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Cardiology

Ventricular Repolarization Disorders Following Overdosage with Tricyclitic Antidepressants Mimicking Myocard Infarcus

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Abstract | **Case Report**

Introduction: Tricyclic antidepressant overdose is the one of the most common in self-poisoning. Amitriptyline is the most common single agent. The high rate of mortality in tricyclic antidepressant overdosing is due to central nervous system and cardiovascular system toxicity. Evidence of cardiovascular toxicity is present in the majority of tricyclic antidepressant overdoses. Cardiotoxicity is hypotension, QRS widening and ventricular arrhythmias. Myocardial infarction however is rare. ***Objective:*** This paper reports a case of overdose of tricyclic antidepressants, resulting in an acute coronary syndrome. ***Case Report***: This is a 59-year-old patient, with a chronic active smoking as cardiovascular risk factor at 53 BP, age and male sex, followed for psychosis under antidepressant treatment for 5 years with poor compliance (amitriptyline 25mg 1cpx2/d), admitted in our training for the management of infarct chest pain dating back to 16 hours, following an overdose in tricyclic antidepressants. This patient ingested probably 450 mg of amitriptyline hydrochloride following a marital dispute. On admission, the patient was conscient, hemodynamically and respiratory stable, with no evidence of right or left heart failure. The ECG was in regular sinus rhythm, with negative T waves in the septo-apical leads, extended to the right. Troponin was positive at 110ng/l. The TTE was free of significant abnormalities, He was commenced on a sodium bicarbonate infusion that was continued overnight and discontinued the following morning. A coronary angiogram performed in the emergency setting showed angiographically healthy coronary arteries. ***Discussion and Conclusion***: Tricyclic antidepressant overdose is known to cause cardiopulmonary and central nervous system complications. As with other cardiovascular complications, amitriptyline toxicity may cause acute myocardial infarction. The physicians should be aware of acute myocardial infarction in patients with tricyclic antidepressant overdose. This complication may occur during the late period of observation in patients without tendency to acute cardiac ischaemia.

Keywords: Tricyclic antidepressant, overdose.

INTRODUCTION

Tricyclic antidepressant overdose is the one of the most common in self-poisoning. Amitriptyline is the most common single agent (Watson *et al*., 2005). The high rate of mortality in tricyclic antidepressant overdosing is due to central nervous system and cardiovascular system toxicity. Evidence of cardiovascular toxicity is present in the majority of tricyclic antidepressant overdoses. Cardiotoxicity is hypotension, QRS widening and ventricular arrhythmias (Smilkstein 1990).

Transient electrocardiographic changes and cardiac arrhythmias are well documented complications of tricyclic antidepressant overdose. Myocardial infarction however is rare [1].

This paper reports a case of overdose of tricyclic antidepressants, resulting in an acute coronary syndrome.

CASE REPORT

This is a 59-year-old patient, with a chronic active smoking as cardiovascular risk factor at 53 BP, age and male sex, followed for psychosis under antidepressant treatment for 5 years with poor compliance (amitriptyline 25mg 1cpx2/d), admitted in our training for the management of infarct chest pain dating back to 16 hours, following an overdose in tricyclic antidepressants. This patient ingested probably 450 mg of amitriptyline hydrochloride following a marital dispute.

On admission, the patient was conscient, hemodynamically and respiratory stable, with no evidence of right or left heart failure.

The ECG was in regular sinus rhythm, with negative T waves in the septo-apical leads, extended to the right. Troponin was positive at 110ng/l.

