



Tako-Tsubo-like syndrome during anaphylactic reaction

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Abstract

Tako-Tsubo's syndrome (apical ballooning or broken heart syndrome) is a reversible left ventricular dysfunction due to apical asynergy that occurs typically after sudden emotional stress in a subject without coronary disease. It is characterized by acute onset of chest pain or dyspnoea or both and is associated with electrocardiographic changes such as ST segment elevation and/or T wave inversion. Myocardial biomarkers may be normal or slightly elevated [Tsuchihashi K, Ueshima K, Uchida T, et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. *J Am Coll Cardiol* 2001;38:11–8.].

Anaphylaxis is a severe, life-threatening, generalized hypersensitivity reaction, most often starting with urticaria and/or angioedema, that may involve cardiovascular and respiratory systems [Johansson SGO, Hourihane JOB, Bousquet J, et al. A revised nomenclature for allergy. *Allergy* 2001;56:813–24.]. Cardiovascular symptoms, including hypotension, cardiac arrhythmia and chest pain, are presumably linked to cardiac mast cell mediator release [Marone G, Bova M, Detoraki A, Onorati AM, Rossi FW, Spadaro G. The human heart as a shock organ in anaphylaxis. *Novartis Found Symp* 2004;257:133–49.]. We describe the case of a young woman who experienced a profound reversible cardiomyopathy with typical features of Tako-Tsubo's syndrome during an anaphylactic reaction.

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1. Case report

A 31-year-old woman arrived at the Emergency Department with severe dyspnoea associated with nausea, vomiting, dizziness, cardiopalmus, hand paresthesias and severe hypotension (80/40 mm Hg) immediately following a Chinese restaurant meal. These clinical signs were preceded by short-lived flushing and itching of the palms of the hands. The patient did not report any previous emotional stress. On admission, blood-gas analysis showed mild hypoxemia (pO_2 79 mm Hg, pCO_2 36 mm Hg, pH 7.40) and oxygen therapy was administered. Electrocardiography showed sinus rhythm (heart rate 110 bpm) with negative T wave in lead D1 and a VL

and biphasic T wave in leads V5–V6. Cardiac enzymes, including creatinine kinase, creatinine kinase MB fraction and troponins, were normal. Chest radiography showed bilateral infiltrates in an acute respiratory distress-like syndrome and echocardiography revealed severe systolic dysfunction caused by diffuse left ventricular hypokinesia with normal basal contraction [Ejection Fraction (EF) 15%]. Atrial, ventricular and septal sizes were normal, excluding any baseline cardiac defects. The clinical manifestations rapidly worsened with loss of consciousness and the patient was treated with assisted invasive ventilation, i.v. dopamine and fluid therapy (crystalloid 2000 cc). On arrival in the Emergency Department, the patient had been treated with i.v. 6-methylprednisolone (500 mg), but epinephrine and anti-histamines were not administered. After haemodynamic stabilization, the patient underwent coronarography, which showed normal vessels,

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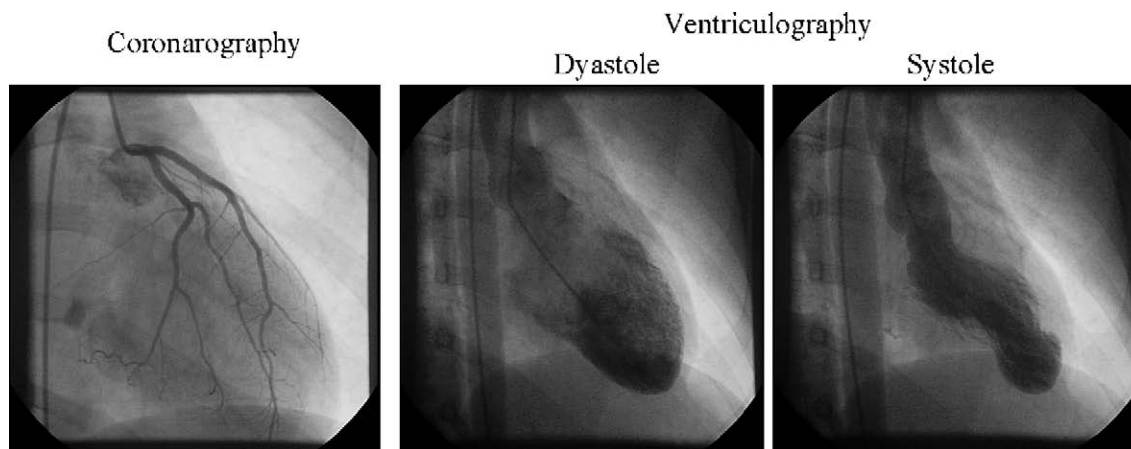


