CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 12-2018: A 30-Year-Old Woman with Cardiac Arrest

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PRESENTATION OF CASE

Dr. Emily C. Cleveland (Emergency Medicine): A 30-year-old woman was brought to the emergency department of this hospital because of cardiac arrest.

On the morning of this presentation, the patient was found unresponsive in her bedroom. Her mother called emergency medical services (EMS) at 8:45 a.m. and initiated cardiopulmonary resuscitation (CPR), which was continued by first responders from the fire department on their arrival. The cardiac rhythm was assessed with an automated external defibrillator, and a shock was delivered. EMS personnel who could provide advanced life support arrived at 8:54 a.m. and found the patient to be pulseless. CPR was continued, and intraosseous access was established. Electrocardiography performed with an external monitor and defibrillator reportedly revealed wide-complex bradycardia. CPR was continued, the trachea was intubated, and sodium bicarbonate, epinephrine, and calcium chloride were administered intraosseously. Spontaneous circulation returned.

While the patient was being transported from her home to the ambulance, pulselessness recurred. CPR was resumed, and epinephrine was administered; a pulse was restored. At 9:16 a.m., the pulse was 94 beats per minute, the blood pressure 66/30 mm Hg, and the respiratory rate 7 breaths per minute. A peripheral intravenous catheter was inserted, and a bolus of normal saline was administered; thereafter, the blood pressure was 54/24 mm Hg. A continuous infusion of dopamine was begun, and the patient was transported to the emergency department of this hospital, arriving at 9:38 a.m.

On the patient's arrival in the emergency department, the available history was limited. The patient's mother reported that the patient drank alcohol in a binge pattern and had appeared to be intoxicated the previous evening but had seemed well at 7:45 a.m., before she went into her bedroom. The patient also smoked cigarettes and had a history of depression, anxiety, substance use disorder (including the use of alcohol, opioids, and cocaine), and skin abscesses due to methicillin-resistant *Staphylococcus aureus*. Current medications were unknown; a review of the electronic medical record revealed an allergy to amoxicillin–clavulanic acid. The

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Presentation
Hematocrit (%)	36.0–46.0	35.4
Hemoglobin (g/dl)	12.0–16.0	11.0
White-cell count (per mm^3)	4500–11,000	13,950
Differential count (%)		
Neutrophils	40–70	64.3
Bands	0–10	0.9
Lymphocytes	22–44	26.1
Monocytes	4–11	5.2
Basophils	0–3	0.9
Myelocytes	0	1.7
Metamyelocytes	0	0.9
Platelet count (per mm^3)	150,000–400,000	290,000
Red-cell count (per mm^3)	4,000,000–5,200,000	3,400,000
Mean corpuscular volume (fl)	80.0–100.0	104.1
Mean corpuscular hemoglobin (pg)	26.0–34.0	32.4
Mean corpuscular hemoglobin level (g/dl)	31.0–37.0	31.1
Red-cell distribution width (%)	11.5–14.5	14.3
Prothrombin time (sec)	11.0–14.0	15.4
Prothrombin-time international normalized ratio	0.9–1.1	1.2
Activated partial-thromboplastin time (sec)	22.0–35.0	29.6
Sodium (mmol/liter)	135–145	146
Potassium (mmol/liter)	3.4–5.0	3.5
Chloride (mmol/liter)	98–108	105
Carbon dioxide (mmol/liter)	23–32	21
Anion gap (mmol/liter)	3–17	20
Calcium (mg/dl)	8.5–10.5	9.0
Phosphorus (mg/dl)	2.6–4.5	8.4
Magnesium (mg/dl)	1.7–2.4	2.9
Glucose (mg/dl)	70–110	176
Urea nitrogen (mg/dl)	8–25	6
Creatinine (mg/dl)	0.60–1.50	1.22
Estimated glomerular filtration rate (ml/min/1.73 m^2)‡	>60	52
Alanine aminotransferase (IU/liter)	7–33	147
Aspartate aminotransferase (IU/liter)	9–32	137
Alkaline phosphatase (U/liter)	30–100	60
Bilirubin (mg/dl)		
Total	0–1.0	0.3
Direct	0–0.4	<0.2
Protein (g/dl)		
Total	6.0–8.3	5.5
Albumin	3.3–5.0	3.5
Globulin	1.9–4.1	2.0

Table 1. (Continued.)

