

CASE REPORT

Upside down you're turning me: inverted Takotsubo pattern cardiomyopathy

V. Richards-Chin A Choi¹, I. Ceelie¹, E.L.A. van Dorp¹, N. Ajmone², F. de Wit³, D.J. van Westerloo³

Departments of ¹Anaesthesiology, ²Cardiology and ³Intensive Care Medicine, Leiden University Medical Centre, Leiden, the Netherlands

Correspondence

V. Richards-Chin A Choi: vanessarichards@hotmail.com

Keywords - Intensive Care, Takotsubo cardiomyopathy, pheochromocytoma, paraganglioma

Abstract

We present the case of a 17-year-old male paraganglioma patient who presented in shock to our emergency department. During workup, an inverted Takotsubo pattern cardiomyopathy was identified. Treatment consisted of blocking catecholamine synthesis as well as supportive care with inotropic medication and high flow nasal cannula oxygen administration. The case is described in detail and the phenomenon of inverted type Takotsubo cardiomyopathy is discussed.

Introduction

Paraganglioma is a neuroendocrine tumour of the autonomic nervous system, which produces catecholamines. The term pheochromocytoma is reserved for paraganglioma located in the adrenal medulla. Pheochromocytomas are rare tumours, which classically present with symptoms of hyperactivity of the sympathetic nervous system, such as paroxysmal hypertension, palpitations, headaches and anxiety. Paraganglioma and pheochromocytoma have been known to cause reversible cardiomyopathy.^[1] Takotsubo cardiomyopathy is a clinical syndrome of transient left ventricular dysfunction in the absence of obstructive coronary disease. It is named after a Japanese octopus trap, 'tako-tsubo'.^[2]

In the clinical presentation, patients may present with symptoms and ECG abnormalities similar to an acute coronary syndrome. On echocardiography, typical findings include ballooning of the cardiac apex and a hyperdynamic base.

Case report

A 17-year-old man presented to the emergency room with a painful left knee. During a minor incident, in which he slipped when opening the front door, he had fallen on his knee. His previous medical history was significant for a large (about 200 cm³) para-aortic paraganglioma caudal to his left kidney, which had unfortunately metastasised to his bones. Bone metastases were present in his skull, thoracic lamina, costa, left ilium

and both femurs. He had undergone a surgical procedure five months prior to presentation, which was intended to resect the neuroendocrine active tumour in the left sympathetic trunk.

On arrival to the emergency department, he received 60 µg of fentanyl and his left leg was immobilised using a vacuum splint. The patient was afebrile with a blood pressure of 160/100 mmHg, a heart rate 140 beats/min, a respiratory rate of 20 breaths/min and an oxygen saturation of 91% on a non-rebreathing mask.

Investigations

Laboratory examination revealed a leucocytosis of 31 x 10⁹/l. Arterial blood gas analysis showed a pH of 7.25, pO₂ 13.8 kPa, pCO₂ 5.9 kPa and a lactate level of 1.9 mmol/l. ECG showed sinus tachycardia, an inverted T wave in lead aVL and upsloping ST segments in leads V3-V5 (*figure 1*). Chest radiography showed consolidation in the right lower lobe. The X-ray of his left thigh showed a fracture of the proximal femur.

Diagnosis and treatment

For haemodynamic monitoring and treatment, the patient was admitted to our medium care unit. Because of a worsening hypoxaemia, high flow nasal cannula oxygen was initiated. Our initial working diagnosis was blood loss due to a fracture of the femur resulting in tachycardia, with hypotension. However, severe bleeding in his femur was not observed. Surprisingly, the troponin level was elevated (1.58 µg/l, normal range: 0.000-0.050 µg/l). At the time of admission the metanephrine/creatinine ratio was significantly increased. By indexing urinary metanephrine levels by urinary creatinine levels, errors of underestimating or overestimating metanephrine excretion can be avoided.^[3] A transthoracic echocardiogram was performed, showing hypokinesia of the basal segments with hyperkinesia of the apical segments in an inverted Takotsubo-type pattern (*figure 2; online video file 1*). Milrinone was started at a dose of 0.25 µg/kg/min to support left ventricular function. Metirosine



Figure 1: Mason Likar ECG at the time of presentation.

