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Takotsubo cardiomyopathy: important differential diagnosis of chest pain in the emergency room

Miocardiopatia de Takotsubo: importante diagnóstico diferencial de dor torácica na emergência

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ABSTRACT: Takotsubo cardiomyopathy is a form of acute, usually reversible, heart failure triggered by physical or emotional stress. The clinical presentation is very similar to that of acute coronary syndromes, but without the characteristic vascular obstruction of coronary disease. Here we report a case of a 53-year-old woman who presented at the cardiac emergency room with typical coronary chest pain, dynamic electrocardiogram changes, and increased markers of myocardial necrosis. Cardiac catheterization showed coronary arteries without significant atheromatosis, despite a slight degree of atherosclerosis, and findings suggestive of Takotsubo cardiomyopathy of the apical type. Supportive treatment with antihypertensive drugs was performed, aiming to reduce cardiac workload and remodeling. Markers of myocardial necrosis monitored during hospitalization showed a downward curve. The patient had clinical improvement, being discharged on the 7th day after hospitalization, using angiotensin-converting enzyme inhibitor, third-generation beta-blocker, statin and platelet antiaggregants.

Keywords: Takotsubo cardiomyopathy; Cardiomyopathies; Spasm.

RESUMO: A miocardiopatia de Takotsubo é uma forma de insuficiência cardíaca aguda, geralmente reversível e desencadeada por um estresse físico ou gatilho emocional, cuja apresentação clínica é bastante similar às síndromes coronarianas agudas, porém sem a obstrução vascular característica da doença coronariana. Relatamos o caso de uma mulher de 53 anos que chegou à emergência cardiológica com dor retroesternal tipicamente coronariana, alterações dinâmicas no eletrocardiograma e aumento dos marcadores de necrose miocárdica. Cateterismo cardíaco mostrou coronárias isentas de ateromatose significativa, embora houvesse pequeno grau de aterosclerose, e achados sugestivos de miocardiopatia de Takotsubo do tipo apical. Foi realizado tratamento de suporte com drogas anti-hipertensivas, visando diminuir trabalho e remodelamento cardíacos. Os marcadores de necrose miocárdica acompanhados durante o internamento mostraram curva descendente. Paciente evoluiu com melhora clínica, recebendo alta hospitalar no 7º dia após internamento, em uso de inibidor da enzima conversora de angiotensina, beta bloqueador de 3ª geração, estatina e antiagregante plaquetário.

Descritores: Cardiomiopatia de Takotsubo; Cardiopatias; Espasmo.

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INTRODUCTION

The Takotsubo syndrome was initially described in 1990 by Sato et al.[1], receiving several designations, such as Takotsubo cardiomyopathy (TCM) and broken heart syndrome[2]. It is a form of acute heart failure, possibly reversible, and usually triggered by physical or emotional stress[3].

The clinical presentation of TCM is very similar to that in acute coronary syndrome (ACS), but without the vascular obstruction characteristic of coronary disease[3,4], being an important differential diagnosis in emergency cases[4].

It is estimated that TCM occurs in 1–2% of hospitalizations due to ACS, with a significant increase in the detection of new cases due to the increasingly common presence of hemodynamic laboratories in cardiac emergency room[3].

CASE REPORT

We report the case of a 53-year-old woman who sought medical attention after an episode of dyspnea and chest pain, triggered by strong emotional stress due to the murder of her son. The electrocardiogram (ECG) result upon admission was normal, but after a few hours and during a further episode of chest pain, the examination was repeated, showing dynamic changes of plus-minus type (T-wave inversion in V3–5) and elevation of troponin level (2.72 ng/mL). The patient was then referred to the cardiac emergency department for constrictive retrosternal pain with irradiation in the back 16 h earlier, in addition to orthopnea. The patient also reported persistence of pain despite previous analgesia use. She presented with a history of systemic arterial hypertension and denied diabetes mellitus. Clinical examination showed a regular general condition, mild tachypnea, and absence of edema in the lower limbs. No changes were noted upon cardiac and respiratory auscultation. The new ECG result showed dynamic changes in the plus-minus type anterior wall, with T-wave inversion in V3–5. Laboratory tests revealed an increase in troponin level, with a value of 4.25 ng/mL, and creatine kinase mass concentration, with a value of 25 U/L. Cardiac catheterization (Figure 1) showed the absence of significant lesions on the anterior descending artery, despite a slight degree of atherosclerosis, and discretely enlarged dimensions of the left ventricle (LV), with marked basal hypercontractility and apical akinesia, findings suggestive of apical TCM. The patient was then admitted for longitudinal evaluation. Antihypertensive drugs were administered to reduce cardiac workload and remodeling. Markers of myocardial necrosis that were monitored during hospitalization showed a downward curve (Table 1). On the third day of hospitalization, a transthoracic echocardiogram (TTE) was performed, which showed a LV with normal cavity, septal hypokinesia, preserved global systolic function, and mild diastolic dysfunction. The patient had a clinical improvement, using angiotensin-converting enzyme (ACE) inhibitor, third-generation beta-blocker, statin and platelet antiaggregants, being discharged on the 7th day after hospitalization.