Variable	Reference Range, Adults†	On Presentation
Lipase (mmol/liter)	13–60	19
Lactic acid (mmol/liter)	0.5–2.0	7.4
Troponin T (ng/ml)	<0.03	<0.01
N-terminal pro–B-type natriuretic peptide (pg/ml)	0–450	64
Venous blood gases		
Fraction of inspired oxygen		Unspecified
pH	7.30–7.40	7.05
Partial pressure of carbon dioxide (mm Hg)	38–50	84
Partial pressure of oxygen (mm Hg)	35–50	108
Base excess (mmol/liter)	0–3.0	–9.4

* To convert the values for calcium to millimoles per liter, multiply by 0.250. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229. To convert the values for magnesium to millimoles per liter, multiply by 0.4114. To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for lactic acid to milligrams per deciliter, divide by 0.1110.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

‡ If the patient is black, multiply the result by 1.21.

this case. This young woman was found unresponsive and in cardiac arrest at home. Early communication from EMS personnel allowed us to generate a preliminary differential diagnosis while preparing for her arrival in the emergency department.

When cardiac arrest occurs in a young adult such as this patient, the underlying cause is usually a cardiac, neurologic, traumatic, toxicologic, or metabolic disorder. Among patients between 16 and 35 years of age, the most common causes are traumatic and cardiac disorders and the most common rhythms are asystole, pulseless electrical activity, and ventricular fibrillation or tachycardia.[1]

In this case, the fact that an automated external defibrillator attempted defibrillation suggests that the initial rhythm was most likely ventricular fibrillation or tachycardia, although a shock might have also been triggered by another wide-complex rhythm. EMS personnel reported that, after the shock had been delivered, the patient had a wide-complex rhythm, sometimes with a palpable pulse and sometimes without. This description prompted us to consider ventricular tachycardia and other wide-complex rhythms, with pulseless electrical activity being unlikely. Wide-complex rhythms can be caused by myocardial ischemia, supraventricular tachycardia with an accessory pathway or aberrant conduction, hypothermia, hyperkalemia, and the use of medications such as sodium-channel blockers. Ventricular tachycardia can occur in the context of acquired prolongation of the QTc interval, which can result from an abnormal potassium, magnesium, or calcium level or from the use of one of several types of medications, including antiarrhythmic, antibiotic, antihistamine, antiemetic, antipsychotic, and antidepressant agents.

Once the patient arrived in the emergency department, the primary evaluation proceeded in parallel with resuscitation. The evaluation included an attempt to obtain additional history, such as a medication list and the last time the patient was known to be well, which we determined to be 60 minutes before she had been found unresponsive. In the initial physical examination, we confirmed that the airway was secure, listened for breath sounds, and ensured that the patient had an adequate blood pressure. We then examined the chest for scars that would suggest a history of heart surgery or pacemaker placement, listened for heart murmurs, assessed for signs of heart failure, examined the arms and legs for a fistula associated with dialysis or track marks associated with the use of injection

drugs, and checked the rectal temperature to evaluate for hypothermia; none of these findings were present. A rapid survey for signs of injury was unrevealing, lowering the likelihood that trauma was the cause of cardiac arrest. A primary neurologic event, such as stroke or subarachnoid hemorrhage, was still possible, although the patient was younger than most patients with these conditions. A toxidrome, possibly caused by medication use or overdose, remained high on the differential diagnosis, as did a derangement of an electrolyte, such as potassium or magnesium.

Tests performed at the bedside and point-of-care laboratory testing may rapidly provide information about the cause of cardiac arrest. A fingerstick glucose test can be performed immediately to rule out hypoglycemia, and bedside ultrasonography facilitates the rapid assessment of left ventricular function and the identification of abnormalities such as cardiac tamponade, right ventricular strain, and pneumothorax. In this patient, the initial evaluation did not reveal the cause of the cardiac arrest. Blood samples were obtained for a complete blood count and measurement of electrolytes (including potassium, magnesium, and calcium), and blood and urine samples were obtained for toxicology screens.

