CASE REPORT

Apical ballooning (takotsubo) syndrome with concurrent ST-segment elevation myocardial infarction

Mohsin A Hussain,¹ Andrew T Cox,¹ Rachel Bastiaenen,¹ Abhiram Prasad²

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bcr-2017-220145>).

¹Cardiology Clinical Academic Group, St George's Hospital's NHS Foundation Trust and St George's University of London, London, UK

²Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota, USA

Correspondence to

Dr Abhiram Prasad, prasad.abhiram@mayo.edu

Accepted 26 June 2017

SUMMARY

We present the case of a 61-year-old woman admitted with chest pain and an ECG demonstrating ST-segment elevation in the lateral leads. Emergency coronary angiography demonstrated an occluded obtuse marginal branch. Percutaneous intervention was unsuccessful as the lesion could not be crossed with a wire. Left ventriculography and transthoracic echocardiography demonstrated hypokinesis of the entire apex but preserved contractility of the basal segments, consistent with a diagnosis of apical ballooning syndrome (ABS). Cardiac MRI demonstrated myocardial oedema in all mid to apical segments, with a left ventricular ejection fraction (LVEF) of 38%. Repeat study at 5 months demonstrated an infarct in the distribution of the occluded artery with late gadolinium enhancement, consistent with a diagnosis of a lateral wall myocardial infarction and an improvement in the LVEF to 51%. The case illustrates the novel observation that ABS and acute myocardial infarction may rarely occur simultaneously.

BACKGROUND

Apical ballooning syndrome (ABS; also known as takotsubo cardiomyopathy/syndrome after the Japanese octopus trap and stress cardiomyopathy) is an acute reversible condition that was first described in the early 1990s.¹ Over 90% of patients who develop ABS are women, the vast majority being postmenopausal. This unique syndrome accounts for 5%–10% of women that are initially suspected of an acute myocardial infarction (AMI) at the time of presentation. The clinical and ECG features of ABS are similar to an AMI.² However, patients with ABS typically have normal coronary arteries or non-occlusive coronary plaques. The transient cardiomyopathy is a diagnosis of exclusion with current diagnostic criteria requiring the absence of a culprit occlusive coronary lesion to confirm a diagnosis of ABS.^{3,4}

CASE PRESENTATION

A 61-year-old woman presented with a 2-hour history of acute onset retrosternal chest pain without radiation. There were no associated symptoms. The patient had previously been in good health and did not suffer from any comorbidity. There was no significant family history. The pulse and blood pressure were 83 beats per min and 100/67 mm Hg, respectively. Physical examination

was normal. ECG demonstrated ST-segment elevation in leads I, aVL and V4–V6 (figure 1). Emergency coronary angiography was performed in view of a presentation consistent with a lateral ST-segment elevation AMI.

INVESTIGATIONS

Angiography demonstrated an occluded terminal branch of the major obtuse marginal segment of the left circumflex coronary artery. The remainder of the coronary arteries were normal (figure 2, see online supplementary videos 1 and 2). A LV angiogram revealed extensive regional wall motion abnormality (RWMA) of the mid and apical segments with preserved basal function resulting in the classic appearance of apical ballooning associated with impairment of global systolic function (see online supplementary video 3). The distribution of RWMA extended well beyond that of the occluded obtuse marginal artery, and involved the territories perfused by the left anterior descending and right coronary arteries. Percutaneous coronary intervention was attempted to restore blood flow in the obtuse marginal and relieve symptoms, but the occlusion could not be crossed with a wire. The cardiac troponin I level at admission was 18 761 ng/L, and peaked at 40 759 ng/L (normal range <50 ng/L). A transthoracic echocardiogram on Day two demonstrated persistent RWMA in all three vascular territories. There was evidence of preserved basal contraction and persistent akinesia of all the apical segments. The left ventricular (LV) systolic function remained impaired with a global ejection fraction of 40%. (figure 3, see online supplementary videos 4 and 5).

