Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Cardiology

Tako-Tsubo Syndrome Following Tricyclics Overdose

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DOI: 10.36347/sjmcr.2022.v10i04.029 | **Received:** 12.03.2022 | **Accepted:** 23.04.2022 | **Published:** 29.04.2022

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Abstract **Case Report**

Background: Tako-tsubo syndrome (TTS) refers to the apical ballooning of the left ventricle observed when angiographic ventriculography is performed in patients presenting with electrocardiographic changes suggestive of acute coronary syndrome (new transient ST-segment deviation (>0.05 mV) or T-wave inversion (>0.2 mV)), mild elevation of cardiac markers, but normal coronary arteries at the angiogram. ***Case report*:** A 49-year-old woman developed the characteristic features of TTS 24 hours following tricyclics (amitriptyline hydrochloride) overdose. The admission ECG showed inverted deep T waves in lateral leads (I, AVL). There was an increase in us- troponin level. Transthoracic echocardiography showed hypokinetic anterior and anterolateral segments in the median slice with apical akinesia. Her angiogram was normal. The ventriculography showed an apical ballooning of left ventricle. In contrast, a complete recovery of left ventricular function was observed within one week. ***Discussion:*** The pathophysiology of TTS, a variant of myocardial stunning, is still incompletely understood but could be related to sympathetic overstimulation. The possibility of TTS following toxic tricyclics exposure is discussed.

Keywords: Tako-tsubo syndrome (TTS), pathophysiology, sympathetic overstimulation.

INTRODUCTION

"Taku-tsubo" is the Japanese name for a fishing pot with a round bottom and narrow neck that is used for trapping octopus. However, it refers also to the left ventricular apical ballooning observed in patients with ECG changes suggestive of acute coronary syndrome (ST segment elevation or T wave inversion), mildly elevated cardiac markers, left ventricular wall motion abnormalities in the apical region, but normal coronary arteries at the angiogram [1]. To our best knowledge, apical ballooning syndrome or "tako-tsubo" syndrome (TTS) was never clearly identified following tricyclics overdose.

CASE REPORT

A 49-year-old Mediterranean woman arrived by ambulance in the emergency department for ongoing angina following tricyclic antidepressants (TCA) overdose. This patient ingested probably 800 mg of amitriptyline hydrochloride 8 hours prior admission after a familial conflict.

Her vital signs were the following: temperature, 36˚C; respiratory rate, 20/min; heart rate, 74/min; and arterial blood pressure, 125/65 mm Hg. The admission Glasgow Coma Score was 14/15.

The admission electrocardiogram exhibited a sinus rhythm of 74/min, narrow QRS complex (146 msec) and a QTc interval of 429 msec, with inverted T wave in lateral leads (I, AVL) (Figure 1). Laboratory data showed creatine kinase of 125 IU/l (<200), troponin I of 271 ng/ml (<13). The hemodynamic condition remained perfectly stable during ICU stay. The serum concentration of amitriptyline hydrochloride on admission was measured at 1,568 µg/l. She was commenced on a sodium bicarbonate infusion at 25 mEq/h that was continued overnight and discontinued the following morning. Echocardiography showed hypokinetic anterior and anteroseptal segments in the medial slice, apical akinesia with mild decreased systolic function. Twelve hours after ICU admission, the patient was transferred to catheterization laboratory. Cardiac catheterization confirmed the apical ballooning characteristic of "tako-tsubo" syndrome (Figure 2) and showed normal coronary arteries. No increase either in CK-MB or troponin I was measured in the blood samples. The patient was treated daily by 75 mg acetylsalicylic acid and 5 mg bisoprolol. The patient was discharged by the same day. On the ECG obtained 1 week later, there were no repolarization disorders. CT-scan did not show any adrenal mass. The transthoracic echocardiography was normal as well with preserved ejection fraction. The prescription of

bisoprolol was discontinued and the patient was referred to a psychiatric unit for the management of her mixed anxiety-depressive disorder.

DISCUSSION

Takotsubo cardiomyopathy, also known as left ventricular apical ballooning syndrome and stress-induced cardiomyopathy, is typically characterized by transient systolic dysfunction of the apical and mid-segments of the left ventricle, in the absence of obstructive coronary artery lesions. Patients may present with symptoms and signs of acute coronary syndrome, and the provider is challenged to differentiate between these conditions.

TTC was incorporated into the American Heart Association (AHA) classification of cardiomyopathies as a unique cardiomyopathy in 2006 and entered into National Center for Biotechnology Information (NCBI) databases as a distinct clinical entity in 2008 [2].

