

Apical ballooning syndrome or Takotsubo cardiomyopathy: A new challenge in acute cardiac care

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Abstract

Apical ballooning syndrome (ABS) is a unique acute cardiac syndrome characterized by symptoms and electrocardiographic changes that mimic acute myocardial infarction. It occurs in patients without evidence of significant obstructive coronary artery disease and is associated with transient extensive wall motion abnormalities of the apical and mid portions of the left ventricle. The onset of ABS is preceded by a stressful event, either emotional or physical in around 65% of cases. The underlying pathophysiology for ABS remains unclear; however, several mechanisms have been proposed including multivessel epicardial spasm, microvascular spasm, catecholamine induced myocardial stunning and myocarditis. The treatment of ABS remains entirely empirical and should be individualized according to the patient's clinical picture at the time of presentation. It should be initially managed according to the guidelines for acute coronary syndrome. Once the diagnosis of ABS is made, supportive care usually leads to spontaneous recovery. The prognosis of patients with Takotsubo cardiomyopathy is generally favourable. The left ventricular systolic dysfunction usually resolves within a few weeks. In-hospital mortality is low, less than 2%, and recurrence rate is no more than 10%. The aim of this article is to clarify, for the clinicians dealing with acute cardiac care, when they should suspect ABS and how they should confirm the diagnosis and subsequently manage it. (Cardiol J 2008; 15: 572–577)

Key words: apical ballooning syndrome, Takotsubo cardiomyopathy, left ventricular dysfunction, acute coronary syndrome

Introduction

Apical ballooning syndrome (ABS) is a unique acute cardiac syndrome characterized by symptoms and electrocardiographic (ECG) changes that mimic acute myocardial infarction [1]. It occurs in patients without evidence of significant obstructive coronary artery disease and is associated with transient extensive wall motion abnormalities of the apical and mid portions of the left ventricle. Apical ballooning syndrome was initially described in Japanese

patients in 1991 by Dote et al. [2], and was given the name Takotsubo cardiomyopathy [3]. The latter is a fishing pot with a round bottom and a narrow neck that is used for trapping octopuses in Japan. It was named so, on the basis of the characteristic appearance of the left ventricle.

The current review article aims to clarify, for the clinicians dealing with acute cardiac care, when they should suspect ABS and how they should confirm the diagnosis and subsequently manage it.

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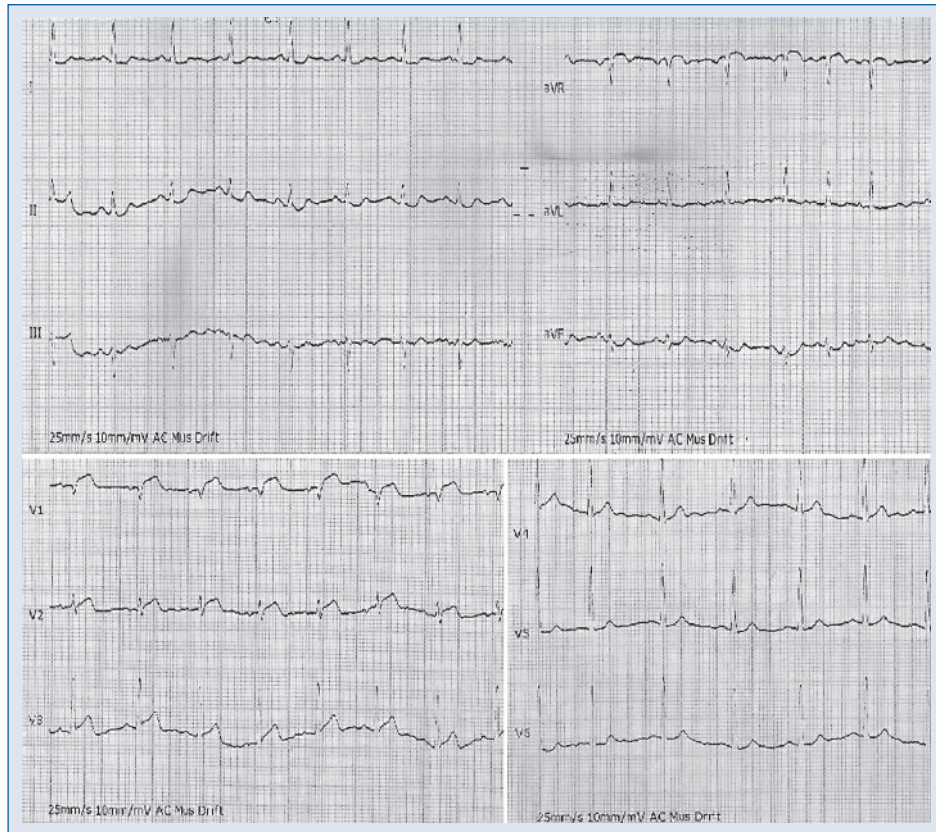


