

Takotsubo Syndrome

Aude Charvet

Key Points

Acute stress cardiomyopathy and differential diagnosis of acute coronary syndrome, Takotsubo syndrome is rare.

Nevertheless, this pathology may necessitate cardiovascular resuscitation.

Introduction

Takotsubo syndrome, also known as transient apical ballooning syndrome of the left ventricle, is a stress cardiomyopathy initially witnessed in Japan and increasingly frequent amongst the Caucasian population [1]. It affects predominantly female elderly patients and mirrors an acute coronary syndrome, most often stress induced. Clinically, it presents itself as an acute haemodynamic failure associated to thoracic pain, electrocardiogram anomalies, and a moderate increase of cardiac enzymes, without significant lesions of coronary arteries. Diagnosis is supported by the echocardiogram showing an apical systolic dilation of the left ventricle. The development of this pathology has spontaneously favourable outcomes, although resuscitation can be necessary. The pathophysiology of Takotsubo syndrome is still open for debate.

A. Charvet (✉)

Service d'anesthésie et de réanimation, Hôpital Nord Assistance
Publique-Hôpitaux de Marseille, Université de la Méditerranée,
Chemin des Bourrelly 13915 Marseille Cedex 20, France
e-mail: Aude.CHARVET@ap-hm.fr

History

This pathology was first observed in Japan in 1990 by Sato et al. The name “Takotsubo cardiomyopathy” was given to this syndrome due to the ultrasound appearance of the left ventricle during the systolic phase: with a dilated background and a narrow neck, it resembles a ceramic amphora-shaped pot called a Takotsubo, used for octopus fishing in Japan. The majority of publications that followed were principally Japanese, so that it was initially thought of as a phenomenon limited to Asia up to the years 2000. Then, numerous incidences were reported throughout the world, especially in Europe, the United States and Australia. In 2006, Takotsubo syndrome is included within the acquired cardiomyopathies classification by the American Heart Foundation [2].

Epidemiology

The exact occurrence of Takotsubo syndrome is unknown, due to the novelty of this pathology, the varying of its symptomatology and its changing diagnostical criteria. Nonetheless, most studies find a similar incidence, around one to two percent of patients admitted for acute coronary syndrome [1]. Contributing factors are equally found in a unanimous fashion: this syndrome usually affects post-menopausal women and is the result of a stressor. Indeed, about 90 % of all reported cases are linked to the female gender, within an age range from 58 to 75 years [3]. It is unknown as to why there exists a strong predominance of female cases. Several hypotheses have been put forward, such as the pathophysiological role of estrogens, or the fact that the atheromatous illness being frequent among males could conceal this syndrome amongst them. Those female patients do not usually have any noteworthy antecedent or any coronary disease risk factor, except for an ongoing smoking habit found in around 50 % of them. At last, approximately two-thirds of female patients have previously suffered a significant stressor, whether it be physical (surgery, trauma, meningeal hemorrhage, sepsis, severe pain, local or general anesthesia, weaning from opiates, cocaine poisoning, endocrinopathies, electro convulsive treatment, chemotherapy, etc....) and/or psychological (death or severe illness of a loved one, divorce, road traffic accident, etc....) [3].

Clinical

The clinical presentation of Takotsubo syndrome is usually close to acute coronary syndrome, of which it constitutes the main differential diagnosis. Over half of female patients describe a brutal and sudden onset of an angina type chest pain.

Other possible manifestations can be dyspnea and much more rarely fainting, pulmonary oedema or cardiac arrest [3]. A haemodynamic failure is frequent, although cardiogenic shock has only been reported as a rare complication.

Paraclinical

The E.C.G. also suggests acute coronary syndrome, frequently accompanied by a convex elevation of the ST segment (from 34 to 100 % depending on studies), most of the time in the antero-septo-apical area (V1–V4), sometimes in the inferior or lateral areas. Other anomalies indicating myocardial ischemia, such as T-wave negativity in precordials, dielectric constant and AVL, along with occurrence of Q-wave in V3 and V4, are all frequent. Widespread micro-voltage, left branch blocking or QT-interval prolongation have been observed less frequently [4, 5]. The E.C.G. can be normal. In each case, analyzing E.C.G. anomalies does not allow to differentiate Takotsubo syndrome from acute coronary syndrome [4], and does imply a link to the seriousness of ventricular dysfunction, or to its development [5].

Cardiac enzymes levels most of the time show a moderate increase, particularly troponin T peaking within 24 h. However, the increase in these markers is lower than during a genuine acute myocardial infarct, and especially disproportionate to the widespread reach as observed in imaging.

The coronarography is normal amongst most patients [3, 4], but assumes the appearance proper to the ventriculography in late systole: hypokinesia or antero-apical akinesia of the left ventricle, responsible for a ballooning, associated to a reverse basal hypercontractility. The coronarography can sometimes show non-significant coronary lesions, as well as vasospasms, which will fade following local administering of nitrated derivatives. In fact, diagnosing Takotsubo syndrome is most of the time possible during a left ventriculography done on female patients with suspected acute coronary syndrome.

Transthoracic echocardiography is a key examination enabling the diagnosis of Takotsubo syndrome. It mimics anomalies specific to apical or septal segmental kinetics, responsible for a distortion of the left ventricular functioning (left ventricular function of emission of 15–40 % in the acute phase) [6] and for a distal ballooning. Usually there are no right-hearted anomalies, nor a pericardial outpouring. However, an associated right ventricular dysfunction is possible (Fig. 1).

A cardiac M.R.I. can also confirm left ventricular kinetics anomalies, without ischemic attack or necrosis, shown by an absence of contrast after a gadolinium injection. Equally, it allows forecasting the reversibility of noted disorders [6]. When undertaken early, cine-M.R.I. recognizes kinetics-associated disorders, characteristic to this pathology (Fig. 2).

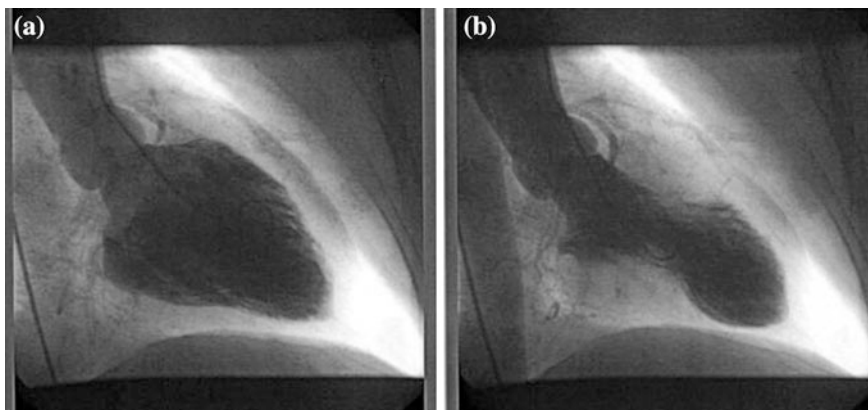


Fig. 1 Left ventriculogram during Takotsubo syndrome, **a** diastole; **b** systole; apical dyskinesia (ballooning) and basal hyperkinesia

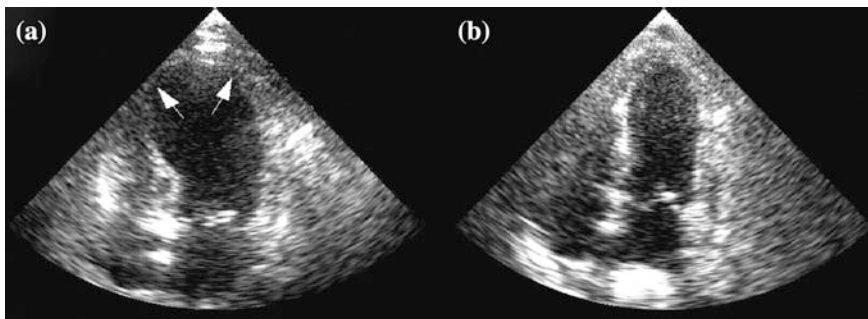


Fig. 2 Echographic image of Takotsubo syndrome, **a** dilatation of the left ventricle in acute phase; **b** spontaneous recovery at day 6

Treatment

The optimal treatment for Takotsubo syndrome has not been defined. Most of the time, patients are already being treated for acute coronary syndrome at the time of diagnosis by the use of antiplatelets, nitrated derivatives, heparin and beta-blockers. Once the illness has been diagnosed and in the absence of ventricular dysfunction, the initial medical treatment may consist of administering renin-angiotensin system inhibitors, beta-blockers and antiplatelets. In the event of coronary spasms observed during the coronarography, calcic inhibitors may be considered. Given the main pathophysiological hypothesis considered in this pathology (an excess of catecholamines), it seems preferable to avoid using amines and beta-agonists. In the event of hemodynamic failure or cardiogenic shock, dobutamine must be used cautiously, and a hemodynamic mechanical support

(extra corporal membranous oxygenation) must be considered rapidly in case of serious dysfunction. The treatment of Takotsubo syndrome complications is symptomatic: diuretics, heparin, anti-arrhythmics, etc.... In the acute phase, patients must benefit from a continuous monitoring in intensive care unit or in resuscitation, along with the help of echocardiographic supervision.

Evolution

Takotsubo syndrome myocardial kinetics anomalies are transient, with a return to a normal primary state within a few days or weeks (3–6). Only the E.C.G. can retain a trace of this event through non-specific signs (repolarization or conduction troubles, lengthening of QT interval). However, short-term prognosis can be clouded by serious, indeed fatal, complications, such as a cardiogenic shock, a left ventricle thrombus, a trouble of ventricular rhythm or of conduction, a mechanical complication.

The death rate is very low (around 1–2 %), even if the clinical picture is worrying by requiring heavy duty resuscitation [4]. The risk of relapse is equally low.

Pathophysiology

Takotsubo syndrome pathophysiology remains little known. A recent stressful event or an important emotional burden appear to be trigger factors for this pathology. The presence of catecholamines at peak level following that stress could well be responsible for a systemic inflammatory reaction and left ventricle fraction [7]. The link between the discharge of catecholamines and ventricular dysfunction is already observed in the meningeal hemorrhage and in pheochromocytoma. The hypothesis of catecholamines released during stress having a toxic and direct influence onto cardiomyocytes is thus plausible [7]. Models based on the use of animals have permitted to copy electrocardiographic modifications and left ventricle kinetics troubles in a rat subjected to a physical stress (forced immobilization). Nevertheless, the concentration of catecholamines released in patients with Takotsubo syndrome is not always high. A microvascular spasm or an intraventricular blocking are other hypotheses put forward, and a multi-factor origin cannot be excluded.

Conclusion

Takotsubo syndrome is a rare and recent concept, most often affecting elderly female patients who have suffered an intense stress. In its acute form, it presents as a particular cardiogenic failure, mimicking a preliminary myocardial infarctus.

Emergency department physicians and anesthetists should familiarize themselves with it, so as to define a quick diagnosis and adapt the required therapies. The evolution is often positive but unpredictable, and sometimes strewn with complications. Treatment is empirical and pathophysiological mechanisms are still to be established.

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