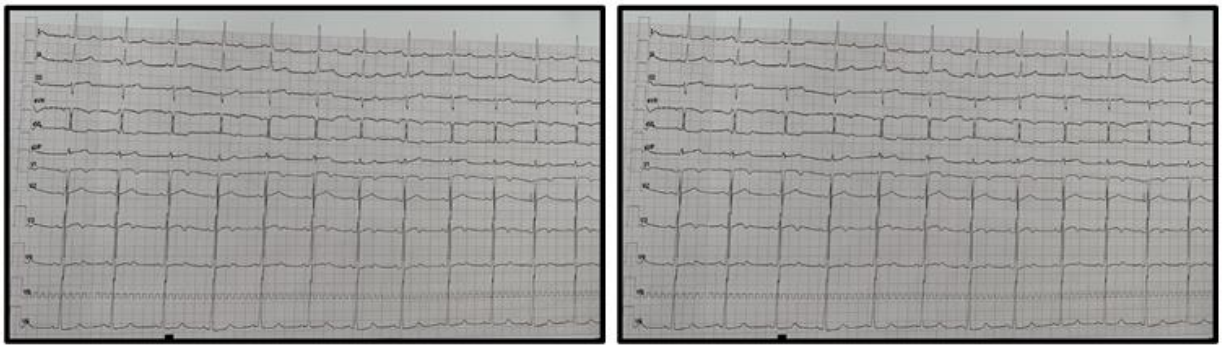

Figure 1: ECG showed negative T waves in septo-apical, extended to right leads

The TTE performed showed a non-dilated, hypertrophied LV with preserved systolic function, LVEF at 66%, preserved segmental and global kinetics, non-dilated atria free of echo, no significant mitro-aortic valve disease, a DV with preserved longitudinal systolic function.

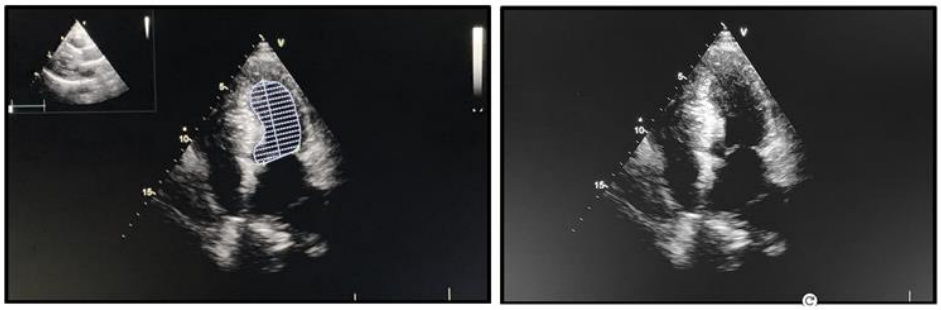

Figure 2: TTE showed a non-dilated, hypertrophied LV with preserved systolic function, LVEF 66%, and preserved segmental and global kinetics

He was commenced on a sodium bicarbonate infusion that was continued overnight and discontinued the following morning

A coronary angiogram performed in the emergency setting showed angiographically healthy coronary arteries.

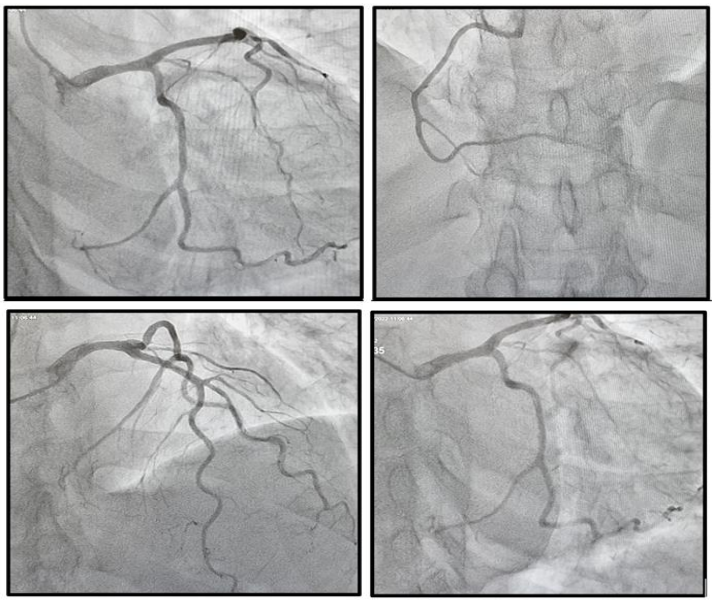

Figure 3: Coronary angiography showed angiographically healthy coronary arteries

On discharge, the patient was referred to a psychiatric unit for the management of his depressive disorder.