While awaiting laboratory test results, empirical treatment for likely causes of cardiac arrest may be initiated. This can include the administration of glucose for potential hypoglycemia, magnesium for potential hypomagnesemia, and sodium bicarbonate for the management of potential toxic effects due to the use of a sodium-channel blocker. Given this patient's young age, the history of psychiatric illness, the fact that she had been known to be well 60 minutes earlier, the wide-complex rhythm, and the absence of an alternative diagnosis, we thought that the cardiac arrest had most likely been caused by a medication effect. We were particularly concerned about toxicity due to the use of a sodium-channel blocker, such as a tricyclic antidepressant, which is associated with altered mental status, prolongation of the QTc interval, and ventricular tachycardia. Therefore, we administered sodium bicarbonate empirically.

Dr. Dudzinski, do the findings on electrocardiography support our working diagnosis of tricyclic antidepressant overdose?

Dr. Dudzinski: In tricyclic antidepressant overdose, classic findings on electrocardiography are sinus tachycardia, a wide QRS complex, a prolonged QTc interval, and rightward shifts of the QRS complex, specifically the terminal forces (a finding that is in part manifested by a positive R wave in lead aVR).[2-4] All these findings were present on this patient's initial electrocardiogram, leading to a high level of suspicion for an acute toxidrome related to tricyclic antidepressant overdose. Other findings that may be seen in tricyclic antidepressant overdose include prolongation of the PR interval and a Brugada pattern.[5]

DR. JOSHUA N. GOLDSTEIN'S DIAGNOSIS

Tricyclic antidepressant overdose.

PATHOLOGICAL DISCUSSION

Dr. Grace Linder: The laboratory testing performed to support the diagnosis in this case was a blood toxicology screen. The basic blood toxicology screen at this hospital consists of quantitative assays that measure levels of acetaminophen, salicylates, and ethanol and a qualitative immunoassay that detects tricyclic antidepressants. Antibody-based immunoassays are widely used for monitoring drug use and have several advantages, including their rapidity, which is important when trying to identify potential toxicants in a critically ill patient such as this one.[6]

The immunoassay for tricyclic antidepressants involves a polyclonal mixture of antibodies directed against the most commonly prescribed tricyclics and their active metabolites. Thus, the immunoassay is nonspecific, and a positive test does not distinguish between single-drug and multidrug exposure. In addition, a positive test can result from tricyclic drug levels ranging from subtherapeutic to toxic and does not necessarily indicate toxicity.[7] Several drugs — including cyclobenzaprine, carbamazepine, and quetiapine — have structural similarities to the tricyclic class and are well-described causes of false positive immunoassays for tricyclic antidepressants.[8] Although diphenhydramine lacks the tricyclic rings, it has also been implicated as a cause of false positive tests.[8] Interpretation of a positive immunoassay for tricyclic antidepressants in

A patient with an unknown medication history (such as this patient) requires consideration of potential exposure to these interferents.

This patient's blood toxicology screen was positive for tricyclic antidepressants and for ethanol, and her urine toxicology screen was positive for cocaine. The diagnosis of tricyclic antidepressant overdose relies on clinicopathological correlation: in this case, the patient had symptoms consistent with toxicity due to the use of tricyclic antidepressants, as well as characteristic findings on electrocardiography and a positive blood immunoassay. Ultimately, two empty bottles of doxepin were found in her bedroom, and approximately 3000 mg of the drug was unaccounted for, which suggests that she took a dose of up to 46 mg per kilogram of body weight. A tricyclic dose of 10 to 20 mg per kilogram leads to clinically significant toxicity.

Dr. Virginia M. Pierce (Pathology): Dr. Erickson, after confirming the diagnosis of tricyclic antidepressant poisoning, how would you treat this patient?