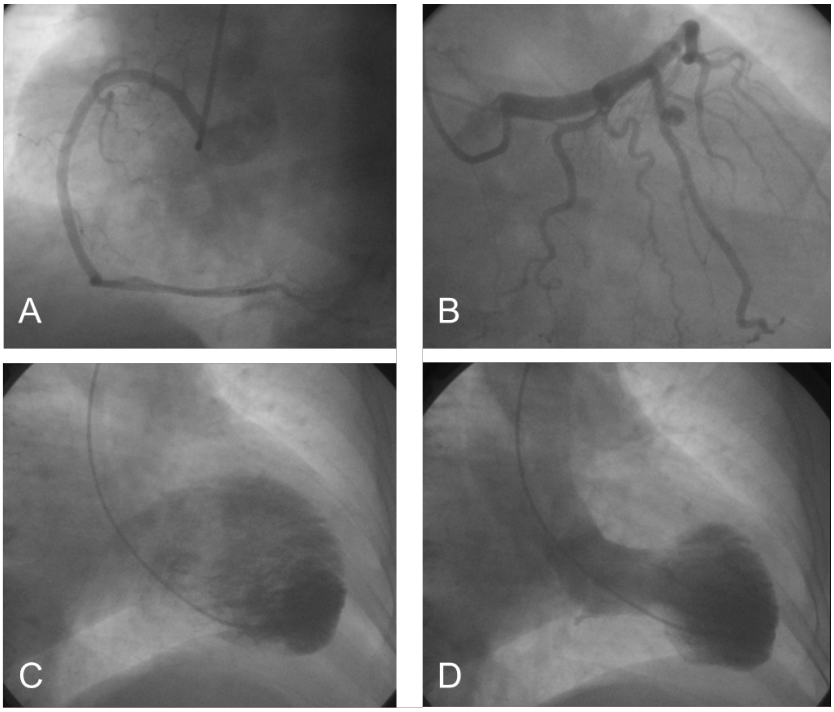

Figure 1. Cardiac catheterization. Right (A) and left (B) coronary arteries without significant atheromatosis. Left ventriculography in diastole (C) and systole (D) showing apical ballooning

Table 1. Values of serum markers of myocardial necrosis: troponin and CK-MB mass

Variables	Day 1	Day 3	Day 4	Day 5	Day 6	Day 7*	Reference value
Troponin (ng/ mL)	4.255	0.211	0.211	0.084	0.084	0.084	< 0.034
CK-MB mass (U/ L)	25	7.66	7.66	7.66	7.66	7.66	0-16

CK-MB: creatine kinase mass
*Day 7: time of hospital discharge for outpatient follow-up

DISCUSSION

TCM is characterized by acute LV dysfunction in patients without coronary atheromatosis capable of triggering the clinical manifestation of myocardial ischemia. Another characteristic of this cardiomyopathy is the possible reversal of cardiac function in up to 18 days[5].

In a study of more than 3,000 patients, Kurowski et al.[6] found a TCM prevalence of 1.2% in patients with ACS and a positive troponin result. These results were extremely similar to those found by Gianni et al.,[7] in a systematic review: 1.7–2.2% of suspected cases of ACS with supra-ST, with an estimated recurrence rate of 1.8% per year[8]. About 90% of cases occur in women aged between 67 and 70 years[8,9], with women aged > 55 years having a TCM risk of at least 5 times greater than women below that age and 10 times higher than men[10]. Regarding the prevalence based on race, the current data are conflicting, due to the lack of more consistent studies[11].

The pathophysiology of TCM remains uncertain, but there are a number of theories that have attempted to explain it: 1) cardiotoxicity caused by catecholamines; 2) metabolic disorders; 3) disorders of the coronary microvasculature; and 4) vasospasm of multiple coronary epicardial vessels[1]. Despite the various theories, TCM seems to be multifactorial and it is widely accepted that the exacerbated release of catecholamines could well be the trigger for myocardial stunning[12]. According to the latter theory, studies show that a significant portion of patients with pheochromocytoma are susceptible to a similar cardiomyopathy during a catecholaminergic crisis[13-15]. However, other studies suggest that septal thickening causes LV splitting, resulting in apical ballooning, which may be responsible for dyskinesia of the anterior wall[16].

LV dysfunction, observed in ventriculography or echocardiography, may occur through hypokinesia, dyskinesia, or akinesia, allowing the classification of TCM into the following types: a) apical (most common and characterized by LV apical ballooning and basement wall hyperkinesia, as observed in the case reported and present in more than 80% of patients), b) medium-ventricular (hypokinesia restricted to the middle ventricle, with a relative preservation of the apex, occurring in approximately 14% of cases), c) basal (also known as inverted Takotsubo) (characterized by hypokinesia of the base with preservation of the middle ventricle and apex, occurring in slightly more than 2% of cases), and d) focal (rare variant characterized by dysfunction of an isolated segment [more often, the anterolateral segment]); e) global (rarest of all, characterized by global cardiac hypokinesia)[8].

