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Cardiology

Salbutamol Induced Takotsubo Cardiomyopathy- A Case Report

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Abstract **Case Report**

Stress induced cardiomyopathy also known as Takotsubo cardiomyopathy (TCM) is characterized by an apical ballooning of the left ventricle related to transient and reversible apical and mid-ventricular hypokinesis that occurs in the majority of cases after an acute stress. The clinical presentation mimics acute coronary syndrome usually leading to urgent coronary angiography with no evidence of lesions or plaque rupture.
We describe an unusual case of salbutamol induced cardiomyopathy of a 78 year-old man with a chronic asthma stable so far, followed by a review of the literature.
Keywords: Salbutamol, Takotsubo cardiomyopathy, catecholamine.

INTRODUCTION

Stress induced cardiomyopathy also known as Takotsubo cardiomyopathy (TCM), is an uncommon syndrome, first described in Japan, with a higher prevalence all over the world due to better knowledge and diagnosis. The exact mechanism of myocardial dysfunction of TCM is unknown, a high circulating catecholamine level is usually found [1, 2].

The clinical presentation is similar to an acute coronary syndrome. The electrocardiogram shows typical repolarization abnormalities with ST elevation like following by negative T waves. The echocardiography shows a systolic dysfunction of the LV apex and/or mid-segment leading to urgent coronary angiography without obstructive coronary artery disease, followed by complete functional recovery in a few weeks. The diagnosis based on the modified Mayo clinic criteria requires the presence of all the four following criteria [3]:

- Transient hypokinesis, dyskinesis, or akinesis of midsegments (with or without apical involvement) that extends beyond a single vessel distribution, a stressful trigger not always found
- No evidence of occlusive coronary disease or plaque rupture on angiography
- New EKG abnormalities (repolarization abnormalities) or mild / moderate elevation in troponine
- Absence of pheochromocytoma or myocarditis

We are reporting a case of Salbutamol induced TCM in patient admitted for severe asthma exacerbation to shed light on an unrecognized etiology for TCM

CASE REPORT

A 87-year-old man with a past medical history of chronic asthma presented to our emergency department with chest discomfort and a rapidly progressive dyspnea with signs of respiratory distress, he already tried salbutamol inhaler and at baseline he used a combination inhaler (budesonide and formoterol) that contained an inhaled corticosteroid and a long-acting beta agonist up to 2 times a day. The patient had no acute stress or emotional event. He was immediately admitted to intensive care unit, on physical examination the patient had tachypnea with respiratory rate at 50 /min, nasal flaring and intercostals retractions with no sign of heart failure. The saturation on arrival was 80%, An arterial-blood gas (ABG) showed pH 7.23; PCO2 at 70mmHg; PO2 at 114 mmHg; HCO_3- at 29.8mmol/l. The patient was put under continuous intravenous salbutamol 5mg / 5ml: 2mg / h and non-invasive ventilation. The electrocardiogram was normal, and the first troponine level was at 0.7 ng/mL (normal value: 0–0.03 ng/mL). An echocardiogram was performed, that revealed severe impairment of the middle and apical segments of the left ventricle, with preserved overall ejection fraction of 60 %, and no evidence of LV thrombus (Figures 1 and 2).In short order, the patient was taken for coronary angiography, that does not show any obstruction or stenosis (Figures 3).

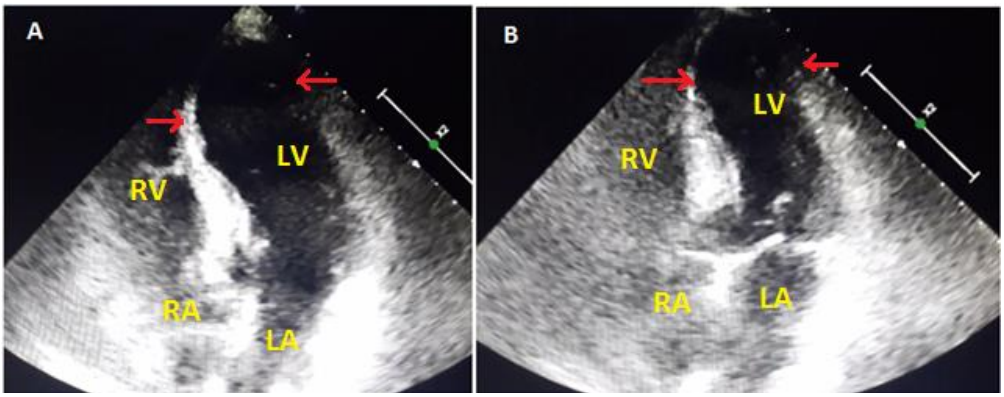

Fig-1: Apical four chamber echocardiography view shows the left ventricle in diastolic phase (A) and systolic phase (B) revealing severe dysfunction of the apex (red arrows). LV: left ventricle, LA: left atrium, RV: right ventricle, RA: right atrium