DISCUSSION OF MANAGEMENT

Dr. Timothy B. Erickson: In patients with tricyclic antidepressant poisoning, close monitoring of vital signs and serial examinations for evidence of antimuscarinic toxicity and for cardiac and neurologic manifestations can be used to guide treatment strategies. As was seen in this patient, symptoms of tricyclic antidepressant toxicity usually develop within 60 minutes after ingestion, and major signs of toxicity are clinically apparent within 2 hours.[9] Among patients who are asymptomatic more than 6 hours after ingestion, symptoms are unlikely to develop; however, delayed toxic effects may occur, particularly if there are coingestants that delay gastrointestinal motility. Most fatalities occur within the first 24 hours after exposure.[9] Survival after ingestion of large doses of tricyclic antidepressants has been documented even after prolonged ventricular tachycardia with maximum resuscitation efforts.[10]

The first steps in the treatment of this patient would be securing control of the airway, ensuring adequate oxygenation and ventilatory support, and initiating resuscitation with intravenous isotonic crystalloid fluids. Then, the following principal management strategies would be considered: gastrointestinal decontamination, the administration of sodium bicarbonate, the administration of direct-acting vasopressors for the management of refractory hypotension, intravenous lipid emulsion therapy, extracorporeal supportive measures, and the administration of antiarrhythmic agents (Table 2).

GASTROINTESTINAL DECONTAMINATION

Because tricyclic antidepressant poisoning is potentially lethal, gastrointestinal decontamination with activated charcoal may be considered if the patient is alert and cooperative and presents within 1 hour after ingestion with no overt signs of acute toxicity. Activated charcoal could not be administered in this patient because of her altered mental status and the risk of pulmonary aspiration. Decontamination with gastric lavage is no longer recommended.

SODIUM BICARBONATE

Sodium bicarbonate, which was administered empirically in this patient by EMS personnel and in the emergency department, is the cornerstone of treatment for patients with tricyclic antidepressant poisoning. The administration of sodium bicarbonate is indicated in patients who have hemodynamic instability or a QRS width that exceeds 100 msec.[18] This patient was hypotensive, with a blood pressure of 60/24 mm Hg, and the QRS width was up to 220 msec. On the basis of these findings, she met the criteria for the administration of sodium bicarbonate.

Tricyclic antidepressant–induced sodium-channel blockade, which is indicated by a QRS width of more than 100 msec, is predictive of seizures; a QRS width of more than 160 msec is predictive of arrhythmias.[19] The electrocardiographic findings of an R/S ratio in lead aVR of more than 0.7 and an R-wave height in lead aVR of more than 3 mm are also predictive of seizures and arrhythmias.[20] In patients who have these signs, the administration of sodium bicarbonate alkalinizes the blood, alters polarization of the cells, and increases protein binding, thereby reducing free drug levels. It also stabilizes the myocardial sodium channels by increasing the sodium level, thereby overriding sodium-channel blockade.[13]

The dose of sodium bicarbonate can vary.[13,14] Patients with severe tricyclic antidepressant poi-

Table 2. Management of Tricyclic Antidepressant Overdose.