The most common clinical presentation is typical retrosternal pain in a woman aged 67 to 70 years, with a history of strong emotional stress prior to symptoms. All these factors are present in this case, except for the age of the patient. Less commonly, some patients present with dyspnea, syncope, tachyarrhythmias (especially ventricular fibrillation and ventricular tachycardia), bradyarrhythmias, acute pulmonary edema, mitral regurgitation, sudden cardiac arrest, or only electrocardiographic abnormalities. Psychiatric (depression, anxiety) and neurological (stroke, subarachnoid hemorrhage, seizures) disorders may sometimes be present[17]. Up to 10% of patients may develop cardiogenic shock[18]. The absence of Q-wave abnormality, in addition to the ST V4–6/V1–3 >1, demonstrates high sensitivity and specificity for the diagnosis.[1] Fewer dynamic ECG changes may occur, as in the present case, when the first ECG result was initially normal, but when repeated, the examination of a new episode of chest pain revealed T-wave inversion in V3–5. Laboratory tests usually show elevation of markers of myocardial necrosis. Troponin, although elevated, typically does not reach levels as high as those in ACS cases[8]. When this occurs in a patient with TCM, it is predictive of a worse clinical outcome.[8] Another frequent change is the elevation of the B-type and N-terminal prohormones of the brain natriuretic peptide (NT-proBNP), which reach their peak 24 to 48 h after the onset of the clinical picture.[19] According to Nguyen et al.[19], the elevation of NT-proBNP is proportional to the degree of sympathetic activation, LV systolic dysfunction and C-reactive protein levels.

TTE shows alterations of segmental contraction, and cardiac catheterization is essential to demonstrate the absence of significant atheromatous lesions[2], as shown in the present case. Cardiac magnetic resonance imaging (MRI) may be used for the diagnosis of TCM, especially when TTE is technically limited and/or there is coexisting coronary disease. Late gadolinium enhancement is absent in TCM but present in myocarditis and myocardial infarction. In the MRI of the patient with stress cardiomyopathy, focal edema can be observed, precisely in areas with

abnormality of movement, allowing an exact anatomical location. Eitel et al.[20] have demonstrated that up to 81% of patients with TCM have this edema at the site with abnormality of movement, but myocardial edema is also observed in acute myocardial infarction and myocarditis. MRI also allows the identification of thrombus in one of the ventricles, which is sometimes not observed in TTE[21]. Although coronary angiography with vetriculography is the gold standard method for diagnosis or exclusion of TCM, the European Society of Cardiology recommends the use of the InterTAK Diagnostic Score (Table 2), which may aid in the identification and stratification of this cardiomyopathy. Using only the clinical and electrocardiographic criteria, the score is an accessible and simple tool for use in the emergency room[18,22].

Table 2. InterTAK Diagnostic Score for initial evaluation of the probability of Takotsubo cardiomyopathy

Criteria	Pointing
Female	25 points
Emotional stress	24 points
Physical stress	13 points
No segment ST* depression	12 points
Psychiatric disorders	11 points
Neurological disorders	9 points
QTc prolongation	6 points
Interpretation	
Low/middle probability of TCM	≤ 70 points
High probability of TCM	> 70 points

*Except in aVR derivation; QTc: corrected QT interval; TCM: Takotsubo cardiomyopathy

Initial treatment is supportive, depending on the comorbidities and hemodynamic status of the patient. In cases of cardiogenic shock in the absence of LV outflow tract obstruction, the careful use of inotropes may be considered[4].

Among the therapeutic possibilities for the follow-up of TCM, ACE inhibitors or beta-blockers, or even the combination of these two classes, may be used. Brunetti et al.[23] concluded in a meta-analysis that ACE inhibitors are significantly associated with lower rates of TCM recurrence compared to beta-blockers, confirming the need for further prospective randomized trials. In the absence of such randomized studies aimed at evaluating the most effective treatment for patients with TCM, the choice is empirical and individualized case by case. However, the international literature has recommended a combination therapy of beta-blockers and ACE inhibitors, especially in patients with significant LV dysfunction[24]. If coronary atherosclerosis is present concomitantly, statin and aspirin are indicated[22].

Although the majority of patients with TCM recover, rates of in-hospital complications are similar to those observed in ACS[8]. The International Takotsubo Registry[8], when comparing TCM with ACS, found rates of 19.1% versus 19.3% respectively, and 3% for the risk of cardiogenic shock, use of invasive or noninvasive mechanical ventilation, cardiopulmonary resuscitation and death. In a systematic review, Singh et al.[25] also showed that acute complications are relatively frequent in TCM, with acute heart failure in approximately 30%, acute lung edema in 21%, cardiogenic shock in 8% and death in 3.5% of patients. The rate of early recurrence (up to six months) was estimated to be 1.5% and 5% when a time frame of up to six years after the first episode was considered.

CONCLUSION

The case reported is important because the patient was younger than expected in a case of Takotsubo cardiomyopathy, in addition to the occurrence of akinesia of the left ventricle anterior wall, characterizing the apical type. Thus, this cardiomyopathy is an important differential diagnosis to be considered in patients with a clinical presentation of acute coronary syndrome.

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