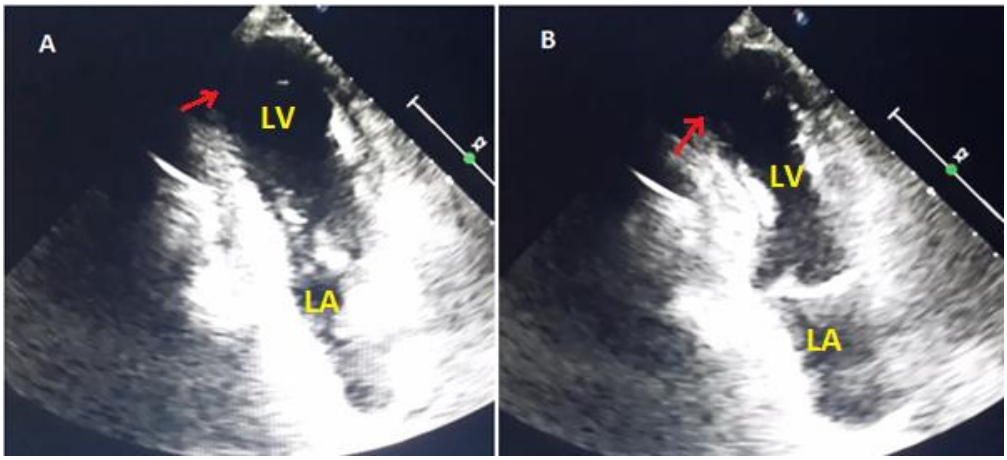

Fig-2: Apical two chamber echocardiography view shows the left ventricle in diastolic phase (A) and systolic phase (B) revealing severe dysfunction of the apex (red arrows). LV: left ventricle, LA: left atrium

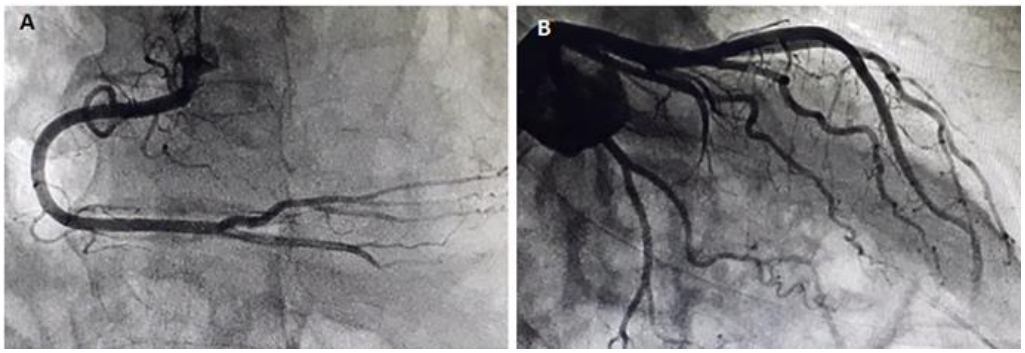

Fig-3: Coronary angiography with noncritical disease

We completed by cardiac magnetic resonance imaging that confirmed the echocardiographic findings , showing a non-dilated left ventricle, and a preserved LVEF associated with hypokinesis of the apex, the apical and middle segments of anterior wall with aneurysmal atrial septum with no late enhancement after gadolinium injection (Figures 4,5).

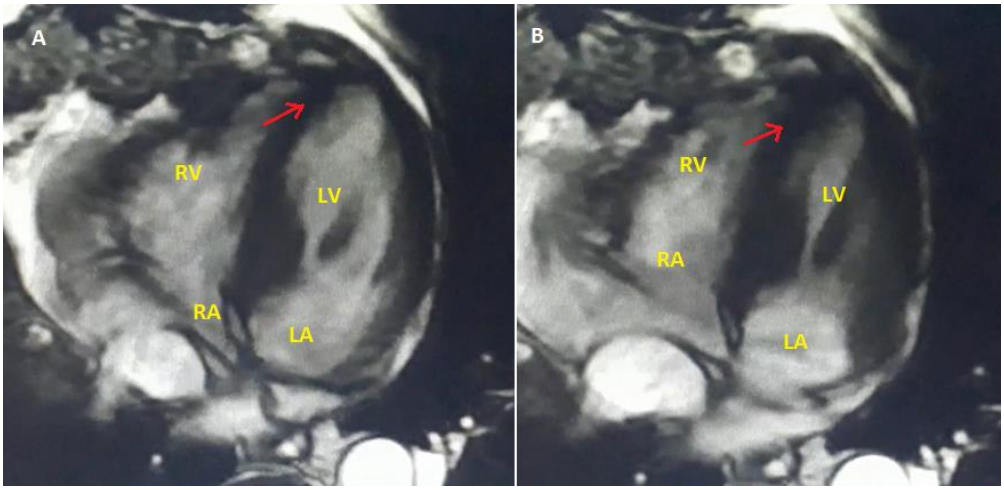

Fig-4: Cardiac MRI 4 chamber view shows the left ventricle in diastolic phase (A) and systolic phase (B) revealing severe dysfunction of the apex (red arrows). LV: left ventricle, LA: left atrium, RV: right ventricle, RA: right atrium