Strategy	Recommendation
Stabilization	Initiate airway control, oxygenation, ventilatory support, and resuscitation with intravenous isotonic crystalloid fluids.
Gastric decontamination[11,12]	Perform if the patient is alert and cooperative and presents within 1 hour after ingestion with no overt signs of toxicity. Administer oral activated charcoal at a dose of 50 to 100 g (or 1 g per kilogram of body weight) if the tricyclic antidepressant dose is unknown. If the tricyclic antidepressant dose is known, administer oral activated charcoal at a dose of 10 g per 1 g of tricyclic antidepressant or until the treatment causes unacceptable side effects.
Sodium bicarbonate administration[13-15]	Administer if the patient has hemodynamic instability or a QRS width of >100 msec. Other indications are an R/S ratio in lead aVR of >0.7, an R-wave height in lead aVR of >3 mm, and rightward deflection in the terminal portion of the QRS complex of 40 msec. In adults, administer intravenous sodium bicarbonate at a loading dose of 50 to 100 meq (i.e., one to two 50-ml ampules of 8.4% solution) and assess for QRS narrowing. This dose may be repeated if QRS narrowing does not occur. Then administer a continuous infusion of 150 meq of sodium bicarbonate mixed with 1 liter of water with 5% dextrose, at a rate of 150 to 250 ml per hour, until the pH in arterial blood is 7.45 to 7.55, while monitoring the potassium level. (An alternative solution is 150 meq of sodium bicarbonate and 40 meq of potassium mixed with 850 ml of water with 5% dextrose.)
Vasopressor administration	Administer if the patient has tricyclic antidepressant–induced hypotension that is refractory to treatment with crystalloid fluids and sodium bicarbonate. In adults, administer a continuous infusion of norepinephrine at an initial rate of 8 to 12 μg per minute. (The usual maintenance rate is 2 to 4 μg per minute.) Increase the rate every 5 minutes, up to a maximum rate of 0.5 to 1.5 μg per kilogram per minute, until the mean arterial pressure is >65 mm Hg or the systolic blood pressure is >90 mm Hg. Alternatively, administer a continuous infusion of epinephrine at an initial rate of 1 μg per minute. Those with severe cardiac dysfunction may receive the infusion at a rate of >10 μg per minute, up to a maximum rate of 20 μg per minute in a patient who weighs 70 kg.
Intravenous lipid emulsion therapy[16,17]	Consider in patients with hemodynamic instability that is refractory to the interventions described above. Do not use as first-line therapy. In adults, administer an infusion of 20% solution, at a dose of 1.5 ml per kilogram or 100 ml, over a period of 2 to 3 minutes. Then administer an infusion of 20% solution, at a rate of 0.25 ml per kilogram per minute. After 3 minutes, assess for a response. If there is a response, the infusion rate may be adjusted to 0.025 ml per kilogram per minute (10% of the initial rate).
Antiarrhythmic-agent administration	In patients with a prolonged corrected QT interval, administer intravenous magnesium (1 to 2 g). Alternatively, administer a class IB agent, such as lidocaine (1 to 1.5 mg per kilogram). Use caution in patients with seizure activity.
Other considerations	Consider extracorporeal membrane oxygenation and plasmapheresis. In patients who have had cardiac arrest with a return of spontaneous circulation, consider therapeutic hypothermia.
Management of seizures	In adults, administer intravenous benzodiazepine: lorazepam (1 to 2 mg) or diazepam (5 to 10 mg). Alternatively, administer intravenous midazolam (loading dose, 0.2 mg per kilogram; rate of maintenance infusion, 0.05 to 2 mg per kilogram per hour). In patients with refractory seizures, administer intravenous phenobarbital (loading dose, 15 to 20 mg per kilogram) or propofol (loading dose, 1 to 2 mg per kilogram; rate of maintenance infusion, 0.1 to 0.2 mg per kilogram per minute). In those with intractable seizures, a rapid sequence that involves the administration of induction agents followed by the initiation of airway control, intubation, and therapeutic paralysis is recommended.
Agents to avoid	Avoid class IA (procainamide), class IC (flecainide), and class III (beta-blockers) antiarrhythmic agents. Reserve physostigmine for symptomatic patients who have overdose of a pure anticholinergic drug and have a normal QRS complex and corrected QT interval. Use of flumazenil can cause seizures in patients who are receiving long-term benzodiazepine therapy or a proconvulsant drug.

soning may need large amounts of sodium bicarbonate to facilitate resuscitation.[21] This therapy is associated with a risk of hypokalemia, and therefore, frequent monitoring of the potassium level and appropriate repletion are recommended. Given the ongoing shortage of sodium bicarbonate in the United States that began in early 2017, adjunct but less effective therapies for tricyclic antidepressant poisoning with associated cardiac toxicity may be administered. These include therapeutic hyperventilation to an arterial blood pH of 7.50 to 7.55 (especially if hypernatremia is a concern) or the administration of hypertonic saline (3% in adults) after the patient's arterial blood pH has reached the maximal alkaline level.

VASOPRESSORS

In patients with tricyclic antidepressant–induced hypotension that is not responsive to aggressive fluid resuscitation or to the intravenous administration of sodium bicarbonate, direct-acting vasopressors may be administered. Because tricyclic antidepressants cause peripheral alpha-adrenergic blockade, norepinephrine and epinephrine are preferred over dopamine. Although dopamine was administered in this patient by EMS personnel, I would recommend switching to another agent, such as norepinephrine, after the patient's arrival in the emergency department.

INTRAVENOUS LIPID EMULSION THERAPY

Intravenous lipid emulsion therapy has emerged as a rescue intervention for toxicity due to local anesthetic agents and has also gained acceptance as a potential treatment for overdoses of other lipid-soluble drugs, including tricyclic antidepressants. The most widely accepted proposed mechanism of action is the creation of a "lipid sink" in the intravascular compartment, which sequesters lipophilic drugs and reduces their bioavailability. Other proposed mechanisms include facilitation of the use of myocardial free fatty acid, decreased nitric oxide–induced vasodilatation, and generalized cardiotonic effects.[22]

It is unclear whether intravenous lipid emulsion therapy is efficacious in the context of tricyclic antidepressant poisoning,[23,24] but some case reports suggest that it may be of benefit.[25-28] Intravenous lipid emulsion therapy may be considered in hemodynamically unstable patients with tricyclic antidepressant overdose who do not have a response to standard doses of sodium bicarbonate and vasopressors; it should not be used as first-line therapy.[29,30] Given that this patient had persistent hemodynamic instability despite receiving conventional therapy, it would be reasonable to initiate intravenous lipid emulsion therapy. Of note, this therapy causes interference in many blood tests, potentially causes pancreatitis and the acute respiratory distress syndrome, and may reduce the effectiveness of other antidotes.[31,32] Therefore, a risk–benefit assessment of this therapy should be performed on a case-by-case basis.[32]

EXTRACORPOREAL SUPPORTIVE MEASURES

Since tricyclic antidepressants are highly protein-bound and have an extensive volume of distribution, enhanced elimination with an extracorporeal method, such as hemodialysis or hemoperfusion, is generally ineffective.[33] Some reports indicate that plasmapheresis[28] and extracorporeal membrane oxygenation may be useful and potentially lifesaving if they are instituted early after ingestion of a large dose of tricyclic antidepressants with associated hemodynamic instability.[34] Current guidelines recommend therapeutic hypothermia for patients who are unconscious after out-of-hospital cardiac arrest with a return of spontaneous circulation, because this therapy may improve functional neurologic outcomes. A recent report suggests that mild therapeutic hypothermia is safe even after intoxication with a drug known to cause serious cardiac conduction disturbances and arrhythmia, such as a tricyclic antidepressant.[35] Therefore, therapeutic hypothermia would be a reasonable strategy to consider in this patient.

ANTIARRHYTHMIC AGENTS

Antiarrhythmic agents that can be used for the treatment of patients with tricyclic antidepressant poisoning include intravenous magnesium (if there is evidence of a prolonged QTc interval) and class IB antiarrhythmics, such as lidocaine.[36] However, lidocaine should be administered cautiously in patients with seizures. Class IA and IC antiarrhythmics should be avoided. Class III agents, such as beta-blockers and amiodarone, may exacerbate hypotension and conduction abnormalities,[33] although one study in animals showed no harmful effects from amiodarone in tricyclic antidepressant poisoning.[37]

OTHER CONSIDERATIONS

Of note, tricyclic antidepressants not only have anticholinergic properties but also lead to alpha-receptor antagonism, norepinephrine-reuptake blockade, and sodium-channel inhibition. Therefore, administration of an anticholinesterase drug such as physostigmine in a patient with tricyclic antidepressant poisoning would be less effective than usual and potentially detrimental. The acetylcholinesterase inhibitor physostigmine is clinically efficacious in symptomatic patients who have poisoning due to a pure anticholinergic drug and have a normal QRS complex (e.g., those with diphenhydramine toxicity),[38-40] but the use of this agent should be avoided in patients with tricyclic antidepressant overdose, particularly in those who have bradycardia or bundle-branch block and have atrioventricular block with a wide QRS complex or a prolonged QTc interval.[15] In such patients, rare adverse effects, such as complete heart block and asystole, have been reported.[41]

Tricyclic antidepressant poisoning can cause seizures. These are typically self-limited and resolve with the administration of intravenous benzodiazepines. For refractory seizures, phenobarbital or propofol may be indicated.[33] If the seizures are intractable, a rapid sequence that involves the administration of induction agents followed by the initiation of airway control, intubation, and therapeutic paralysis is recommended to avoid worsening metabolic acidosis from lactic-acid production and accumulation. Acidosis decreases protein binding and increases the free drug level of tricyclic antidepressants, leading to increased neurologic and cardiac toxicity.