Cardiac MR (CMR) on day 3 demonstrated a normal size left ventricle with akinesia of all mid-apical segments and preserved contraction of the basal segments. The global LV systolic function was moderately impaired with an ejection fraction of 38%. On T2 short tau inversion recovery imaging, high-signal intensity was present subendocardially in all mid and apical segments suggesting the presence of oedema. There was partial thickness (<50%) subendocardial late gadolinium enhancement (LGE) in the mid to apical anterolateral wall of the left ventricle with evidence of microvascular obstruction (figure 4, see online supplementary videos 6 and 7).

CrossMark

To cite: Hussain MA, Cox AT, Bastiaenen R, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220145

Figure 1 Twelve-lead ECG demonstrating lateral ST segment elevation.

DIFFERENTIAL DIAGNOSIS

The two main differential diagnoses at this stage were ABS and AMI.

TREATMENT

Initial treatment was initiated according to the ST-segment elevation AMI pathway and included aspirin, ticagrelor and intravenous heparin. Following the angiogram, heparin was discontinued and oral beta blocker and ACE-inhibitor therapy was initiated for the LV systolic dysfunction.

OUTCOME AND FOLLOW-UP

The patient was seen at 6 weeks follow-up, and was well without cardiac symptoms. A repeat CMR scan at 5 months following the initial admission demonstrated a mildly dilated left ventricle with recovery of the LV ejection fraction at 51% (normal $\geq 55\%$). The only persistent RWMA was akinesis of the mid to apical

anterolateral wall segments along with full thickness (75%–100%) LGE. Adenosine stress perfusion imaging demonstrated a fixed defect in the same distribution as the LGE (figure 5, see online supplementary videos 8 and 9). At 2-year follow-up, the patient remained free of recurrence of ABS or AMI. These detailed and serial imaging findings confirm the simultaneous occurrence of AMI and ABS.

DISCUSSION

ABS is typically associated with symptoms and ECG features of myocardial ischaemia and laboratory findings of myonecrosis, but despite the extensive RWMA at presentation, it is characterised by complete recovery of LV function without infarction. Our case clearly illustrates that, not only does ABS mimic an AMI, but that the two conditions may rarely coexist at the time of acute presentation. AMI may have been the primary stressor triggering ABS in our patient. However, the presence of otherwise angiographically near normal coronary arteries makes AMI and plaque rupture unlikely to have been the cause of the coronary occlusion. Conversely, ABS may have been complicated by either thromboembolism, spasm or dissection of the obtuse marginal artery, resulting in AMI as a secondary event. Abreu

Figure 2 Coronary angiography—LAO view of the RCA (A). RAO caudal view of the left coronary system (B) with an occluded branch of an obtuse marginal branch (white arrow). Left ventricular angiography views in diastole (C) and systole (D) demonstrating apical ballooning. LAO, left anterior oblique; RAO, right anterior oblique.

Figure 3 Transthoracic echocardiography demonstrating evidence of good basal wall contraction and apical ballooning—apical 4 chamber views in diastole (A) and systole (C); apical 2 chamber view in diastole (B) and systole (D).

Figure 4 Cardiac MRI on day 3—four-chamber view in diastole (A) and systole (B) demonstrating preserved basal contraction and apical ballooning. T2 STIR imaging (C) demonstrates high-signal intensity subendocardially in all mid to apical segments indicating oedema. Late gadolinium enhancement seen in the mid to apical anterolateral wall with evidence of microvascular obstruction (D). STIR, short tau inversion recovery.

and colleagues have recently reported a similar case of ABS in which there was also isolated occlusion of terminal branches of an obtuse marginal branch. They proposed that AMI was the trigger for ABS, but the distal occlusion of multiple terminal

Figure 5 Cardiac MRI 5 months following presentation—four-chamber view in diastole (A) and systole (B) demonstrating mildly impaired systolic function with akinesis of mid to apical anterolateral wall. There is an almost full thickness mid to apical anterolateral infarct with LGE evident in the four-chamber (C) and short-axis views (D).

branches, in an otherwise mildly diseased coronary tree, raises the possibility of an embolic occlusion secondary to ABS.⁵ Maeda *et al* have reported a case of ABS in which there was a proximal occlusion of an obtuse marginal branch that was treated with emergency percutaneous intervention; and the patient had lateral wall LGE on CMR.⁶ They also proposed that the lateral AMI was the trigger for the ABS. However, if that were so, given that there are millions of cases of AMI per year globally, one would expect a higher incidence of concomitant ABS. The case highlights the need to interpret current ABS diagnostic criteria with caution with respect to the need to exclude patients with plaque rupture or intracoronary thrombosis.²⁻⁴