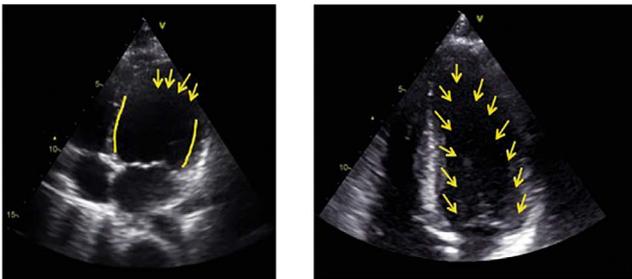


Figure 2: Transthoracic echocardiogram (apical 4 chamber view): hypokinesia in the basal segments with hyperkinesia of the apical segments in an inverted-Takotsubo type pattern

was started to inhibit catecholamine synthesis. After 1 day, the milrinone was stopped and alpha blockage with doxazosin was started. The patient was transferred to the ward for further medical treatment. Eight days later, the transthoracic echocardiogram was repeated, showing a good ventricular function with no residual regional wall motion abnormalities (*online video file 2*). The patient was discharged home after two weeks with continuation of the doxazosin therapy and was subsequently re-admitted for elective surgery for osteosynthesis of the pathological femur fracture.

Discussion

Takotsubo cardiomyopathy was first described in Japan in 1991, including transient left ventricular dysfunction with apical ballooning and a hyperkinetic base of the heart.^[1] Cardiac enzymes are usually slightly elevated and the ECG may show elevated ST segments and/or T wave inversion.^[4] There is no significant coronary stenosis on coronary angiography. According to the Mayo Clinical Diagnostic Criteria, the diagnosis of Takotsubo cardiomyopathy requires all of the following criteria: (1) transient hypokinesia, akinesia, or dyskinesia of the left ventricular mid-segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often but not always present, (2) absence of obstructive coronary disease or angiographic evidence of acute plaque rupture, (3) new electrocardiographic abnormalities (either ST-segment elevation and/or T-wave

inversion) or modest elevation in cardiac troponin, (4) absence of pheochromocytoma or myocarditis.^[2,5] Although the exact pathophysiological mechanism behind the development of Takotsubo is unknown it is well recognised that it frequently occurs in patients suffering from intense emotions, hence its nickname 'broken heart syndrome'. The working hypothesis is that catecholamine surges during these emotional states are mechanistically important.^[2,5,6]

In contrast to a regular Takotsubo cardiomyopathy, the subtype of an inverted or reversed Takotsubo cardiomyopathy is characterised on echocardiography by a hyperkinetic apex and a dynamic base.^[2,5,6] This specific type is much less prevalent, occurring in about 2% of patients in the International Takotsubo Registry study.^[7] Although an inverted type of Takotsubo is therefore quite rare, it has been reported in all patient groups. However, it seems to be preferentially reported in pheochromocytoma patients.^[2,5,6]

There are different hypotheses to explain the different patterns. One hypothesis is the different anatomical distribution of beta-1 and beta-2 adrenoceptors in the myocardium in different individuals or regional anatomic differences in catecholamine sensitivity. Other theories include coronary vasospasm and transient microthrombi.^[6] In inverted Takotsubo cardiomyopathy related to pheochromocytoma, there are persistently higher levels of catecholamines compared with the transient normalising levels of catecholamines in normal variant Takotsubo cardiomyopathy, which may influence the specific form of cardiomyopathy observed.^[5] The inverted Takotsubo cardiomyopathy seems to occur more often in pheochromocytoma patients but may be seen in non-affected patients as well. In those patients, it has been observed that younger individuals (median age of 50 years) have a higher incidence of inverted type Takotsubo as compared with the patients with normal variant Takotsubo cardiomyopathy, which usually presents around the sixth decade.^[5] Both types seem to predominantly affect females.^[2,5]

Taken together, we describe a patient with a paraganglioma who presented with a rare and unexpected Takotsubo variant. Although this variant of inverted Takotsubo has been described in these patients before, the mechanistic explanation for this association remains to be elucidated. It is, however, of great importance to be aware of the association of pheochromocytomas and Takotsubo cardiomyopathy and realise that in these patients an upside down pattern Takotsubo may be encountered.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

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Online you'll find the videos mentioned in the text.

Video file 1: Transthoracic echocardiogram (parasternal short axis view at basal, mid and apical level): hypokinesia of the basal segments with hyperkinesia of the apical segments in an inverted-Takotsubo type pattern

<https://www.njcc.nl/njcc-17-68-chin-choi-video-1>

Video file 2: Transthoracic echocardiogram repeated after eight days (parasternal short axis view at basal, mid and apical level): good ventricular function with no residual wall motion abnormalities.

<https://www.njcc.nl/njcc-17-68-chin-choi-video-2>

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