Dr. Pierce: Dr. Cleveland, would you tell us what happened with this patient?

Dr. Cleveland: On the patient's arrival in the emergency department, intravenous fluids were administered, dopamine was stopped, and a continuous infusion of norepinephrine was begun. Sodium bicarbonate was administered, both in intermittent doses and as a continuous infusion. The patient's pulse was weak and then was lost. After CPR was performed and epinephrine and additional doses of sodium bicarbonate were administered, spontaneous circulation returned. The patient was noted to have twitching movements, and midazolam was administered for suspected seizures. After hemodynamic stabilization was achieved, therapeutic hypothermia was initiated. Once the results of the blood toxicology screen became available, management decisions were made in consultation with poison control experts. Electrocardiography continued to show a wide-complex rhythm. The administration of sodium bicarbonate was continued, and intravenous lipid emulsion therapy and therapeutic hyperventilation were begun. Arterial blood gas measurements were obtained and electrocardiography was performed on an hourly basis.

Dr. Pierce: Dr. Dudzinski, how did the findings on electrocardiography change during this patient's treatment?

Dr. Dudzinski: When a patient with tricyclic antidepressant poisoning is treated with sodium bicarbonate, there are decreases in the QRS width, the R-wave height and R/S ratio in lead aVR, and the QTc interval, and the frontal-plane axis of the QRS complex becomes less rightward. Three hours after this patient's presentation, after she had received treatment with sodium bicarbonate (600 meq) and intravenous lipid emulsion therapy, the QRS width had decreased to 140 msec, the R-wave height in lead aVR had decreased, atrial activity had become visible (with probable sinus tachycardia at a rate of 110 beats per minute and with a first-degree atrioventricular delay), and the frontal-plane axis had become less rightward (Fig. 2A). By 7 hours after presentation, the R/S ratio in lead aVR had become negative. By 24 hours after presentation, the heart rate had decreased to 84 beats per minute and the QRS width was approximately 110 msec (Fig. 2B).[42]

Dr. Cleveland: The patient was admitted to the medical intensive care unit, where continuous infusions of sodium bicarbonate, norepinephrine, midazolam, and hydromorphone were administered. On the second hospital day, at which point the results on electrocardiography had normalized, sodium bicarbonate was discontinued; on the third hospital day, the patient was rewarmed. She was also treated for aspiration pneumonia. The hypotension had resolved by the third hospital day, and the next day, the patient was extubated. Thereafter, she was treated for both delirium and presumed alcohol withdrawal.

Additional interviews revealed that the patient had had two previous hospitalizations that followed suicide attempts. She had been abstinent

