



Electrocardiographical case. A man found unconscious

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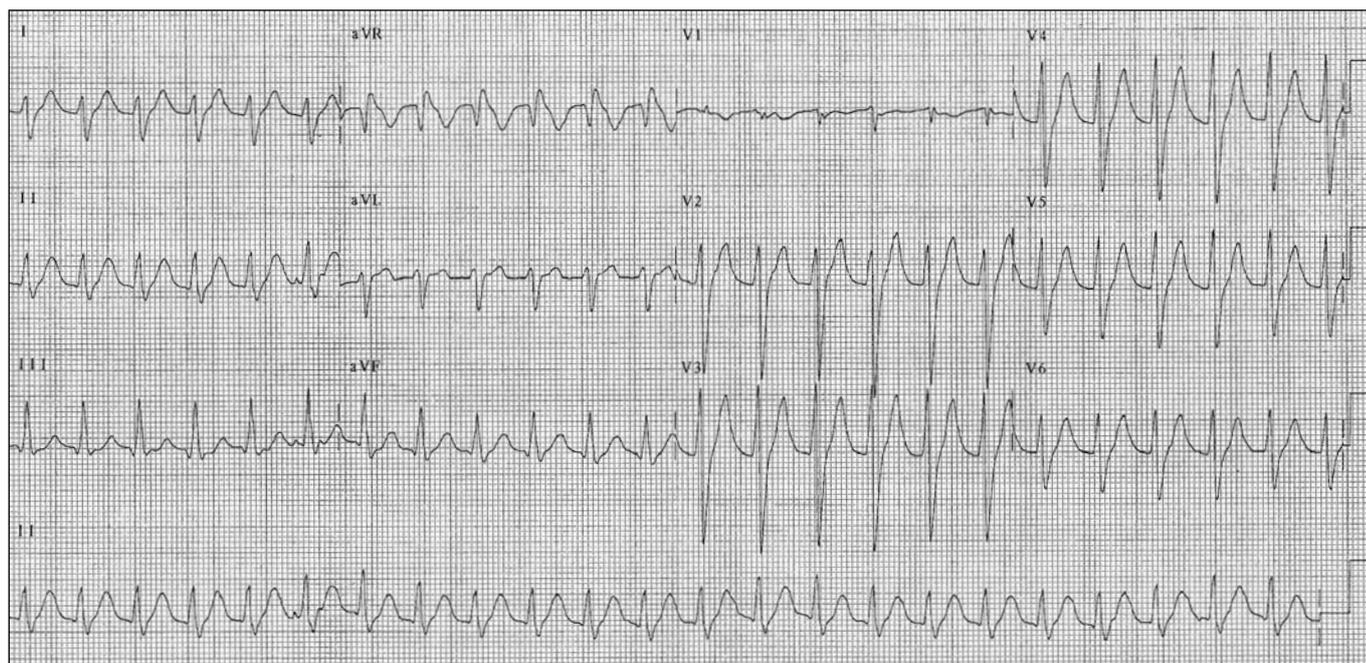


Fig. 1 ECG obtained on arrival.

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CLINICAL PRESENTATION

A 25-year-old man was found lying on the pavement late at night. He was unresponsive, and brought to the hospital. On examination, his vital signs were: body temperature 37.3°C, heart rate 140/min, respiratory

rate 20/min, and blood pressure 95/60 mmHg. The patient's Glasgow Coma Scale was three. His bedside blood glucose level was 4.8 mmol/L. Electrocardiography (ECG) (Fig. 1) was done. What does his ECG show? What is your diagnosis?