Figure 1. Admission electrocardiogram of a patient who presented with chest pain reveals ST elevation in leads V1 to V3.

Prevalence, patient demographics and clinical presentation

Even though the exact prevalence of ABS remains unknown, there is evidence to suggest that it accounts for around 1% to 2% of patients who present with a suspected acute myocardial infarction [4–6]. In a systemic review by Gianni et al. [1], it was found that almost 90% of the patients with ABS were women and more than 95% of them were above the age of 50.

Chest pain is the most common presenting complaint among patients with Takotsubo cardiomyopathy [1, 5]. The second most common presentation is dyspnoea and other less frequent clinical presentations include cardiogenic shock, syncope and cardiac arrest [1, 7].

The onset of ABS is preceded by a stressful event, either emotional (e.g. unexpected death of a relative, financial crisis, catastrophic medical diagnosis etc.) or physical (e.g. exhausting work, trauma, exacerbation of a systemic disorder, etc) in around 65% of cases [1, 5]. In approximately 35% of cases no trigger can be identified.

Investigations

Electrocardiographic features

The most frequent electrocardiographic changes are ST-segment elevation, usually in the precordial leads, and T wave inversion (Fig. 1, 2) [1, 5]. However, the ECG could be normal or show non-specific changes.

Cardiac biomarkers and catecholamines

Troponin I or T and the MB fraction of CK are usually only mildly raised in the majority of patients [1, 8, 9]. Plasma levels of catecholamines have also been found to be raised in most patients with ABS [1].

Echocardiography, left ventriculography and coronary angiography

The latter shows no evidence of significant coronary artery stenoses [3]. Echocardiography and left ventriculography usually reveal marked left ventricular dysfunction which is subsequently followed by dramatic improvement over a period of days to weeks [1]. The wall motion abnormalities include moderate to severe dysfunction of the

