Early and prolonged ECG alterations resembling a myocardial injury after severe amitriptyline poisoning

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ABSTRACT

Evidence of cardiovascular toxicity is present in the majority of tricyclic antidepressant overdoses. We report the case of a 63-year-old woman admitted to our department with a severe amitriptyline poisoning. The ECG at admission showed a pattern mimicking an acute anteroseptal subepicardial infarction.
This pattern persisted for 11 days. Myocardial enzymes and echocardiographic findings never confirmed an ischemic event. At discharge, the ECG returned normal without cardiac or neurologic sequelae.
Our experience suggest that after severe tricyclic antidepressant ingestion, ECG alterations resembling myocardial injury may occur early and last for a longer period than previously reported.

Keywords: *tricyclic antidepressant poisoning, amitriptylin overdose, ECG abnormalities, myocardial infarction.*

CASE REPORT

A 63-year-old woman was admitted to our Intensive Care Unit (ICU) four hours after ingesting 7000 mg of amitriptyline as a suicide attempt. She had no history of diabetes, heart disease or other illness, except for a major depressive syndrome, treated with amitriptyline and clomipramine.
She was found at home comatose (Glasgow Coma Score 3) with normal pupils reactive to light. Blood pressure was 90/80, the heart rate was 110 beats/min and the SpO_2 was 80%. In the Emergency Room, she was tracheally intubated and was admitted to the ICU. Aiming to remove as more pills as possible, a gastric lavage was performed, followed by the administration of active charcoal.
Arterial blood gases, pH, serum electrolytes and myocardial enzymes were normal. Toxicological studies were negative for other substance abuse. A baseline ECG tracing obtained from a previous admission to hospital for a surgical intervention was available for comparison. It showed a sinus tachycardia and an anterior left hemiblock.
The 12-lead ECG (Figure 1, column 2) on admission showed sinus tachycardia, anterior left hemiblock, prolonged QT interval (360 ms), QRS widening (140 ms) and a marked ST tract elevation in leads V1-V6 and aVR.
The terminal 40 ms of the frontal plane QRS vector (T40ms) did not show remarkable variations from the baseline ECG tracing. The pattern reported was consistent with an acute anteroseptal subepicardial infarction along with a possible Brugada syndrome.

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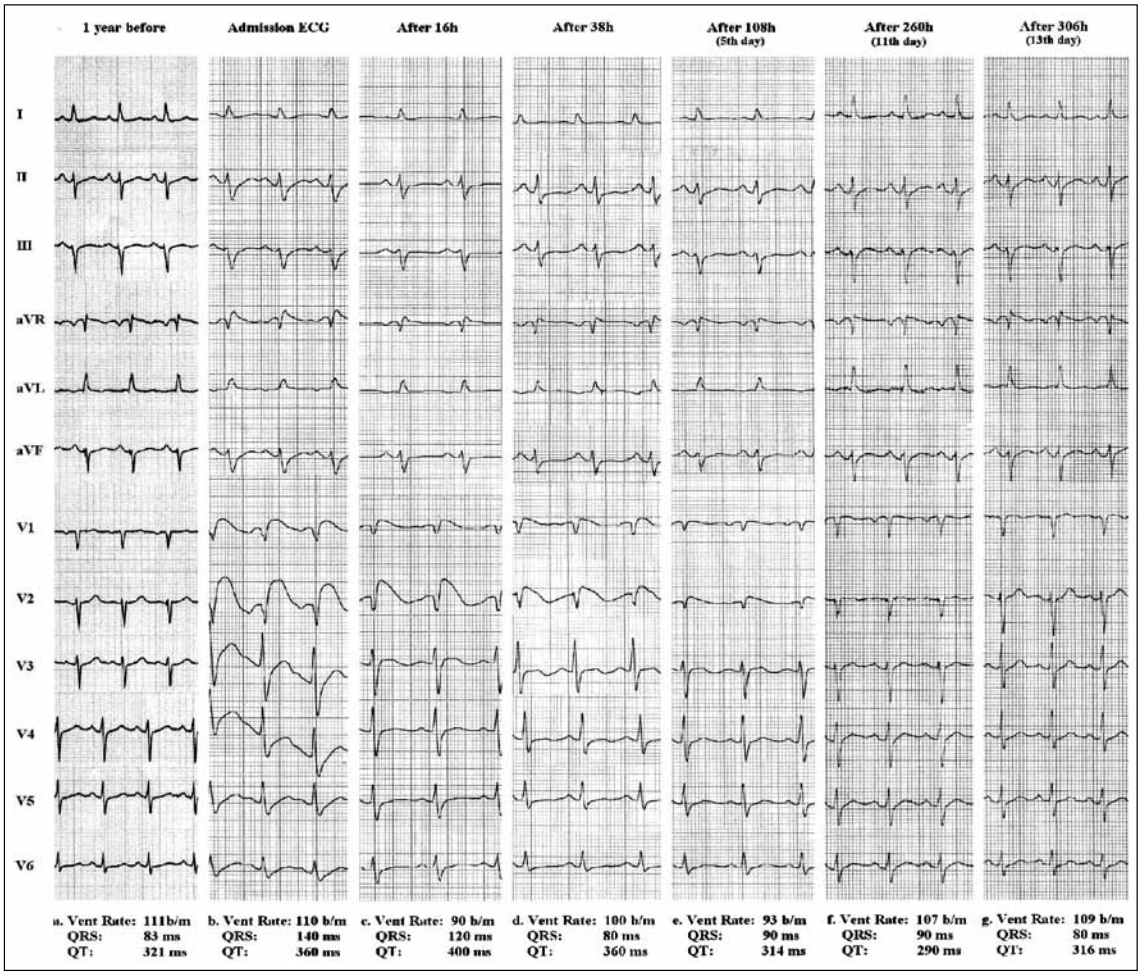

Figure 1 - *Serial ECGs recorded during hospitalisation.*

Echocardiographic findings, including ventricular segmental kinesis, were normal. No episodes of arrhythmias were recorded. Serial ECG showed abnormal ventricular repolarization, mimicking a myocardial injury for eleven days. Measurements of creatine kinase (CK), CK isoenzyme MB and troponin T were always normal.