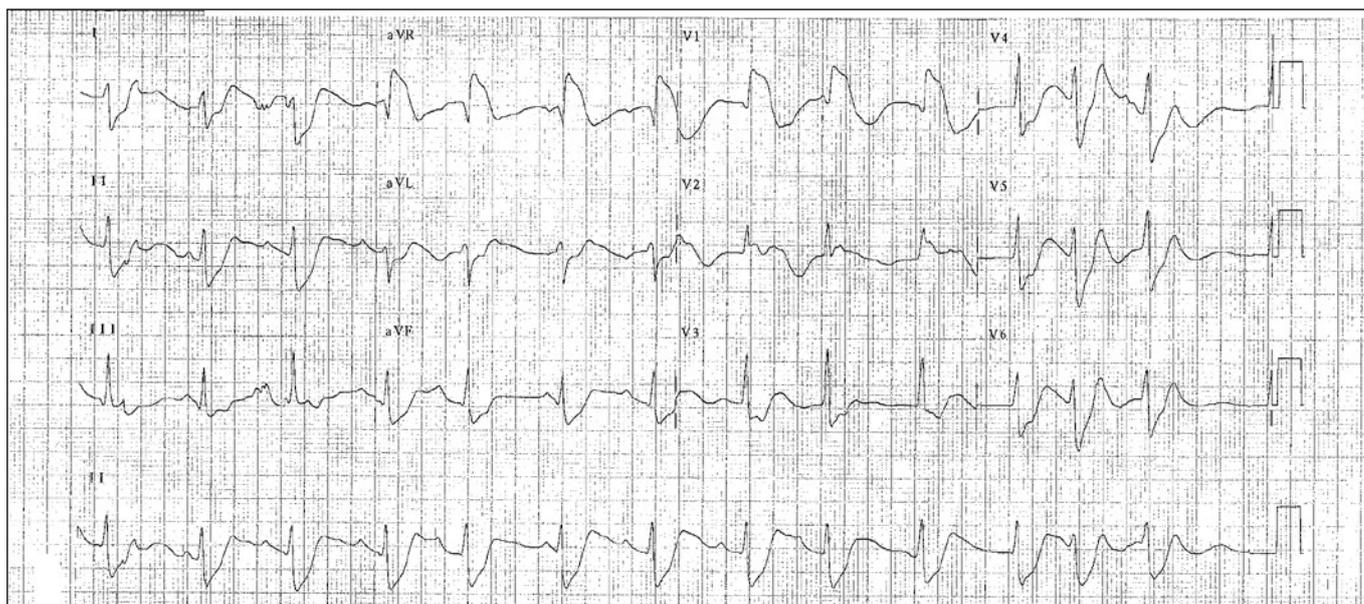


Fig. 2 ECG (obtained at 58 min after arrival) shows that the QRS complexes have widened further. Note the positive terminal R wave in lead aVR, and the negative S wave in lead I.