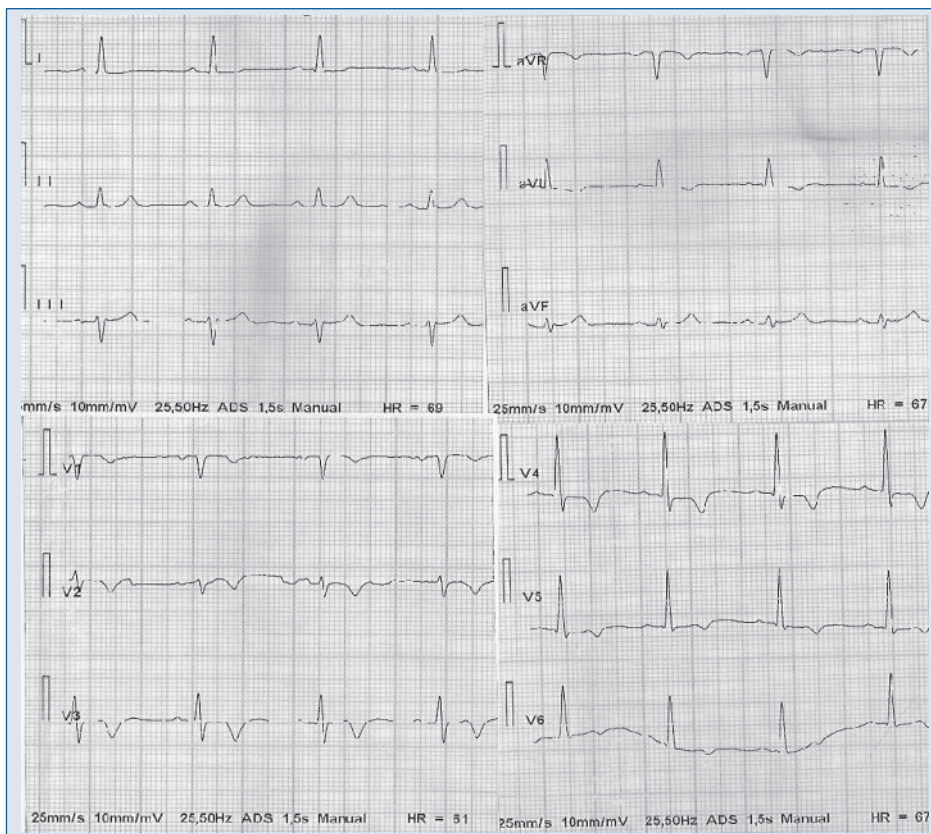


Figure 2. Predischarge electrocardiogram of the same patient reveals T wave inversion in all the precordial leads.

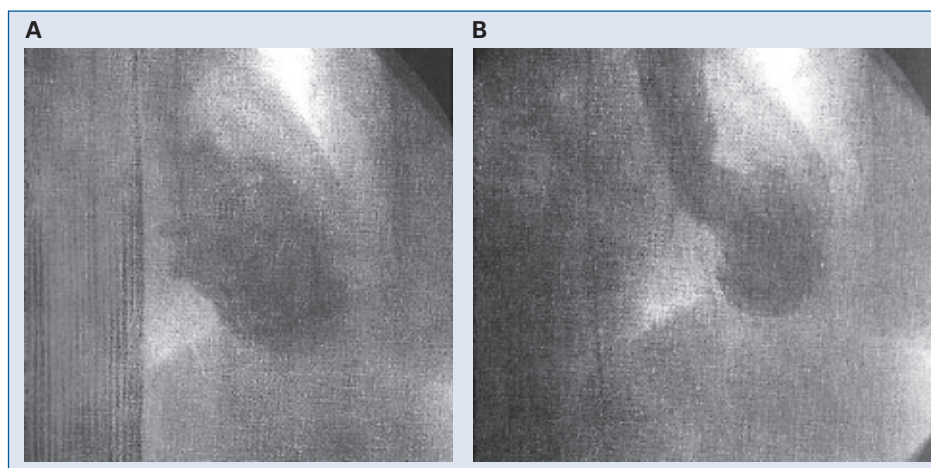


Figure 3. Left ventriculography of the same patient, in diastole (A) and systole (B) reveals wall-motion abnormality consistent with Takotsubo cardiomyopathy. The apical segment of the left ventricle is akinetic with sparing and hyperkinesis of the basal segment.

mid-segment and the apical segment of the left ventricle with sparing and usually hyperkinesis of the basal segment (Fig. 3). The wall motion abnormalities extend beyond the distribution of any single coronary artery [5].

Cardiac magnetic resonance imaging

This technique is very useful because it can demonstrate preserved myocardial viability very well and rule out myocardial infarction or myocarditis [8, 10–12].

Pathophysiology

The underlying pathophysiology for Takotsubo cardiomyopathy remains unclear; however several mechanisms have been proposed including multi-vessel epicardial spasm, microvascular spasm, catecholamine induced myocardial stunning and myocarditis [5].

Multivessel spasm has been postulated to be the cause of ABC. Some investigators used provocative tests, such as infusion of ergonovine, to induce coronary spasm [1, 13, 14]. It was shown that less than 30% of the evaluated patients experienced multivessel spasm after infusion of a provocative agent. The latter suggests that large-vessel spasm is an unlikely explanation of ABC in the majority of patients.

Coronary microcirculation dysfunction is present in the majority of patients who present with this syndrome [4, 15, 16]. Ito et al showed that myocardial perfusion assessed by single photon emission computed tomography is impaired at the time of presentation but improves considerably at 3–5 days [6]. In the absence of obstructive coronary lesions, these findings suggest that impaired microcirculation is the underlying cause of this syndrome. However, it is still not clear whether microvascular dysfunction is the primary mechanism or is an epiphenomenon [5].