The patient was administered intravenous sodium bicarbonate 8,4 % for four days and underwent mechanical ventilation for ten days. She was progressively weaned from mechanical ventilation, extubated and discharged to a Medical ward after eleven days free of cardiovascular and neurologic sequelae. After twelve days her blood levels of amitriptyline were still above the therapeutic range (490 ng/ml; normal values between 100-250 ng/ml) but ECG abnormalities were no longer present (Figure 1, column 1 and column 7).

DISCUSSION

TCA overdose accounts for 25 % of severe drug abuse, with a mortality rate up to 10 % (1). It is known that TCA can induce car-

diac electrical alteration at therapeutic or toxic serum levels.

The mechanism of toxicity is related to four pharmacological actions: an anticholinergic effect, a α1-antiadrenergic action, the adrenergic reuptake inhibition at nerve terminals and the fast sodium channel blockade, acting with a quinidine-like effect in the heart (2).

A recent study showed that the action of tryciclic antidepressant on intracellular calcium handing in cardiac myocytes likely involves direct effects on calsequestrin (CSQ), type 2 ryanodine receptor channel (RyR), and sarcoplasmic reticulum Ca^{++}-ATPase (SERCA) (3). It has been suggested that augmentation of RyR mediated Ca^{++} leak can lead to proarrhythmogenic delayed or early after depolarizations that are common features of the failing heart (4).

The longer action of TCA to promote sarcoplasmic reticulum Ca^{++} depletion would most likely lead to negative inotropism. Common alterations include sinus tachycardia, prolongation of the PR, QRS and QT intervals, usually returning normal after four days (5, 6).

As previously reported (5, 6), in the present case the QT fully recovered after 108 hours, while QRS duration remained above 100 ms for only 38 hours, probably due to early administration of sodium bicarbonate.

Experimental data suggest that cardiac arrhythmias and broad QRS complexes react to aggressive treatment with $NaHCO_3$. (7, 8) $NaHCO_3$ diminishes direct cardiac toxicity and facilitates binding of TCA to proteins which, in turn, lowers the free fraction of TCA (7). Bundle branch block and atrioventricular block can be seen in TCA intoxication, while ST segment and T wave changes mimicking a myocardial infarction are unusual (5).

Similarly, a Brugada electrocardiographic pattern after TCA intentional ingestion is uncommon (less than 3 % of patients) (9).

Brugada syndrome (BS) is a genetic myocardial sodium channel dysfunction that results in slow inward current and ventricular dysrhythmias.

It is a clinical and electrocardiogram (ECG) entity whose features include sudden cardiac death, right bundle branch block (RBBB), and unusual St-segment elevation in leads V1–V3 (10).

Various reports of a Brugada electrocardiographic pattern after intentional amitryptiline overdose have been reported (8, 11, 12), which can be likely ascribed to a TCA-dependent reduction in the inward sodium current and a prominent outward current result in a shortened action potential in the right ventricular epicardial tissue leading to a heterogeneity of action potential duration between the epicardium and the endocardium which ultimately causes the ST segment elevation in leads V1–V3 (8).

According to the Second Consensus Conference on the Brugada Syndrome (10), in our patient a Brugada syndrome could be excluded because of the absence of right bundle block and the presence of ST- segment elevation in leads V1-V6 and aVR.

After TCA ingestion, the admission ECG tracing is usually still normal or showing moderate alterations with abnormalities developing after several hours (6).

In the present case, a notably wide ST tract elevation was already present at admission, four hours after amitriptyline ingestion. In two previous reports (5, 6), a precordial ST tract elevation has been described, but it was evident respectively 14 and 16 hours after admission.

In addition, in our patient the abnormalities resembling an anteroseptal subepicardial injury persisted for eleven days.

To our knowledge, a so exceedingly long period after amitriptyline overdose has never been reported before. This is probably due to the large amount of drug ingested.

Previous reports showed the ECG returning normal respectively after 84 hours and four days after ingestion (5, 6).
Unlike other cases with a classic enzyme pattern consistent with acute myocardial infarction (13, 14), in our patient serial myocardial enzymes never confirmed an ischemic event.
It is likely that such changes in conduction were due either to the quinidine-like activity of TCA, or to an alteration in membrane permeability, allowing differences in potassium concentration between various areas of the myocardium, rather than to an ischemic injury (2).
TCA poisoning outcome is unpredictable since severe cardiac complications have been reported in patient who took only 300 mg of amitriptyline (13, 14), a dose much lower than that of our patient.
However, the dose ingested is a poor predictor of the subsequent clinical outcome.
Individual variation in absorption, protein binding and metabolism make plasma levels an unreliable predictor of toxicity (14).

CONCLUSIONS

Our experience suggests that, after a severe antidepressant drug intoxication, ECG abnormalities resembling myocardial infarction may also occur during the early period of observation even in patients without history of heart disease.
These alteration can last for a notably longer period than commonly reported, without cardiac or neurologic long-term complications.
Furthermore, in any comatose patient with ECG showing an acute myocardial injury and a psychiatric history, TCA intoxication should be strongly suspected.

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