricular and interventricular conduction delay resulting in delayed right ventricular activation. From an emergency medicine perspective, this value is best estimated by qualitatively looking for a deep, slurred S wave in leads I and VL, and an R wave in lead AVR (R/S ratio in aVR >0.7). This finding is important both diagnostically and prognostically. A large meta-analysis indicated that a patient

with a T40-ms axis of $130\text{--}270^\circ$ (evidenced by the qualitative bedside measurement previously described) is more likely to have a seizure (positive LR 1.79) and suffer fatality (positive LR 1.14) when compared to TCA overdoses without this finding.⁸ In addition to ECG, quantitative serum drug levels are also used in evaluating toxicity related to overdose. Bailey *et al*⁸ found TCA concentration performed similarly to ECG in predicting complications in TCA overdose; however, both tests demonstrated only moderate sensitivity and specificity.

A recent review of the literature¹¹ suggested that ECG changes may be noted on arrival or may present within 2–6 h after arrival. It is important to note that few studies or cases in the literature are able to depict a clear timeline of ingestion. Liebelt *et al*¹² reported a median time of 2.0 h postingestion for 25 patients presenting to the ED; however, the authors did not specify cardiac or neurological sequelae by time postingestion for these patients. As the current case illustrates, ECG abnormalities may present much earlier than previously documented in cases of severe TCA overdose. In this case, severe cardiotoxicity was noted within 45 min of TCA overdose. Cardiac abnormalities included bradycardia, AV block, hypotension, a widened QRS and prolonged QTc interval, deep, slurred S wave in leads I and VL, and a slurred terminal wave in aVR with an R/S ratio of 1.67. An EKG approximately 45 min after initial sodium bicarbonate treatment and subsequent drip showed improvements in cardiac conduction abnormalities on EKG. The patient's haemodynamic instability did not initially improve

Figure 4 A rhythm strip taken approximately 7 h postingestion demonstrating narrowing of the QRS <100 ms.

Figure 5 An EKG approximately 65 h postingestion indicated normal cardiac functioning. QRS was no longer widened and QTc was no longer elongated.

with bicarbonate and intravenous fluids and subsequently required vasopressor therapy with norepinephrine. Overall, the cardiac abnormalities improved after 3 days of treatment in the ICU and no long-term sequelae have been noted.

The most recent GEMNet guidelines,⁶ published in December 2011, make seven recommendations based on the best existing evidence for the diagnosis and treatment of TCA overdose in the ED setting. Briefly, initial management consists of (1) airway management based on GCS greater than or less than 8, (2) determining need for gastric decontamination based on time of ingestion and airway protection, (3) initial ECG assessment for QRS widening, QTc prolongation and/or aVR R/S ratio changes, (4) risk stratification based on blood pH and appropriate alkalisation, (5) treatment of haemodynamic instability with intravenous fluids and various adjunct therapies, (6) seizure management with benzodiazepines, and (7) disposition of patients based on symptoms and laboratory findings. Following the GEMNet flowchart for the management of TCA overdose provided the emergency medicine physicians with a series of evidence-based recommendations for utilising equipment, medications and resources available in all ED settings. Immediately assessing the patient's airway, breathing and circulation while adhering to these guidelines resulted in a full recovery without any neurological or cardiac sequelae.

In many cases of TCA overdose, time since ingestion is unknown. However, in the current case, we provide a timeline indicating that severe neurological and cardiac sequelae were evident within 45 min of ingestion. Based on the EKG findings, seizures and GCS score, our patient presented with life threatening sequelae of TCA overdose. Our management of this patient was concordant with the GEMNet Guideline for the Management of Tricyclic Antidepressant Overdose with respect to ECG on admission to the ED, initial management of cardiac arrhythmias and hypotension with sodium bicarbonate, intravenous fluid boluses and vasopressors as necessary, single-dose charcoal admission within 1 h, and utilisation of benzodiazepines for convulsions (with avoidance of phenytoin). These treatments were highly effective, and the patient recovered with no long-term physical sequelae.

Learning points

- Initial assessment of the patient with suspected tricyclic antidepressant (TCA) overdose should focus on the standard ABC's of resuscitation (airway, breathing and circulation).
- Rapid diagnosis of clinically significant TCA toxicity can be made with an EKG, as this fast and inexpensive bedside tool provides the majority of the diagnostic and prognostic information that will lead to proper treatment. These findings include QRS prolongation (>100 ms), delayed right ventricular activation (manifested by a deep, slurred S wave in leads I and AVL, and an R wave in lead AVR) and an R/S ratio in aVR >0.7.
- Immediately on obtaining an EKG suggestive of clinically significant TCA toxicity, intravenous bicarbonate therapy should be initiated.
- In the haemodynamically unstable patient whose hypotension is refractory to bicarbonate and intravenous fluid boluses, vasopressor therapy with either norepinephrine or epinephrine should be initiated.

Competing interests None declared.

Patient consent Obtained.

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