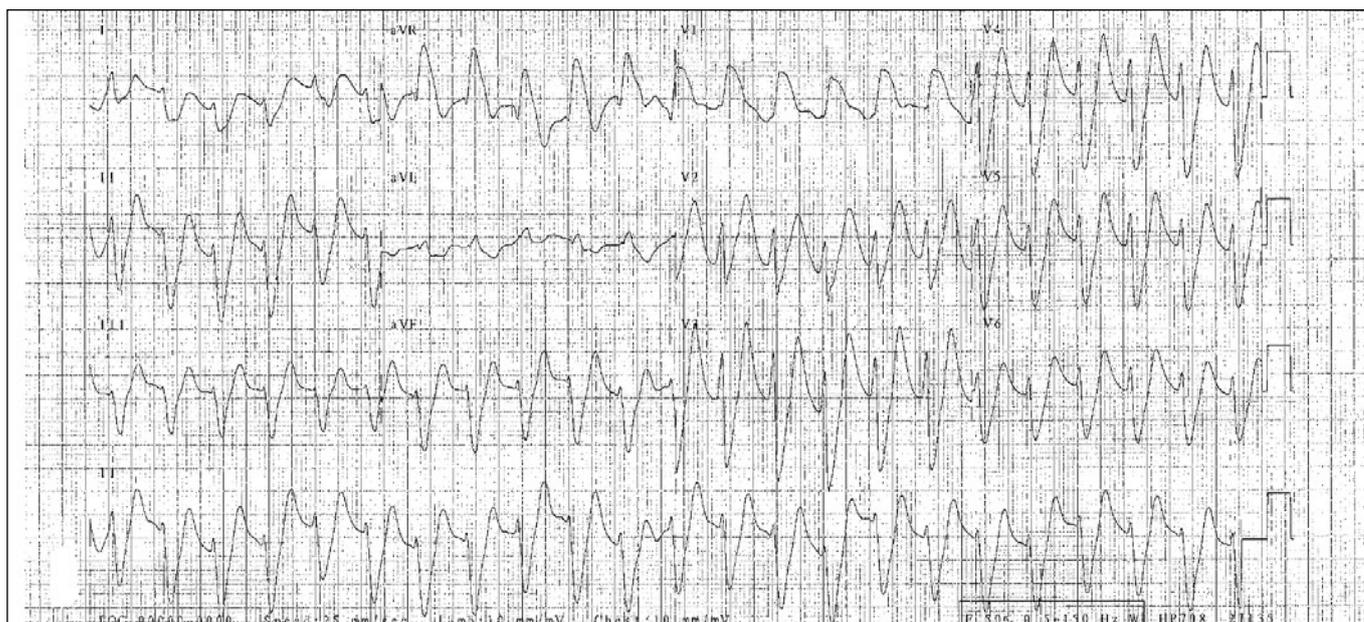


Fig. 3 ECG (obtained at 63 min after arrival) shows that the patient has gone into ventricular tachycardia.

ECG INTERPRETATION

The ECG (Fig. 1) showed sinus tachycardia of rate 140/min. There was right axis deviation. The QTc was prolonged at 490 ms, and the QRS complexes widened at 137 ms. There was a positive R wave (3 mm) in lead aVR.

DIAGNOSIS

Tricyclic antidepressant overdose.

CLINICAL COURSE

The patient was managed in the resuscitation room, with haemodynamic and continuous cardiac monitoring. The patient's airway was secured with endotracheal intubation. He was mechanically ventilated. A large-bore nasogastric tube was inserted and gastric lavage performed. Activated charcoal 50 g was also administered, via nasogastric tube.

