The Journal of Laryngology & Otology (2016), ***130***, *883–886*.

doi:10.1017/S0022215116008288

CLINICAL RECORD

Management of airway obstruction with nebulised adrenaline resulting in takotsubo cardiomyopathy: case report

F KESHTKAR, O T DALE, W O BENNETT, C E HALL

Department of Otolaryngology, Gloucestershire Royal Hospital, Gloucester, UK

Abstract

Background: Takotsubo cardiomyopathy has been associated with the use of catecholamines; however, its development after the use of nebulised adrenaline for the management of acute airway obstruction has not previously been described.

Case report: A 66-year-old man with squamous cell carcinoma of the larynx, with tumour–node–metastasis staging of $T_3N_{2c}M_0$, confirmed by biopsy and computed tomography, presented to the emergency department with acute airway obstruction. He was treated twice with nebulised adrenaline and intravenous dexamethasone. After a period of 24 hours, cardiac rhythm changes were noted on telemetry. A 12-lead electrocardiogram showed widespread T-wave inversion and QT prolongation suggestive of an acute coronary syndrome. Coronary angiography demonstrated no coronary artery disease, but left ventricular angiography showed marked apical ballooning and apical wall akinesia consistent with a diagnosis of takotsubo cardiomyopathy.

Conclusion: Takotsubo cardiomyopathy can mimic true ischaemic heart disease and the diagnosis requires a high index of suspicion in patients managed with nebulised adrenaline.

Key words: Takotsubo Cardiomyopathy; Takotsubo Syndrome; Stress Cardiomyopathy; Broken Heart Syndrome; Transient Apical Ballooning Syndrome; Apical Ballooning Syndrome; Laryngeal Neoplasm; Adrenaline; Epinephrine; Catecholamines; Airway Obstruction

Introduction

Airway obstruction is a common presentation in patients with laryngeal cancer. Management of acute obstruction in these patients focuses on securing the airway without compromising oncological outcome. In such cases, medical adjuncts including nebulised adrenaline and intravenous steroids are often used.

We present a case of takotsubo cardiomyopathy resulting from nebulised adrenaline administered for the management of acute airway obstruction in a patient with laryngeal cancer.

Case report

A 66-year-old man with squamous cell carcinoma of the larynx, with tumour–node–metastasis staging of $T_3N_{2c}M_0$, confirmed by biopsy and computed tomography, presented to the emergency department with acute airway obstruction. Nasendoscopy demonstrated an irregular mass affecting the left hemilarynx and extending to the subglottis, with vocal fold fixation. He was treated with 1 µg/5 ml of nebulised adrenaline and 8 mg of intravenous dexamethasone. He was transferred to the intensive care unit for airway observation pending a laryngectomy. On the intensive care unit, the patient required further treatment with nebulised adrenaline.

After a period of 24 hours, cardiac rhythm changes were noted on telemetry. A 12-lead electrocardiogram (ECG) showed widespread T-wave inversion and QT prolongation (Figure 1). Throughout this episode, the patient reported no chest pain or other symptoms of an acute coronary syndrome. Analyses of serum cardiac enzymes conducted 6 and 12 hours after ECG changes demonstrated high levels of troponin T. The ECG changes and raised cardiac enzyme levels indicated possible myocardial ischaemia.

Urgent coronary angiography was performed. This demonstrated no coronary artery disease (Figure 2). However, left ventricular angiography showed marked apical ballooning and apical wall akinesia (Figure 3). A subsequent transthoracic echocardiogram confirmed a hypokinetic apical segment of the left ventricle and a left ventricular ejection fraction by Simpson's method of 42 per cent. These findings are consistent with a diagnosis of takotsubo cardiomyopathy. The patient subsequently underwent laryngectomy for his laryngeal carcinoma.

Discussion

Takotsubo cardiomyopathy is also referred to as apical ballooning syndrome, broken heart syndrome, stress cardiomyopathy and Japanese octopus syndrome.[1–3] It describes the transient regional left ventricular dysfunction manifesting in global ECG changes and raised cardiac biomarkers that mimic myocardial infarction. It is distinguishable from myocardial infarction based on angiographic evidence suggesting no coronary artery disease or plaque rupture.[3–10] Approximately 15 per cent of those with takotsubo cardiomyopathy also have some level of coronary artery disease. If coronary artery

Accepted for publication 12 March 2016 First published online 5 July 2016

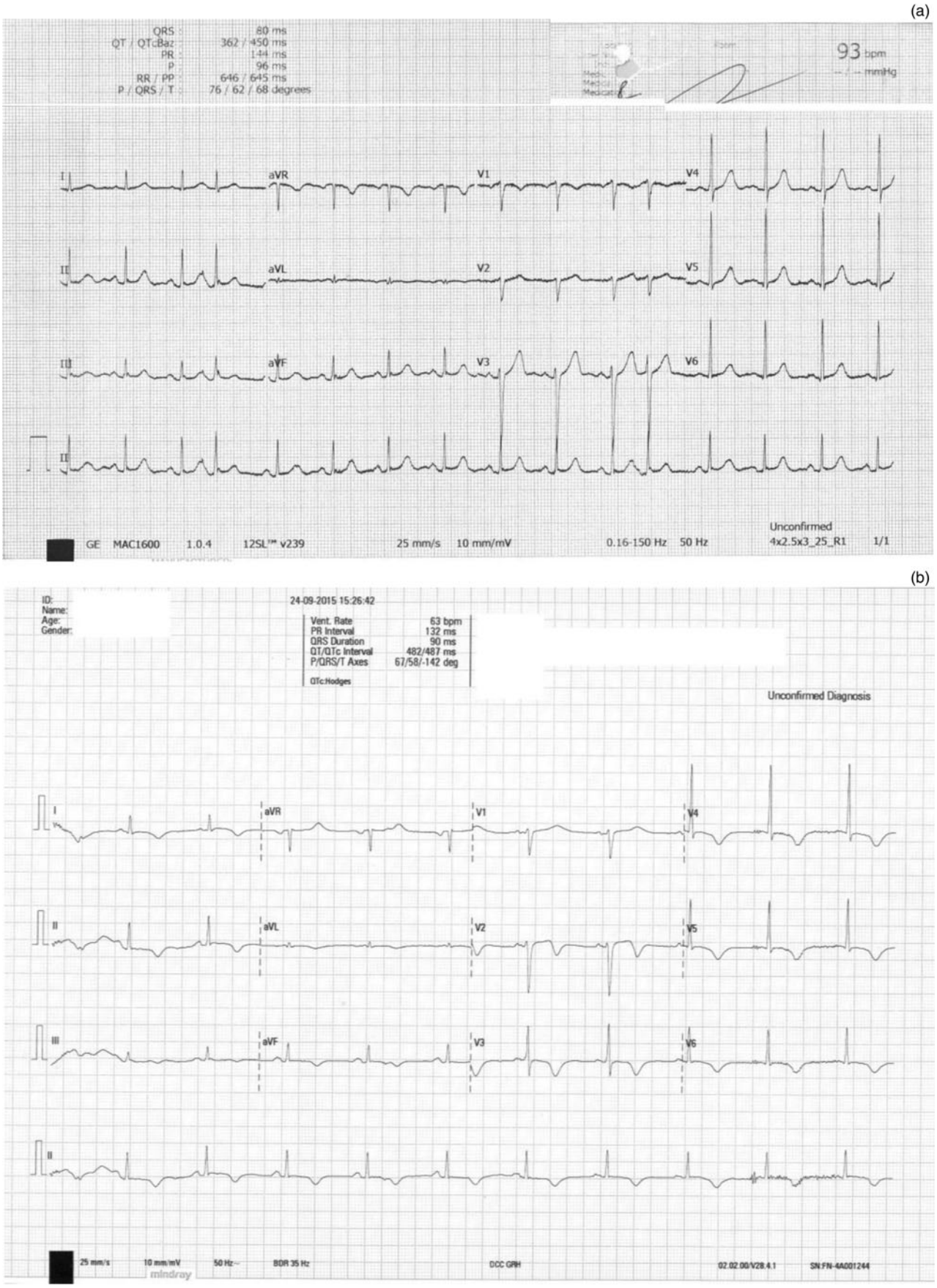

FIG. 1

(a) Electrocardiogram on admission to the emergency department showing tachycardia and no evidence of ischaemic heart disease. (b) Electrocardiogram 24 hours after admission (following administration of nebulised adrenaline) showing widespread T-wave inversion and QT prolongation. V1–V6 represent pre-cordial electrode placements. Bpm = beats per minute; aVR = augmented vector right; aVL = augmented vector left; aVF = augmented vector foot; vent = ventricular; deg = degrees

https://doi.org/10.1017/S0022215116008288 Published online by Cambridge University Press

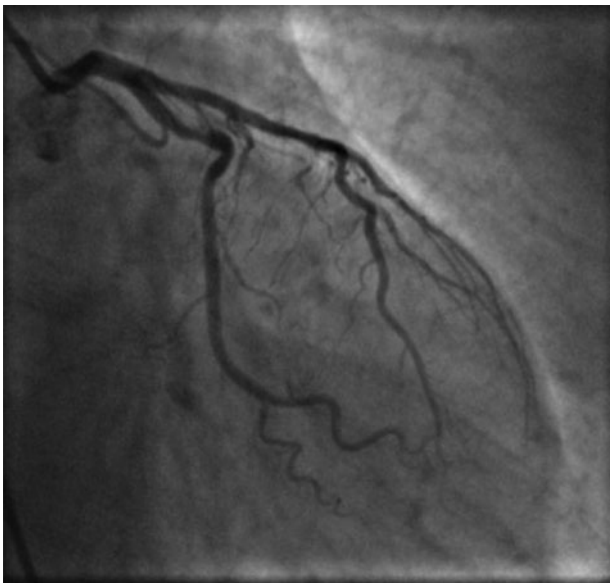

FIG. 2
Angiography showing normal coronary artery, with no defect in filling.

disease is found, takotsubo cardiomyopathy can be diagnosed if the changes in ECG are beyond the territory perfused by a single epicardial coronary artery and the wall motion abnormalities are not in the distribution of the coronary disease.[11]

The condition was first described in 1990 in Japan. The term 'takotsubo' means octopus trap, which is a vase that has a similar shape to the systolic apical ballooning appearance of the left ventricle, created as a result of depression of the mid and apical segments and hypokinesis of the basal walls.[12–15]

Patients often present with chest pain, retrosternal pain or dyspnoea, but a significant number are asymptomatic and the condition is found on routine investigation.[11] It affects women more than men and 80 per cent of those diagnosed are post-menopausal. The prevalence is not known; however, 1–2 per cent of patients presenting with troponin-positive suspected acute coronary syndrome are thought to have takotsubo cardiomyopathy.[12–14]

- **Takotsubo cardiomyopathy following the use of nebulised adrenaline for airway obstruction has not previously been reported**
- **It may mimic true ischaemic heart disease; the possibility of takotsubo cardiomyopathy should be considered in this context**
- **It can mimic myocardial infarction, with electrocardiogram (ECG) and biochemical evidence of ischaemic heart disease**
- **It is distinguished from a myocardial infarct based on angiographic and ECG evidence**
- **There is systolic apical ballooning of the left ventricle resulting from depression of mid and apical segments and hypokinesis of basal walls**

The exact pathogenesis of the disease is not known, particularly the reason for the primary involvement of the mid and apical segments of the left ventricle.[15–17] Takotsubo

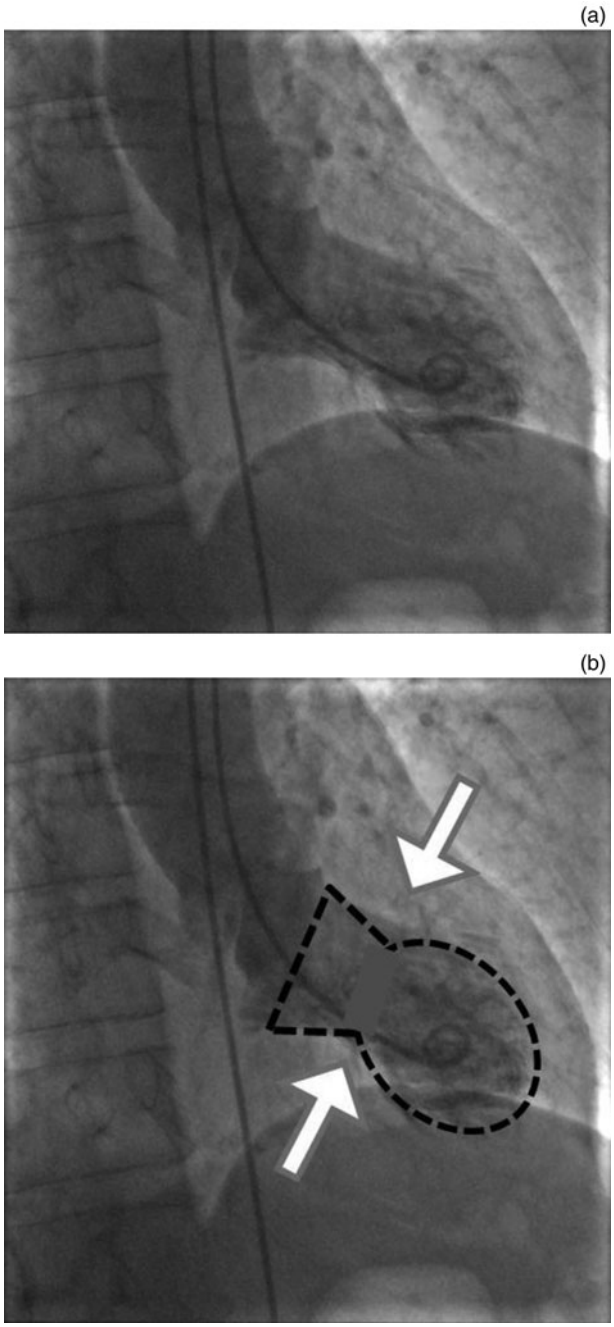

FIG. 3
(a) Left ventricular angiography shows apical ballooning and mid-cavity ventricular abnormality. (b) Vase-like appearance of the cavity.

cardiomyopathy is often but not always precipitated by extreme physical or emotional distress, such as the death of a relative, natural disasters or after sepsis.[2,4,18] This has led to the hypothesis that excess catecholamine release leads to coronary artery spasm and microvascular abnormalities, causing myocardial stunning.[19] This idea has been reinforced by studies that have demonstrated high levels of plasma adrenaline in patients found to have takotsubo cardiomyopathy in the intensive care setting.[15] This has not been replicated in all subsequent studies, with some authors demonstrating no difference in the plasma adrenaline levels found in those with takotsubo cardiomyopathy and those who had a myocardial infarct.[20] However, the findings of

https://doi.org/10.1017/S0022215116008288 Published online by Cambridge University Press

vasospasm on angiography and hypoperfusion of the myocardium which resolves following improvement in myopathy strengthen the argument for catecholamine-induced takotsubo cardiomyopathy.[4,7,21,22]

Conclusion

Takotsubo cardiomyopathy has not previously been reported following the use of nebulised adrenaline for airway obstruction. It may mimic true ischaemic heart disease and it is important to consider the possibility of takotsubo cardiomyopathy in this context.

The diagnosis requires a high index of suspicion in patients with ECG and biochemical evidence of ischaemic heart disease in the absence of physical symptoms.

Takotsubo cardiomyopathy is confirmed by ECG, with or without angiography, demonstrating normal coronary vessels. Treatment involves removing the causative agent. Left ventricular hypokinesis is transient and often resolves.

References

1 Dote K, Sato H, Tateishi H, Huchida T, Ishihara M. Myocardial stunning due to simultaneous multivessel coronary spasms: a review of 5 cases. *J Cardiol* 1991;**21**:203–13
2 Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS *et al*. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med* 2004;**141**:858–65
3 Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M *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
4 Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol* 2003;**41**:737–42
5 Wittstein IS, Thiemann DR, Lima JA, Boughman KL, Schulman SP, Girstenblit G *et al*. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;**352**:539–48
6 Desmet WJ, Adriaenssens BF, Dens JA. Apical ballooning of the left ventricle: first series in white patients. *Heart* 2003;**89**:1027–31
7 Dec GW. Recognition of the apical ballooning syndrome in the United States. *Circulation* 2005;**111**:388–90
8 Aurigemma GP, Tighe DA. Echocardiography and reversible left ventricular dysfunction. *Am J Med* 2006;**119**:18–21
9 Bybee KA, Prasad A. Stress-related cardiomyopathy syndromes. *Circulation* 2008;**118**:397–409
10 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
11 Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M *et al*. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. *N Engl J Med* 2015;**373**:929–38
12 Kurowski V, Kaiser A, von Hof K, Killermann DP, Mayer B, Hartmann F *et al*. Apical and midventricular transient left ventricular dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. *Chest* 2007;**132**:809–16
13 Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J* 2006;**27**:1523–9
14 Prasad A, Dangas G, Srinivasan M, Yu J, Gersh BJ, Mehran R *et al*. Incidence and angiographic characteristics of patients with apical ballooning syndrome (takotsubo/stress cardiomyopathy) in the HORIZONS-AMI trial: an analysis from a multicenter, international study of ST-elevation myocardial infarction. *Catheter Cardiovasc Interv* 2014;**83**:343–8
15 Park JH, Kang SJ, Song JK, Kim HK, Lim CM, Kang DH *et al*. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. *Chest* 2005;**128**:296–302
16 Medeiros K, O'Connor MJ, Baicu CF, Fitzgibbons TP, Shaw P, Tighe DA *et al*. Systolic and diastolic mechanics in stress cardiomyopathy. *Circulation* 2014;**129**:1659–67
17 Park SM, Prasad A, Rihal C, Bell MR, Oh JK. Left ventricular systolic and diastolic function in patients with apical ballooning syndrome compared with patients with acute anterior ST-segment elevation myocardial infarction: a functional paradox. *Mayo Clin Proc* 2009;**84**:514–21
18 Watanabe H, Kodama M, Okura Y, Aizawa Y, Tanabe N, Chinushi M *et al*. Impact of earthquakes on takotsubo cardiomyopathy. *JAMA* 2005;**294**:305–7
19 Paur H, Wright PT, Sikkel MB, Tranter MH, Mansfield C, O'Gara P *et al*. High levels of circulating epinephrine trigger apical cardiodepression in a β2-adrenergic receptor/Gi-dependent manner: a new model of takotsubo cardiomyopathy. *Circulation* 2012;**126**:697–706
20 Heubach JF, Ravens U, Kaumann AJ. Epinephrine activates both Gs and Gi pathways, but norepinephrine activates only the Gs pathway through human beta2-adrenoceptors overexpressed in mouse heart. *Mol Pharmacol* 2004;**65**:1313–22
21 Lyon AR, Rees PS, Prasad S, Poole-Wilson PA, Harding SE. Stress (takotsubo) cardiomyopathy–a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. *Nat Clin Pract Cardiovasc Med* 2008;**5**:22–9
22 Kurisu S, Sato H, Kawagoe T, Ishihara M, Shimatani Y, Nishioka K *et al*. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* 2002;**143**:448–55

Address for correspondence:
Dr F Keshtkar,
Department of Otolaryngology,
Gloucestershire Royal Hospital,
Great Western Road,
Gloucester GL1 3NN, UK

E-mail: f.keshtkar@doctors.org.uk

Dr F Keshtkar takes responsibility for the integrity of the content of the paper
Competing interests: None declared