DISCUSSION

Tricyclic antidepressants (TCAs) were introduced in the late 1950s for the treatment of depression. With the advent of selective serotonin reuptake inhibitors (SSRIs) and other new antidepressants, the use of TCAs has decreased, although they are still used to treat depression that has not responded to treatment with less toxic agents. In adults, TCAs are also used for migraine headache prophylaxis, treatment of neuralgic pain, including the pain associated with Ciguatera poisoning, and obsessive-compulsive disorder. Despite the current limited use of TCAs, TCA-overdose-associated hospitalizations and fatalities are on the rise [1].

Tricyclic antidepressants impose their therapeutic effects by inhibiting presynaptic reuptake of norepinephrine and serotonin in the central nervous system (CNS). This effect in the CNS can cause seizures. TCAs are weakly basic, and an acidic environment facilitates the formation of the ionized form and potentiates this effect. In cases of toxicity, TCAs block a number of receptors, including peripheral alpha-adrenergic, histaminic, muscarinic, and central serotonin receptors. Blockade of alpha-adrenergic receptors can cause hypotension. Blockade of muscarinic receptors can cause signs of anticholinergic toxicity, such as tachycardia, fever, dry mouth and skin, decreased bowel sounds, and altered mental status. Blockade of histamine receptors can also cause altered mental status. TCAs can cause cardiac toxicity. Blockade of fast sodium channels in myocardial cells slows the action potential and provides a membrane stabilizing effect [2].

The characteristic QRS prolongation seen in TCA overdose occurs secondary to prolongation of phase "0" of the myocardial action potential. This effect can lead to heart block and bradycardia. QT prolongation seen in cases of TCA overdose occurs due to potassium channel blockade that may potentially cause torsades de pointes. TCAs can also exert a quinidine-like toxic effect on the myocardium that can cause decreased cardiac contractility and hypotension [3, 4].

Common electrocardiographic changes associated with tricyclic antidepressant overdose are sinus tachycardia, broadening of the QRS complex, prolonged QT interval, right bundle branch block and right shift of the terminal 40 s of the frontal plane of QRS complex vector. Sinus tachycardia may be attributed to the anticholinergic effects of tricyclic antidepressants. QRS widening in the presence of normal levels of serum electrolytes may be due to either a quinidinelike effect [5] or an abnormal sympathomimetic stimulation.

Although rare, ventricular fibrillation [6] and cardiac arrest have been reported. To our knowledge, there has been only one previous report of myocardial infarction due to a tricyclic antidepressant overdose [7]. Previous reports of transient QRS changes which mimic an acute myocardial infarction [8] may be either due to quinidine-like effect of dothiepin or to an alteration in membrane permeability rather than due to ischaemic changes of the myocardium itself. It is proposed that the intense sympathomimetic stimulation that accompanies an overdose of dothiepin caused the myocardial infarction through intense vasospasm of the coronary arteries.

Hence the importance of repeating serial 12-lead electrocardiograms in patients with initial sinus tachycardia and QRS widening to rule out progressive changes progressive.

Myocardial infarction due to amitriptyline overdose has been reported in literature (Chamsi-Pasha & Barnes 1988). They reported a case of a 22-year-old woman suffering from anteroseptal acute myocardial infarction 26 hr after amitriptyline overdose. The patient's echocardiogram revealed septal hypokinesia but coronary angiography had not been performed.