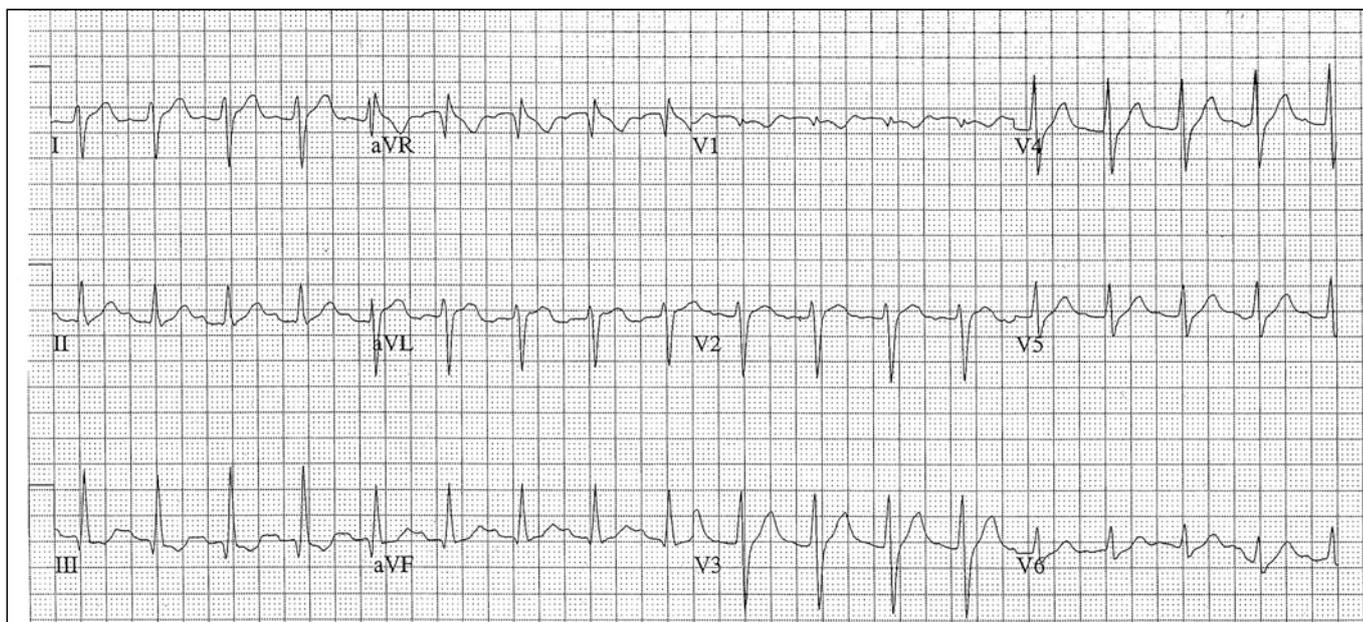


Fig. 4 ECG (obtained at 2 hours after arrival) shows resolution of the widened QRS complexes, although the QTc remains prolonged at 480 ms. The negative S wave in lead I remains while the positive R wave in lead aVR is less now.

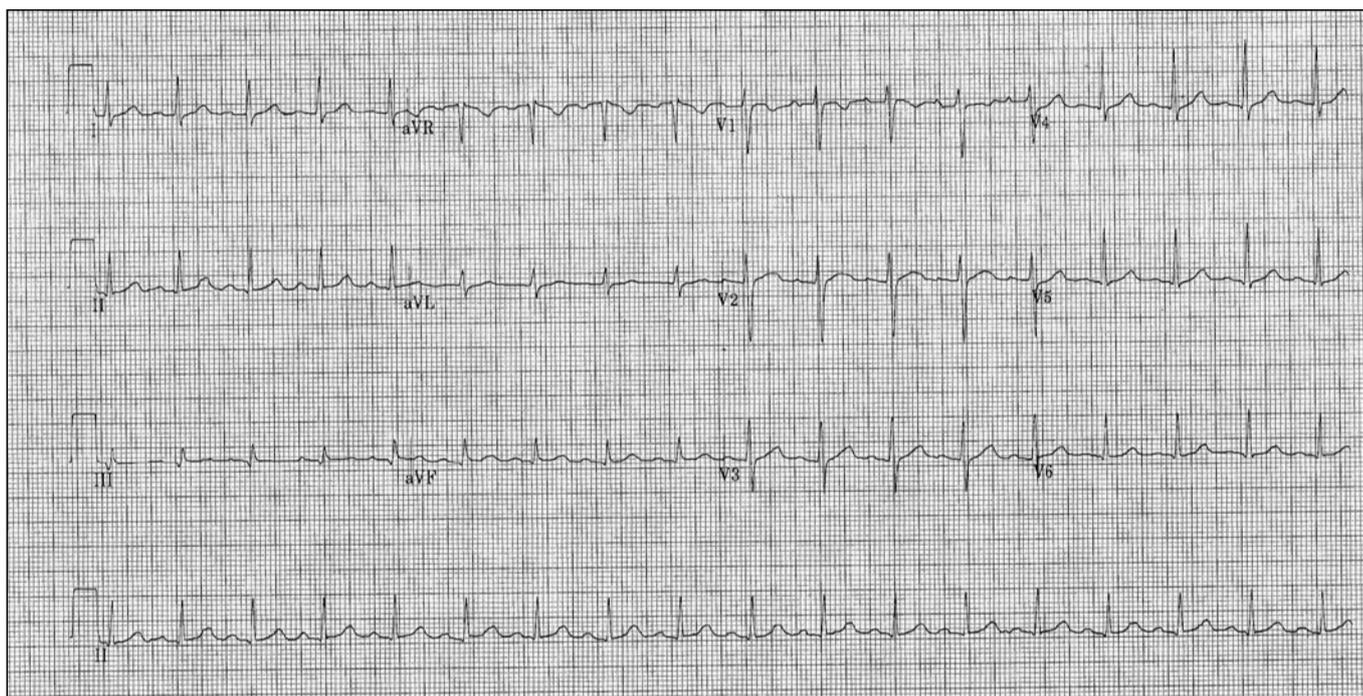


Fig. 5 ECG (on day 4) shows a sinus rhythm. The axis is now normal. The QRS interval has reduced to 422 ms, and note the normal R wave in lead I and S wave in lead aVR.