It has been suggested that enhanced sympathetic activity plays an important role in the origin of this syndrome [17]. ABS may result from stunning of the myocardium in the setting of excess catecholamines; however, it remains unclear whether the catecholamine excess leads to microvascular spasm, direct myocyte toxicity secondary to cyclic adenosine monophosphate-mediated calcium overload or a primary metabolic abnormality [18, 19]. Bybee et al. [20] found that in patients with ABS there is a flow-metabolism mismatch pattern where there is preserved blood flow but reduced glucose uptake. The enhanced adrenergic activity might lead to increased insulin resistance which in turn leads to reduced glucose uptake.

Another explanation that has been suggested is left ventricular outflow tract obstruction in the setting of intense adrenergic activity or hypovolemia [9, 21]. Left ventricular outflow tract obstruction is known to be associated with increased wall stress, raised left ventricular filling pressure and decreased systemic blood pressure. These hemodynamic changes, which are known to increase oxygen demand and reduce coronary perfusion pressure, may produce myocardial ischemia and subsequent stunning.

Myocarditis has also been proposed as a possible underlying cause. However, myocardial biopsies and viral serology screens that have been performed on patients who have been diagnosed for ABS have failed to show any evidence of myocarditis [14, 16, 17]. Another enigmatic finding in patients with ABS is the predilection of the apical and mid-segments of the left ventricle with sparing of the basal segments. There is some evidence to suggest that the apical region is more responsive to sympathetic stimulation and more vulnerable to catecholamine surges [22]. It has also been observed that fatty acid metabolism, which is the predominant source of energy for the myocardium, is more severely impaired than myocardial perfusion in the mid and apical segments during the early phase of this syndrome [23]. An alternative explanation is that there are basal to apical gradients in both perfusion and sympathetic distribution [18, 20, 24].

A different mechanism that has been proposed is that ABS may actually be the paradigm of spontaneously aborted myocardial infarction resulting from an acute atherothrombotic event in the proximal or middle portion of the left anterior descending artery with subsequent rapid and complete lysis of the thrombus [25]. This could be the case in patients with long left anterior descending arteries that wrap around the apex and supply a large area of the inferior wall.

Discussion

The Mayo Clinic has recently proposed the following diagnostic criteria for the clinical diagnosis of ABS [5]:

- Transient hypokinesis, akinesis or dyskinesis of the left ventricular mid segments with or without apical involvement. The regional wall-motion abnormalities extend beyond a single epicardial vascular distribution. However, there are rare exceptions such as those patients in whom the regional wall-motion abnormality is limited to a single coronary territory.
- Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture. However, it is possible that a patient with obstructive coronary atherosclerosis may also develop ABS. This is very rare in the published literature, perhaps because such cases are misdiagnosed as an acute coronary syndrome. It is obvious that in the above circumstances, the diagnosis of ABS should be made with caution, and a clear stressful precipitating trigger must be sought [5].

- New ECG abnormalities (either ST-segment elevation and/or T-wave inversion) or elevated cardiac troponin.
- Absence of recent significant head trauma, intracranial bleeding, pheochromocytoma, myocarditis and hypertrophic cardiomyopathy.

The treatment of ABS remains entirely empirical and should be individualized according to the patient's clinical picture at the time of presentation. It should be initially managed according to the guidelines for acute coronary syndrome. Once the diagnosis of ABS is made, supportive care usually leads to spontaneous recovery [1, 5].

When there is significant hypotension, echocardiography should be performed to rule out dynamic left ventricular outflow tract obstruction [5]. If present, it should be cautiously treated with beta-blockers aiming to reduce the contractility of the basal segment. Treatment with inotropes is contraindicated in this situation. If low blood pressure is secondary to cardiogenic shock, treatment with inotropes and intra-aortic balloon counterpulsation is indicated [5, 9].

The prognosis of patients with Takotsubo cardiomyopathy is generally favourable [5]. In-hospital mortality is low, less than 2%, and recurrence rate is around 10% [1, 26]. Some centres advocate long-term therapy with beta-blockers aiming in this way to reduce the likelihood of recurrence [5].

It is almost certain that many patients over the years have received thrombolysis which was thought to be successful even though it might have been unnecessary, especially if we take into account the suggested incidence of ABS, which is around 1% to 2%, of patients who present with a suspected acute myocardial infarction [5].

Therefore, physicians dealing with acute cardiac care should be able to recognise the characteristic features of this not so rare syndrome, provide supportive therapy and proceed to urgent coronary angiography before giving thrombolytic therapy if the diagnosis of ABS is strongly suspected.

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