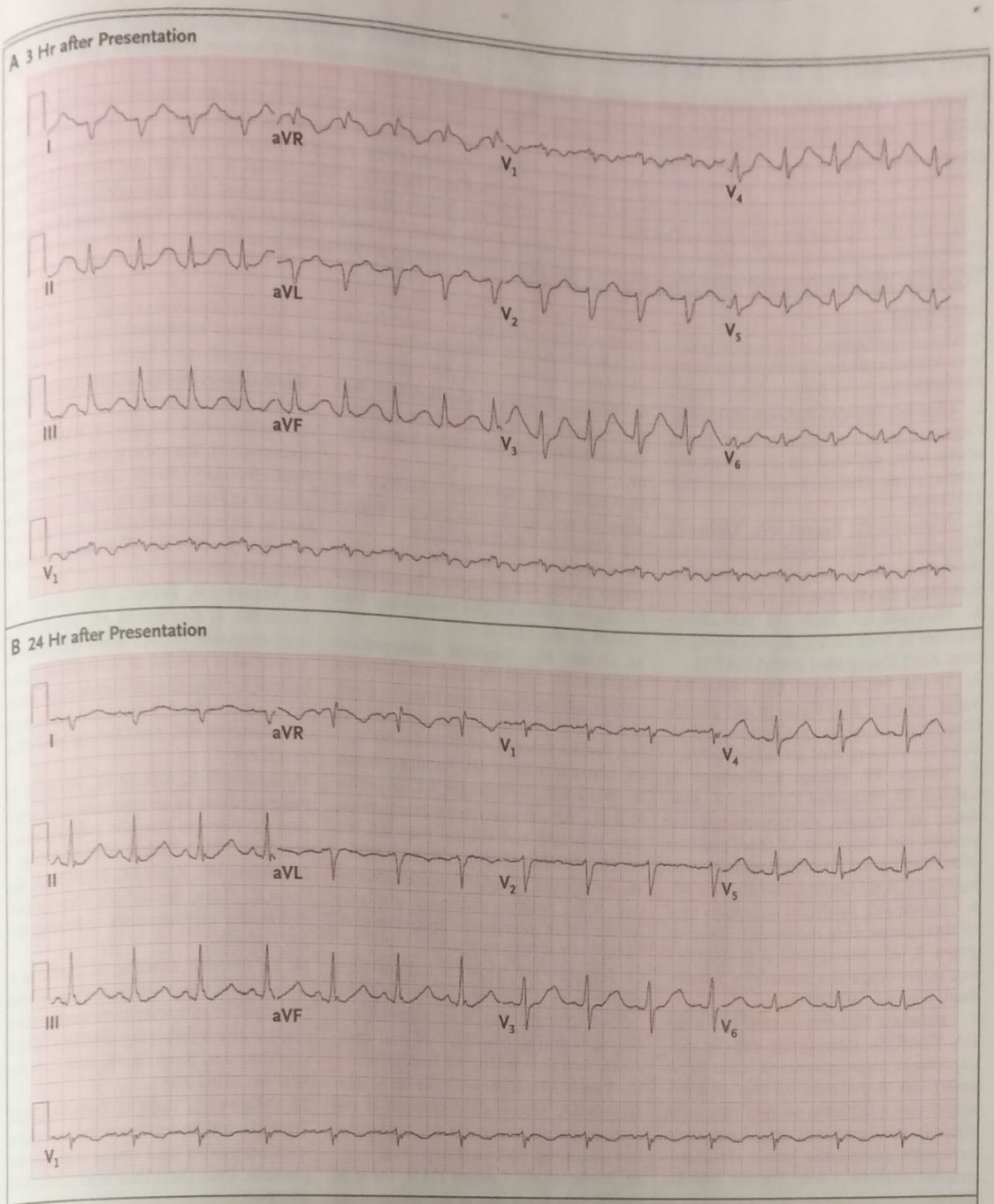

Figure 2. Follow-up Electrocardiograms.

On an electrocardiogram obtained 3 hours after presentation (Panel A), the QRS width has decreased to 140 msec, the R-wave height and R/S ratio in lead aVR have decreased, atrial activity has become visible (with probable sinus tachycardia at a rate of 110 beats per minute and with a first-degree atrioventricular delay), and the frontal-plane axis has moved from northwest to become less rightward. On an electrocardiogram obtained 24 hours after presentation (Panel B), the heart rate has decreased to 84 beats per minute and the QRS width is 110 msec. These findings are consistent with reversal of the toxic effects of tricyclic antidepressants on electrocardiography.

from illicit-drug use for 5 years, until relapsing 2 months before this admission. During those 2 months, she had felt hopelessness and had stopped taking her psychiatric medications.

On the 10th hospital day, the results of magnetic resonance imaging of the head and a neurologic examination were normal, and the patient was transferred from this hospital to an inpa-

tient psychiatric facility. The patient declined inpatient treatment for substance abuse. After 10 days of inpatient psychiatric care, she was discharged home.

FINAL DIAGNOSIS

Tricyclic antidepressant overdose due to doxepin ingestion.

This case was presented at Emergency Medicine Grand Rounds.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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