The patient was also started on sodium bicarbonate therapy consisting of intravenous (IV) 8.4% NaHCO₃ 50 ml over 30 min. Arterial blood gases were closely monitored, and a urinary catheter was placed. The patient had a generalised seizure, which was aborted with IV Diazepam 10 mg. Subsequent ECGs (Figs. 2 & 3) showed further progression.

The patient was given synchronised biphasic cardioversion at 150 J. He was also given another cycle of IV sodium bicarbonate therapy. Repeat ECG (Fig. 4) showed resolution of the widened QRS complexes. The patient was then admitted to the medical intensive care unit (MICU). Repeat ECG on day four showed a sinus rhythm and normal axis (Fig. 5).

The patient was well when discharged. Toxicology studies subsequently showed a toxic amitriptyline level of 2.6 mcg/ml (therapeutic levels <0.3 mcg/ml; Increased risk for developing seizures and cardiotoxicity at levels >1.0 mcg/ml).

DISCUSSION

Tricyclic antidepressants (TCAs) are used primarily to treat major depression. Their other uses are for the treatment of psychiatric conditions such as obsessive-compulsive disorder, attention-deficit disorder, panic and phobia disorders, anxiety disorders and eating disorders, and medical conditions such as chronic pain syndromes, peripheral neuropathies, nocturnal enuresis, migraine headache prophylaxis, and selected drug withdrawal therapies⁽¹⁾.

In Singapore, the commonly-prescribed TCAs are amitriptyline, imipramine, clomipramine, dothiepin and nortriptyline. Although the TCAs possess many pharmacological effects, viz.,

1. Anticholinergic effects-antihistamine and antimuscarinic effects;
2. Inhibition of alpha-adrenergic receptors;
3. Inhibition of amine uptake;
4. Sodium channel blockade;
5. Potassium channel antagonist;
6. Gamma-aminobutyric acid (GABA) receptor antagonist⁽¹⁾;

only a few, such as inhibition of amine uptake (noradrenaline and serotonin), have a direct therapeutic effect. The rest contribute to adverse and potentially life-threatening effects in overdoses.

The single most important factor contributing to mortality in TCA poisoning is TCA-induced cardiotoxicity. The ECG changes associated with TCA poisoning are brought about by two effects, namely: the inhibition of the efflux of potassium ions during repolarisation (potassium channel antagonist), and the inhibition of sodium influx through voltage-dependent sodium channels (sodium channel blockade), of which the latter contributes a significant role in mortality. The effect of potassium channel blockade during repolarisation is seen as prolonged QTc on the ECG. Many TCA overdose patients develop sinus tachycardia, which is partially protective against severe QTc interval prolongation. Torsades de pointes, as a complication of prolonged QTc, is rare in TCA overdose⁽²⁾.

Life-threatening cardiotoxicity results from TCA-induced inhibition of sodium influx. This results in decreased contractility, and prolongation of phase 0 of the action potential, the effect of which is more pronounced with rapid heart rates, hyponatraemia and acidosis. On ECG, this is seen as prolongation of PR and QRS intervals and right axis deviation (RAD), manifest by a terminal R wave in lead aVR and an S wave in lead I.

Although not validated, the following ECG markers are thought to be predictive of arrhythmias, seizures and death^(3,4):

- QRS duration >100 ms
- QTc interval >430 ms
- RAD of 120-270 degrees in the terminal 40 ms frontal plane QRS vector
- R/S ratio >0.7 in lead aVR
- R wave in lead aVR >3 mm⁽⁵⁾

Sodium channel blockade can be overcome in part by serum alkalinisation (pH 7.50-7.55) and increasing sodium concentration. Hence, sodium bicarbonate therapy is employed as it does both. Thus, on top of the supportive management of securing patient's airway, breathing and circulation, gastrointestinal decontamination with activated charcoal and gastric lavage, managing complications (e.g. non-arrhythmic-seizures with benzodiazepines, which are GABA enhancers), sodium bicarbonate therapy remains the cornerstone in the management of life-threatening cardiotoxic effects of TCA overdose.