The pathophysiology of ABS

The underlying pathophysiology of ABS has not been fully understood despite multiple theories being proposed. Myocardial stunning, defined as transient left ventricular systolic dysfunction following a brief period of myocardial ischaemia,⁷ could be a potential explanation. However, the epicardial coronary arteries in ABS are typically normal or have mild atherosclerosis and therefore an alternative cause(s) of myocardial ischaemia needs to be sought. Multivessel coronary vasospasm has been proposed.⁸ However, in a case series of ABS, coronary vasospasm, provoked by using intracoronary acetylcholine, was only seen in 21% of cases.⁹ Microvascular spasm/dysfunction may be an alternative cause for myocardial ischaemia. In support of this, early studies frequently identified that the thrombolysis in myocardial infarction (TIMI) frame count was elevated at presentation in a multiterritory distribution, a marker of diffuse coronary microvascular dysfunction.¹⁰ Another marker of microvascular dysfunction is coronary flow reserve (CFR) when assessed in the absence of epicardial stenosis.¹¹⁻¹³ In a study of eight patients with ABS, decreased CFR was found in all three epicardial coronary arteries during the acute phase. The CFR returned to normal after 3 weeks.¹⁴ The improvement in myocardial perfusion appears to precede and correlate with recovery of left ventricular ejection fraction.¹⁵ More recently, reactive hyperaemia, as a parameter of endothelial function and peripheral vascular response to acute mental stress was assessed in a group of women who had recovered from an episode of ABS and compared with a control group of postmenopausal women without the cardiomyopathy. Impaired peripheral vascular reactivity and endothelial dysfunction was found following acute mental stress in patients with prior ABS.¹⁶ These data suggest that vasomotor dysfunction may be a substrate in the pathogenesis of ABS.

The RWMA of ABS is similar to that seen occasionally in patients following an acute cerebrovascular insults and pheochromocytoma, both conditions associated with sympathetic surges.^{17 18} High level of catecholamines have been documented in ABS, however, this has not been a consistent finding.^{19 20} In a rat model of ABS, the coadministration of an alpha and beta adrenoceptor antagonist prevented the onset of RWMA.²¹ If a surge in catecholamine levels was the primary cause for the cardiomyopathy, one would expect a similar prevalence among men and women. Indeed, if catecholamine surge was the sole mechanism, a case could be made that the condition should be more frequently seen in men due to the greater adrenergic response to mental stress.²

The increased incidence of ABS in postmenopausal suggests a contribution of oestrogen withdrawal. Women who take long-term oestrogen therapy have attenuated catecholamine responses to mental stress.^{22 23} It has been suggested that the

increased incidence of ABS in women may be explained by perimenopausal oestrogen deficiency in conjunction with microvascular dysfunction.²

The mechanisms described above do not explain why ABS leads to the characteristic RWMA with apical ventricular dysfunction. Potential explanations include, regional heterogeneity in ventricular wall structure and hence wall stress, the apex being a border zone of the perfusion regions for the major coronary arteries,⁹ and an apical-basal gradient in beta two receptors and sympathetic innervation.²⁴

Learning points

- ▶ Apical ballooning (Takotsubo) syndrome (ABS) is typically a transient cardiomyopathy with complete recovery of left ventricular systolic function.
- ▶ ABS is an important differential diagnosis of acute myocardial infarction (AMI), especially in postmenopausal women.
- ▶ ABS and AMI may rarely occur simultaneously.
- ▶ Presence of a potential 'culprit lesion' on coronary angiography should not always exclude the diagnosis of ABS.