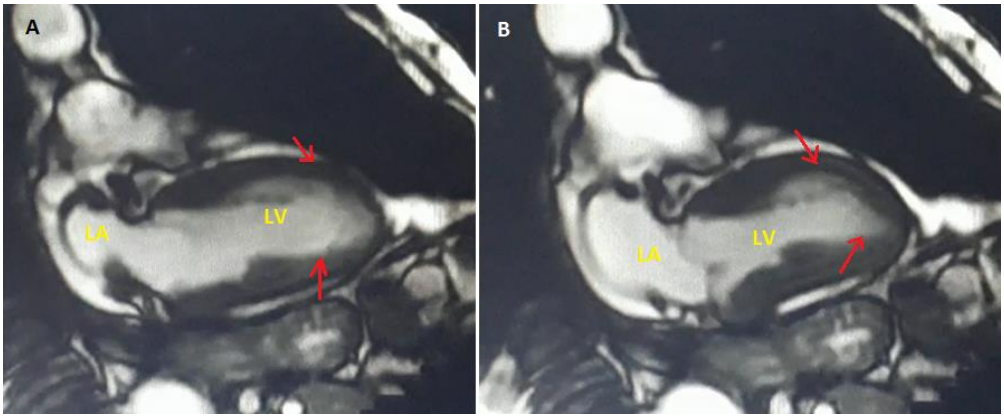

Fig-5: Cardiac MRI 2 chamber view shows the left ventricle in diastolic phase (A) and systolic phase (B) revealing severe dysfunction of the apex (red arrows). LV: left ventricle, LA: left atrium

Our patient was diagnosed with Takotsubo cardiomyopathy, supported by an acute presentation and elevation of troponine, as well as the findings of apical ballooning on left ventricle in cardiac imaging findings and a normal coronary angiography. He was treated in the intensive care unit then transferred to cardiology department for a few days with a medical regimen with good evolution. He was discharged in stable condition. An echocardiography control was performed one month later with a complete normalization of her LV function.

DISCUSSION

Takotsubo or a stress-induced cardiomyopathy mimics acute coronary syndrome without coronary lesions, in which the heart takes the appearance of a Japanese octopus fishing pot called a Takotsubo with hypokinesis of apical and mid ventricular with hyperkinesis of the basal segments leading to the ballooning aspect of the left ventricle. Stress plays a main role with high plasma levels of epinephrine and norepinephrine. The brain responds to an acute stressor by activating the noradrenergic neurons. That leads to cathecholamine massive release by the sympathetic nerve endings directly into the myocardium. It has been demonstrated catheocalamines reaching the heart directly are way more toxic than circulating cathecholamines [4].

The mechanism is not well known but it is presumed that the activation of α and β postsynaptic adrenoceptors has severe consequences. The main mechanism is cathecholamine myocardial direct toxicity by provoking myocellular hypoxia due to supply-demand mismatch with heart rate acceleration [5], producing free radicals leading to myocyte damage [6] and contraction band necrosis due to cAMP mediated calcium overload [7].

The consequences concern also the coronary arteries. A subocclusive epicardial coronary arteries spasm and coronary microvascular dysfunction can result. Small coronary arteries and arterioles receive autonomic innervations, in the context of endothelial dysfunction; a coronary microvascular constriction is observed insead of vasodilataion [8].

Histological studies showed that there is a regional differences in adrenoceptor density. The fact that the left ventricular apex contains a higher concentration of adrenoceptors could explain the adrenergic stimulation pronounced in this area with a ballooning aspect [9].

Exogenous catecholamines were incriminated in pharmacologically induced TCM and the salbutamol induced TCM is a rare case. To our knowledge, there were only 10 similar cases reported in literature between 2000 and 2016 [10-19].

The asthma exacerbation was considered in many publications as a stress factor, Elesber *et al.* reported in a cohort of 100 patients having a TCM, at the Mayo clinic, that 4 patients (4%) had asthma/ COPD exacerbation as the only physical stress [20]. However our patient had a quite stable chronic asthma with no previous remarkable history of difficult medical management or respiratory failure. The likely mechanism of TCM in our case is mediated through the β agonist action of Salbutamol.

Usually TCM occurs in postmenopausal women. Our patient does not fit with the literature findings; same for the clinical presentation that was less severe with a chest discomfort instead of intense chest pain, the EKG was normal but the mild elevations in troponine level was typically similar to the majority of reported cases. The evolution is favorable with total reversibility in a few weeks, the treatment is the same as the treatment of ischemic cardiomyopathy, consist on inhibitors of the conversion enzyme and beta blockers. In case of congestive heart failure it is necessary to put the patient under diuretic treatment, and under vasoactive amines in case of cardiogenic shock.

Conclusion

We conclude that the diagnosis of beta-2 agonists induced TCM should be evoked in front of all unexplained acute coronary syndromes without significant coronary artery disease, in patients with asthma who received high doses of salbutamol.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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