Chamsi-Pasha & Barnes (1988) explained the case with persistent hypotension, which can precipitate acute myocardial infarction. Guthrie & Lott (1986) reported elevation of serum creatine kinase and MB fraction following an amitriptyline overdose without ECG changes in a patient who subsequently had normal coronary angiogram.

Zakynthinos *et al*., (2000) reported ECG changes mimicking acute myocardial infarction associated with tricyclic antidepressant overdose. ST segment elevation was reported in leads of DI, aVL, V1 and V2 mimicking a current of anteroseptal subepicardial injury after amitriptyline overdose, which persisted for four days. Serial cardiac enzyme estimates did not confirm an ischaemicevent Steeds & Muthusamy (2000) reported a case of dothiepin (sulphur-containing analogue of amitriptyline) overdose with a symmetrical T wave repolarization; abnormalities appeared within 9 hr and mimicked acute anteroseptal myocardial infarction. ECG changes persisted for 6 weeks [9].

The authors suggested that the changes were caused by either the quinidine-like activity of dothiepin or by an alteration in membrane permeability allowing differences in potassium concentrations between different areas of the myocardium, rather than by any myocardial ischaemic damage.

Arya *et al*., (2004) also reported ST segment elevation in leads V2 and V3 and T-wave inversion in leads V4, V5 and V6 suggestive of acute myocardial infarction after overdose of dothiepin. ECG changes persisted for 4 weeks.

Although several hypotheses have been, the exact cause of acute myocardial infarction due to tricyclic antidepressant overdose is not yet known. Vasospasm can be a cause of acute myocardial infarction due to tricyclic antidepressant overdose. Coronary artery spasm has been shown to cause myocardial infarction in patients with normal coronary arteries and it has been concluded that spasm may initiate acute myocardial infarction. It has also been hypothesized that the mechanism of acute myocardial infarction is temporary occlusion of the infarct related vessel by spasm or thrombus or a combination (Lindsay & Pichard 1984). It is suggested that the intense sympathomimetic stimulation that accompanies an overdose of tricyclic antidepressant causes the myocardial infarction through intense vasospasm of the coronary arteries (Arya *et al*., 2004).

All patients with suspected TCA overdose should be immediately evaluated, and a 12 lead EKG should be obtained. The therapeutic index of TCAs is narrow, and therefore, the ingestion of 10 to 20 mg/kg is potentially life-threatening. Symptoms usually start in 30 to 40 minutes, and signs of toxicity are usually clinically apparent within 2 hours, but delayed toxicity may occur. History of co-ingestion or access to other medications, including acetaminophen and aspirin, is essential. Close attention to the patient's vital signs and repeated physical examination for evidence of an anticholinergic toxidrome, cardiac toxicity, and neurologic toxicity should be done and will help guide proper management.

Our patient had ingested 300 mg of amitriptyline. This dose may be considered to be low and thus, the development of acute myocardial infarction is surprising in this case. However, to our knowledge the dose ingested is a poor predictor.

Experimental studies suggest that both alkalinisation and sodium loading are effective in reducing cardiotoxicity independently. Species and experimental differences may explain why sodium bicarbonate appears to work by sodium loading in some studies and by a pH change in others. In the only case series, the administration of intravenous sodium bicarbonate to achieve a systemic pH of 7.5–7.55 reduced QRS prolongation, reversed hypotension (although colloid was also given) and improved mental status in patients with moderate to severe tricyclic antidepressant poisoning. This clinical study supports the use of sodium bicarbonate in the management of the cardiovascular complications of tricyclic antidepressant poisoning. However, the clinical indications and dosing recommendations remain to be clarified [10].

CONCLUSION

Tricyclic antidepressant overdose is known to cause cardiopulmonary and central nervous system complications. As with other cardiovascular complications, amitriptyline toxicity may cause acute myocardial infarction.

The physicians should be aware of acute myocardial infarction in patients with tricyclic antidepressant overdose. This complication may occur during the late period of observation in patients without tendency to acute cardiac ischaemia.

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