ECG abnormalities develop within six hours of ingestion, and usually resolve over 36-48 hours. Generally, therapy is started when QRS prolongation is greater than 100 ms. Hyperventilation therapy is a reasonable alternative to sodium bicarbonate in the setting of renal failure, pulmonary oedema or cerebral oedema. The ECG changes of widened QRS and RAD can be seen in toxicity with other drugs, such as carbamazepine, diphenhydramine and class IA anti-arrhythmics. In the emergency room, the initial treatment is identical. Thus, in the setting of an unconscious patient with the presenting ECG, treatment should not be delayed until definitive drug levels become available.

ABSTRACT

A 25-year-old man was brought to the emergency room after being found unconscious. Electrocardiography (ECG)

showed changes classical of tricyclic antidepressant (TCA) poisoning. These included sinus tachycardia, QTc prolongation, QRS complex widening, right axis deviation and positive R waves in lead aVR. This unique ECG highlights the importance of lead aVR, which often tends to be ignored. Treatment is started based on ECG findings.

Keywords: electrocardiogram, poisoning, sodium bicarbonate, tricyclic antidepressants

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

Multiple Choice Questions (Code SMJ 200608B)

	True	False
Question 1: The following are ECG features of tricyclic antidepressant (TCA) poisoning:		
(a) 1st degree heart block.	<input type="checkbox"/>	<input type="checkbox"/>
(b) QRS complex widening.	<input type="checkbox"/>	<input type="checkbox"/>
(c) QT interval narrowing.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Left axis deviation.	<input type="checkbox"/>	<input type="checkbox"/>
Question 2: Regarding ECG changes of TCA poisoning:		
(a) Changes are caused by inhibition of sodium channels.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Ventricular tachycardia is a known complication.	<input type="checkbox"/>	<input type="checkbox"/>
(c) R wave in lead aVR >3 mm is a feature.	<input type="checkbox"/>	<input type="checkbox"/>
(d) May be explained by inhibition of potassium channels during depolarisation.	<input type="checkbox"/>	<input type="checkbox"/>
Question 3: The following are possible complications of TCA poisoning:		
(a) Seizures.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Coma.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Acute myocardial infarction.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Arrhythmias.	<input type="checkbox"/>	<input type="checkbox"/>
Question 4: Regarding the treatment of TCA poisoning:		
(a) Diagnosis must be confirmed by toxic serum levels before treatment is initiated.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Activated charcoal is the mainstay of treatment.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Sodium bicarbonate therapy is initiated when there is QRS complex widening.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Hyperventilation therapy may be used in cases of renal failure.	<input type="checkbox"/>	<input type="checkbox"/>
Question 5: The following statements are true:		
(a) Amitriptyline belongs to the class of TCAs.	<input type="checkbox"/>	<input type="checkbox"/>
(b) TCAs are used to treat major depression.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Inhibition of amine uptake by TCAs contribute to their therapeutic effects.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Serum alkalisation and increasing sodium concentration are important to overcome the cardiotoxic effects of TCA poisoning.	<input type="checkbox"/>	<input type="checkbox"/>

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

Submission instructions:**A. Using this answer form**

1. Photocopy this answer form.
2. Indicate your responses by marking the "True" or "False" box
3. Fill in your professional particulars.
4. Post the answer form to the SMJ at 2 College Road, Singapore 169850.

B. Electronic submission

1. Log on at the SMJ website: URL <<http://www.sma.org.sg/cme/smj>> and select the appropriate set of questions.
2. Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

Deadline for submission: (August 2006 SMJ 3B CME programme): 12 noon, 25 September 2006**Results:**

1. Answers will be published in the SMJ October 2006 issue.
2. The MCR numbers of successful candidates will be posted online at <http://www.sma.org.sg/cme/smj> by 15 October 2006.
3. All online submissions will receive an automatic email acknowledgment.
4. Passing mark is 60%. No mark will be deducted for incorrect answers.
5. The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.