Contributors MAH acquired the data and drafted the manuscript with editing from ATC, RB and AP. All authors (MAH, ATC, RB, AP) made a significant contribution to the manuscript and agree to be held accountable for its contents.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) . All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Sato H, Tateishi H, Uchida T. Takotsubo-type cardiomyopathy due to multivessel spasm. In: Kodama K, Haze K, Hon M, eds. *Clinical aspect of myocardial injury: from ischaemia to heart failure (in Japanese)*. Tokyo: Kagakuyouronsya Co, 1990:56–64.
- 2 Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J* 2008;155:408–17.
- 3 Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on takotsubo syndrome: a position statement from the Taskforce on Takotsubo syndrome of the heart failure association of the European Society of Cardiology. *Eur J Heart Fail* 2016;18:8–27.
- 4 Scantlebury DC, Prasad A. Diagnosis of Takotsubo cardiomyopathy. *Circ J* 2014;78:2129–39.
- 5 Abreu G, Rocha S, Bettencourt N, et al. An unusual trigger causing Takotsubo syndrome. *Int J Cardiol* 2016;223:118–20.
- 6 Maeda S, Tamura A, Kawano Y, et al. Takotsubo cardiomyopathy triggered by lateral wall ST-segment elevation myocardial infarction. *J Cardiol Cases* 2014;9:117–20.
- 7 Braunwald E, Kloner RA. The stunned myocardium: prolonged, postischemic ventricular dysfunction. *Circulation* 1982;66:1146–9.
- 8 Fournier C, Boujon B, Hebert JL, et al. Stunned myocardium following coronary spasm. *Am Heart J* 1991;121:593–5.
- 9 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. angina pectoris-myocardial infarction investigations in Japan. *J Am Coll Cardiol* 2001;38:11–18.
- 10 Bybee KA, Prasad A, Barsness GW, et al. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. *Am J Cardiol* 2004;94:343–6.
- 11 Doucette JW, Corl PD, Payne HM, et al. Validation of a Doppler guide wire for intravascular measurement of coronary artery flow velocity. *Circulation* 1992;85:1899–911.
- 12 Baumgart D, Haude M, Liu F, et al. Current concepts of coronary flow reserve for clinical decision making during cardiac catheterization. *Am Heart J* 1998;136:136–49.
- 13 McGinn AL, White CW, Wilson RF. Interstudy variability of coronary flow reserve. influence of heart rate, arterial pressure, and ventricular preload. *Circulation* 1990;81:1319–30.
- 14 Kume T, Akasaka T, Kawamoto T, et al. Assessment of coronary microcirculation in patients with takotsubo-like left ventricular dysfunction. *Circ J* 2005;69:934–9.
- 15 Jain M, Upadaya S, Zarich SW. Serial evaluation of microcirculatory dysfunction in patients with Takotsubo cardiomyopathy by myocardial contrast echocardiography. *Clin Cardiol* 2013;36:531–4.
- 16 Martin EA, Prasad A, Rihal CS, et al. Endothelial function and vascular response to mental stress are impaired in patients with apical ballooning syndrome. *J Am Coll Cardiol* 2010;56:1840–6.
- 17 Ohtsuka T, Hamada M, Kodama K, et al. Images in cardiovascular medicine. neurogenic stunned myocardium. *Circulation* 2000;101:2122–4.
- 18 Shaw TR, Rafferty P, Tait GW. Transient shock and myocardial impairment caused by pheochromocytoma crisis. *Br Heart J* 1987;57:194–8.
- 19 Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352:539–48.
- 20 Park JH, Kang SJ, Song JK, et al. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. *Chest* 2005;128:296–302.
- 21 Ueyama T, Kasamatsu K, Hano T, et al. Emotional stress induces transient left ventricular hypocontraction in the rat via activation of cardiac adrenoceptors: a possible animal model of 'tako-tsubo' cardiomyopathy. *Circ J* 2002;66:712–3.
- 22 Komesaroff PA, Esler MD, Sudhir K. Estrogen supplementation attenuates glucocorticoid and catecholamine responses to mental stress in perimenopausal women. *J Clin Endocrinol Metab* 1999;84:606–10.
- 23 Sung BH, Ching M, Izzo JL, et al. Estrogen improves abnormal norepinephrine-induced vasoconstriction in postmenopausal women. *J Hypertens* 1999;17:523–8.
- 24 Paur H, Wright PT, Sikkel MB, et al. High levels of circulating epinephrine trigger apical cardiodepression in a β_2 -adrenergic receptor/Gi-dependent manner: a new model of Takotsubo cardiomyopathy. *Circulation* 2012;126:697–706.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow