

Inverted takotsubo cardiomyopathy secondary to adrenaline injection

Introduction

A young woman presented with severe chest pain and an inverted takotsubo cardiomyopathy following adrenaline injection for treatment of an allergic reaction. To the authors' knowledge, this is the first reported case of inverted takotsubo cardiomyopathy following systemic adrenaline administration. The case strongly suggests a central role of catecholamines in the pathogenesis of takotsubo cardiomyopathy.

Discussion

This article reports the first case of inverted takotsubo cardiomyopathy secondary to treatment of anaphylactic reaction by adrenaline injection. Adrenaline is available in a variety of preparations for the management of several medical conditions including treatment of cardiac arrest and other cardiac dysrhythmias, and use in local anaesthetics.

Atypical transient left ventricular dysfunction (inverted takotsubo) has been described in a young woman who suffered an episode of acute pulmonary oedema after local skin infiltration anaesthesia using a combination of lidocaine and epinephrine (Bonnemeier et al, 2007). A similar pattern of contractility was widely described in different conditions with high levels of catecholamines, as described below.

Takotsubo cardiomyopathy is a syndrome of reversible left ventricular dysfunction with apical ballooning. The prevalence of takotsubo cardiomyopathy in the general population is estimated to be between 1.7% and 2.2% in patients who present with suspected acute coronary syndrome.

Takotsubo cardiomyopathy typically presents with signs and symptoms consistent with acute myocardial infarction, including chest pain and shortness of breath, electrocardiogram changes of ST segment elevation later evolving to diffuse T wave inversions, and elevated cardiac enzymes.

More recently 'inverted takotsubo' has been described – characterized by a hyperdynamic left ventricular apex and akinesia of the left ventricular base and mid-portion. It may account for up to 40% of cases of transient left ventricular cardiomyopathy. Subjects presenting with inverted takotsubo cardiomyopathy show an inverted contractile pattern with tall upright T waves following ST segment depression (Kimura et al, 2010). These electrocardiogram changes were noted in this patient.

The pathophysiology of both takotsubo and inverted takotsubo cardiomyopathy is unclear. Various mechanisms have been

proposed, including catecholamine-mediated myocardial dysfunction (Hurst et al, 2006). The occurrence of inverted takotsubo cardiomyopathy following adrenaline injection in this patient supports the central role of catecholamines in the pathophysiology of takotsubo cardiomyopathy. Patients with takotsubo cardiomyopathy have higher catecholamine levels than do patients with myocardial infarction with the same Killip class (Wittstein et al, 2005). On the other hand, this case does not support the hypothesis of myocardial ischaemia secondary to microvascular spasm since coronary arteries only have β_2 receptors which cause vasodilatation in the presence of adrenaline (Sun et al, 2002).

Catecholamine-mediated myocardial stunning may be the central cause of both takotsubo and inverted takotsubo cardiomyopathies. Some (Palecek et al, 2010) but not all (Koulouris et al, 2010) authors rec-

Case Report

A 26-year-old woman with no known medical problems presented with a 2-day history of an erythematous macular rash over her back which had started approximately a day after starting treatment with a proton-pump inhibitor for dyspepsia. She also gave a history of periorbital swelling for a few hours. Her GP administered intramuscular hydrocortisone (200 mg) and adrenaline (500 μ g). Immediately after administration of intramuscular adrenaline, the patient developed severe retrosternal compressive discomfort requiring urgent admission to the local hospital. At emergency room triage, the patient's parameters were stable and no abnormality was detected on physical examination. The initial electrocardiogram showed normal sinus rhythm with ST sagging in leads II, III, aVF, V5 and V6, and non-specific diffuse T-wave flattening. The chest X-ray was within normal limits. Full blood count revealed a slightly elevated neutrophil count (9.55×10^9 /litre). The chest discomfort started to subside slowly after about 25 minutes, but persisted for about 14 hours after admission to hospital. Initial cardiac enzymes were normal but repeated blood tests 6 hours after admission revealed an elevated troponin I level of 6.7 ng/ml (reference range <1.0 ng/ml). The patient was initially treated with intravenous nitrate. Coronary angiography within 24 hours of admission showed normal coronary arteries (Figures 1a and b) while left ventriculography showed moderately impaired global contractility with anterobasal akinesia and inferobasal hypokinesia and hyperkinetic apex; inferior contractility was preserved (Figures 1c and d) (video of this is available at www.bjhm.co.uk). These findings were confirmed on echocardiography the next day (Figures 2a and b). Ejection fraction was estimated to be 42% (using modified Simpson's biplane method). Mild mitral regurgitation was also noted; there was no sign of left ventricular outflow tract obstruction.

The patient received standard heart failure treatment: perindopril and carvedilol. Aspirin was not given as there was no evidence of myocardial ischaemia on coronary angiography. Follow-up electrocardiography showed tall upright T waves in leads II, III, aVF, V3 through V6 (Figure 3). The tallest T waves were seen on day 3 without accompanying hyperkalaemia. The patient was discharged home on day 4. Echocardiography 2 weeks after admission showed normalization of left ventricular systolic function and regional contractility (Figures 2c and d) and complete resolution of mitral insufficiency. The patient remained asymptomatic after 3 months of follow up.

Dr Caroline J Magri is Higher Specialist Trainee in the Department of Cardiac Services, **Professor Stephen Fava** is Consultant Diabetologist and Internal Medicine in the Department of Medicine and **Dr Herbert Felice** is Consultant Cardiologist in the Department of Cardiac Services, Mater Dei Hospital, Tal-Qroqq, Malta

Correspondence to: Dr CJ Magri (cjmagri013@yahoo.com)

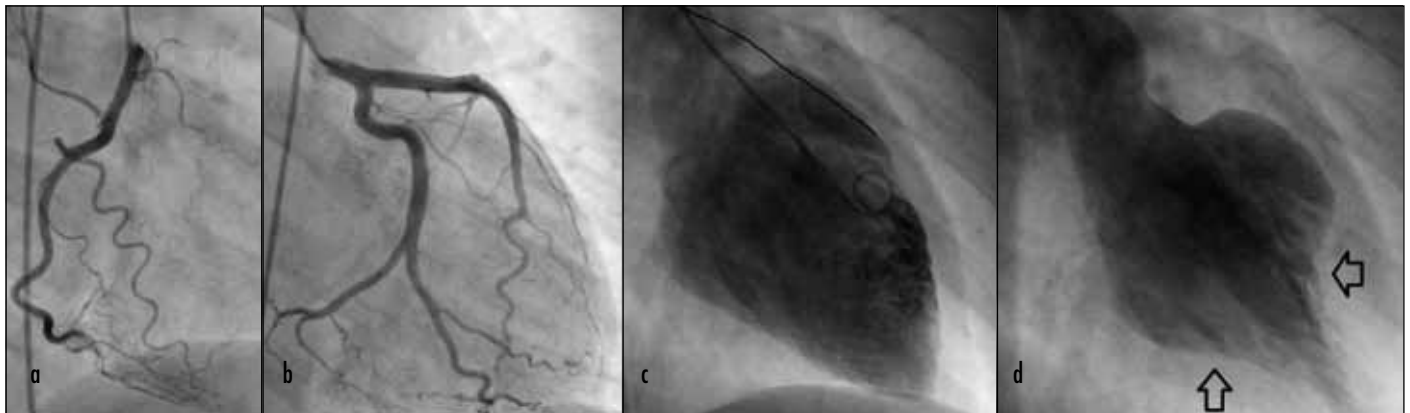


Figure 1. Coronary angiography showing (a) normal right coronary system and (b) normal left coronary system. c. Ventriculogram at end diastole. d. Ventriculogram at end systole showing apical hypercontractility with antero-basal akinesia and infero-basal hypokinesia, characteristic of inverted takotsubo cardiomyopathy.

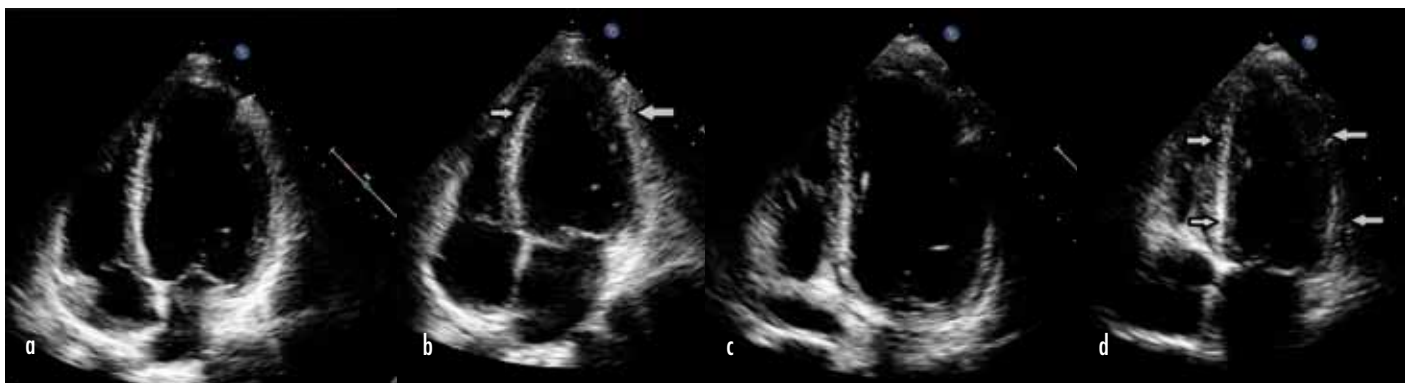


Figure 2. Echocardiography. a. End-diastole and (b) end-systole at diagnosis, showing basal and mid-ventricular hypokinesia with retained contractility in apical segment. c. End-diastole and (d) end-systole 2 weeks post-admission, showing regained left ventricular contractility in basal and mid segments.

commend simultaneous α and β adrenergic blockade. This merits further study. In this patient, the authors used carvedilol which blocks β_1 , β_2 and α_1 adrenergic receptors.

It is unclear why some patients develop classical takotsubo cardiomyopathy while others develop inverted takotsubo left ventricular dysfunction. The authors propose that excessive neural sympathetic stimulation may result in classical takotsubo cardiomyopathy, while excessive circulating catecholamines are more likely to result in the inverted pattern. Thus, in pheochromocytoma, inverted left ventricular dysfunction seems more common. The current case supports this. Exceptions to this may be explained by the heterogenous nerve distribution in the heart. **BJHM**

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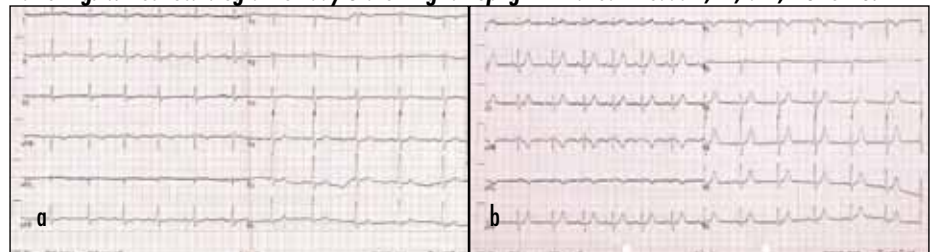
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Figure 3. a. Electrocardiogram on admission showing ST sagging in inferolateral leads with diffuse T-wave flattening. b. Electrocardiogram on day 3 showing tall upright T waves in leads II, III, aVF, V3 to V6.



LEARNING POINTS

- Inverted takotsubo cardiomyopathy can occur following treatment of anaphylactic reaction by adrenaline injection.
- Occurrence of an inverted takotsubo pattern following adrenaline injection indicates a central role of catecholamines in the pathophysiology of this reversible cardiomyopathy.
- Whether a patient develops classical or inverted takotsubo cardiomyopathy may in part depend on the level of circulating catecholamine relative to the degree of sympathetic neural stimulation of the heart, but further research is needed to elucidate this problem.