Fig. 1. Coronarographic and ventriculographic assessment on 10th day. Coronary angiography shows normal coronary arteries. Contrast-enhanced ventriculography during diastole and systole shows apical akinesia and anterior distal hypokinesia in the presence of normal contractility of the base.

with no evidence of vasospasm (Fig. 1). Left ventriculography, showed normal contractility of the base in the presence of anterior distal hypokinesia and apical akinesia with ballooning, which is typical of Tako-Tsubo's syndrome (Fig. 1). The patient also underwent endomyocardial biopsy which showed light lymphomononuclear infiltration without myocyte necrosis (Fig. 2). Intracavitary electrophysiological study excluded the presence of inducible arrhythmia. Serological viral screening was also performed to exclude myocarditis. Serial echocardiographic assessment of EF showed a progressive improvement in left ventricular contractility; at discharge, on the 18th day, EF was 55%. Taking into account the sudden onset of the symptoms, the rapid improvement in cardiac contractility and the negative results of the cardiac examinations, an allergic reaction was suspected, and the patient was referred to our Allergy Department. A detailed allergy history revealed past episodes of angioedema after eating legumes and a quinine-induced severe systemic reaction, without history of asthma and/or rhinitis. The onset of symptoms followed the intake of rice, eggs, pork and fried chicken. Testing for food-

specific IgE antibodies revealed only sensitisation toward peanuts (3.79 kUA/l), with normal levels of total serum IgE. The existence of hyperthyroidism was excluded.

2. Discussion

In this patient we hypothesize a severe anaphylactic reaction with cardiac involvement mimicking Tako-Tsubo's syndrome. Our patient showed few cutaneous paradigmatic signs of anaphylaxis, however, it should be noted that the rapid onset and the severity of the reaction could explain the lack of cutaneous signs, the absence of which would not necessarily rule out an anaphylactic event. In addition, the appearance of flushing, itching, nausea, vomiting, dizziness, cardiopalmus, hypotension and hypoxaemia in strict association with the ingestion of oil contaminated with peanut protein, in a subject with allergy to peanuts, supports the diagnosis of anaphylaxis. We may also assume a synergic IgE-independent mechanism (anaphylactoid), caused by the intake of histamine-rich foods and additives typical of oriental cooking (glutamate).

The term "Tako-Tsubo cardiomyopathy" refers to a specific pattern of left ventricular contractile dysfunction that generally occurs after emotional stress [1]. Moreover, similar patterns have been reported in patients after different types of non-emotional stress [2–5]. This syndrome is most prevalent in elderly women although, as in our case, younger patients are occasionally seen. Our case shows some typical features described in Tako-Tsubo cardiomyopathy, such as the electrocardiographic and echocardiographic changes which resolve completely over a few weeks and the discrepancy between these changes and the lack of increase in markers specific for myocardial injury. However, in contrast to the majority of described cases of Tako-Tsubo cardiomyopathy, our patient did not report any previous emotional stress and did not experience chest pain. To our knowledge, a case of Tako-Tsubo-like syndrome has never been reported during anaphylaxis. However, the involvement of the cardiovascular system is an important clinical finding in anaphylaxis [6,7].

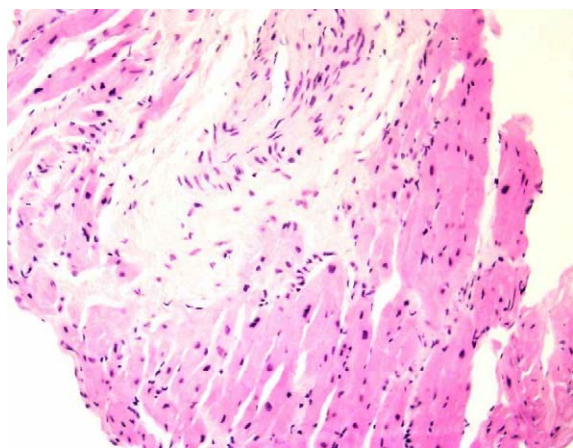


Fig. 2. Endomyocardial biopsy specimen (hematoxylin and eosin). Light lymphocyte and monocyte infiltration of the interstitial myocardial tissue. No signs of necrosis are present.

Myocarditis must be ruled out in the differential diagnosis of transient left ventricular deficiency. Its pathological diagnosis requires the presence of myocyte necrosis, which was not found in our patient, besides inflammatory infiltrate [8]. The histological findings observed in the endomyocardial biopsy of our patient are consistent with the unspecific findings reported in previous cases of Tako-Tsubo-like syndrome [9]. Furthermore, an interstitial mononuclear inflammatory response has been associated with catecholamine toxicity [8], which as we will discuss below, could be involved in the pathophysiology of Tako-Tsubo syndrome. So, the rapid onset of heart involvement, the typical apical ballooning pattern, the absence of fever and of a preceding infection, the normal viral serological titers and the histological findings, make myocarditis a remote possibility in our case.

Profound depression of cardiac systolic function during anaphylaxis has been previously described [10], perhaps caused by the negative inotropic effect of mast cell mediators. Mast cells have been identified in human heart tissue [11], thus activation during anaphylaxis may be responsible for cardiovascular alterations. Mast cell mediators, appear to affect coronary blood flow, heart rate and atrial–ventricular conduction [3], and in particular, decreased myocardial contractility can result from the action of circulating depressant factors, including tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β) [12], secreted by activated mast cells during anaphylaxis [13].

Although the true pathophysiological mechanism of Tako-Tsubo's syndrome remains unknown, some recent reports highlight possible underlying baseline cardiac defects, such as localized mid-ventricular septal thickening [14]; however, this was not present in our patient. A previous angiographic study showed multivessel coronary spasm, at epicardial and microvascular levels during Tako-Tsubo's syndrome [15]. Coronary vasospasm could be related to the exaggerated sympathetic activation that has been recently reported in patients with Tako-Tsubo cardiomyopathy. In addition, Tako-Tsubo patients have higher levels of plasma catecholamines and stress-related peptides than controls [16]. Anaphylaxis is characterized by a rapid movement of intravascular fluid into the extravascular space, which can result in activation of the renin–angiotensin–aldosterone system, causing compensatory catecholamine release [17]. Moreover, it is interesting to remember that histamine, one of the major anaphylaxis mediators, stimulates the release of catecholamines by a direct action on the adrenal medullary cells [18]. Histamine is also synthesized, stored and released by a subpopulation of adult adrenal chromaffin cells [19]. It is likely that the autocrine and endocrine histamine-induced adrenaline secretion by adrenal chromaffin cells plays a protective role against shock. Thus, during anaphylaxis, ventricular contractile dysfunction may be sustained by two non-mutually exclusive mechanisms related to different mast cells mediators and to sympathetic activation. In conclusion, we think that reversible left ventricular

contractile dysfunction may be precipitated by an anaphylactic reaction, such as in our case report. Thus an adverse allergic and non-allergic reaction to foods and/or drugs and/or venom sting should be considered among the potential triggers for Tako-Tsubo's syndrome.

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