The diagnosis is often made when a patient with suspected acute myocardial infarction is found at cardiac catheterization to have no coronary blockage. Revised Mayo Clinic diagnostic criteria include the following [3]:

- Transient dyskinesis of the LV midsegments
- Regional wall motion abnormalities beyond a single epicardial vascular distribution
- Absence of obstructive coronary artery disease or acute plaque rupture
- New electrocardiographic abnormalities or modest troponin elevation
- Absence of pheochromocytoma and myocarditis

The mechanism underlying the association between sympathetic stimulation and myocardial stunning is unknown. A direct myocyte injury has been debated, with contraction-band necrosis that can be demonstrated histologically in certain conditions including pheochromocytoma, subarachnoid hemorrhage, or fatal asthma. Catecholamines have well known vasoconstrictive effects. Epicardial coronary arterial spasm could result in transient ischemia. But the patients usually have contractile abnormalities in multiple vascular territories and multivessel epicardial spasm was never demonstrated at angiogram. Microvascular spasm with sympathetically mediated microcirculatory dysfunction is another possibility.

TTS has been described predominantly in women and frequently occurs after emotional or physical stress [4]. Originally described in the Japanese population, it was also demonstrated in the European and North-American populations [5, 6]. The patients developing TTS have usually cardiovascular risk factors, including arterial hypertension, hyperlipidemia, diabetes mellitus, or smoking [7].

The diagnosis of TTS requires the exclusion of other conditions such as pheochromocytoma, acute myocarditis, hypertrophic cardiomyopathy, or acute neurological disease (particularly subarachnoid hemorrhage). A large number of other underlying disorders have been associated with TTS [1]. However, to our best knowledge, a recent episode of tricyclics overdose has rarely been mentioned among the precipitating factors.

Our patient met the criteria for TTS diagnosis. However, we acknowledge that a provocative test for coronary spasm was not performed during angiography and that we did not exclude atherosclerotic plaque rupture by ultrasound examination.

Is there a possible relationship between this cardiac event and TCA overdose?

Transient ECG changes mimicking acute coronary syndrome are common during the course of TCA overdose [8, 9]. The ECG changes are usually not associated with abnormal regional wall motion at echocardiography. Rarely, elevated cardiac biomarkers consistent with an acute myocardial infarction (troponin or CK-MB) have also been observed as stated below, suggesting a cardiac toxicity. Kiyan *et al.*, reported after the ingestion of 300 mg amitriptyline an “acute myocardial infarction” in a 33-year-old woman without cardiovascular risk factors [10]. Initially, the ECG showed sinus tachycardia and mild QRS widening (120 msec). Forty hours after the ingestion, she complained of chest pain and the ECG was modified with ST segment depression and T-wave inversion in V2 to V5 leads. Creatine kinase and troponin I were elevated. In this case, the echocardiography did not reveal abnormalities such as global or segmental hypokinesia or pericardial effusion. No coronary angiography was obtained because of normal myocardial perfusion at the single photon emission tomography. Similarly, Arya et al. described a case of dothiepin overdose complicated by a typical electrocardiographic feature of acute myocardial infraction [11]. No data were available regarding cardiac markers. While coronary angiography was not performed, echocardiography revealed hypokinesia in the apical and anteroseptal regions. Other authors reported a 22-year-old woman who had ST-segment elevation in the antero-septal leads 26 hours after the ingestion of 300 mg amitriptyline. Creatine kinase MB was increased and the echocardiography revealed hypokinesia of the septum [12]. No coronary angiography was performed and the patient was lost for follow-up. Sophie De Roock et Al. reported a case of a 54-year-old woman who developed the characteristic features of TTS 44 hours following nortriptyline overdose. The admission ECG showed increased QRS duration rapidly reversible after sodium bicarbonate infusion. There was a minimal increase in troponin I level. The ECG performed at the time of chest pain revealed deeply negative T waves in leads I,

II, III, aVF, V1 to V6 and remained abnormal at 5 weeks follow-up. In contrast, a complete recovery of left ventricular function was observed within one week [13].

It remains difficult to speculate about the exact role of amitriptyline hydrochloride in the genesis of TTS. The delay between drug overdose and the onset of chest pain remains imprecise but relatively short. We were also not able to obtain plasma catecholamine levels. When plasma catecholamine levels could be determined in patients with TCA overdose, there was some correlation between QRS duration and plasma norepinephrine levels [14]. However, commensurate physiologic changes were not found in the presence of elevated catecholamine levels. Older publications also suggest that tricyclics could reduce coronary flow in experiments on the isolated heart muscle and could raise the tone of isolated coronary blood vessels [15].

The prognosis in takotsubo cardiomyopathy is typically excellent, with nearly 95% of patients experiencing complete recovery within 4-8 weeks [16, 17].

CONCLUSION

In conclusion, we report a case of TTS following amitriptyline hydrochloride overdose. A recent drug overdose (and perhaps particularly with substances accompanied by an intense sympathetic stimulation) should be added to the list of the precipitating factors.

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