

# Dyspnea as a dominant clinical manifestation in a patient with takotsubo cardiomyopathy treated for chronic obstructive pulmonary disease and hyperthyroidism

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## KEY WORDS

chronic obstructive pulmonary disease, hyperthyroidism, takotsubo cardiomyopathy

## ABSTRACT

This paper discusses the case of a female patient treated for chronic obstructive pulmonary disease and hyperthyroidism, who also had takotsubo cardiomyopathy with dyspnea at rest as a dominant clinical manifestation.

**INTRODUCTION** Transient left ventricular apical ballooning, that is takotsubo cardiomyopathy or stress-induced cardiomyopathy, was first described in Japan by Dote et al. in 1991 and it has been diagnosed increasingly more often in white race patients ever since.<sup>1</sup> A typical clinical presentation involves chest pain that mimics acute myocardial infarction, abnormal electrocardiogram (ECG) findings similar to those encountered in patients with acute coronary syndrome with ST elevation, normal coronary angiography and abnormal echocardiogram. In most cases these abnormalities resolve spontaneously.<sup>2</sup> This paper discusses the case of a female patient treated for chronic obstructive pulmonary disease (COPD) and hyperthyroidism, who also displayed dyspnea at rest as a dominant clinical manifestation of takotsubo cardiomyopathy.

**CASE REPORT** A 59-year-old female patient was admitted to the intensive coronary care unit (ICCU) of the Department of Internal Diseases at the public hospital N° 1 in Lublin, because of dyspnea at rest lasting for several hours. The patient had been treated for COPD with inhaled drugs for 8 years at irregular intervals. She had smoked about 20 cigarettes a day for 30 years. Lung function tests performed the previous year revealed signs of moderate bronchial obstruction: forced vital capacity (FVC) – 2.67 l (81%

of the normal value), forced expiratory volume in one second (FEV1) – 1.60 l (57% of the predicted value), FEV1/FVC ratio – 59.8%, peak expiratory flow – 3.54 l/s (53% of the predicted value), forced expiratory flow at 50% of FVC – 0.894 l/s (22% of the predicted value), airway resistance – 0.333 kPa/l/s (as compared with the normal value of <0.3), intrathoracic gas volume – 4.72 l (167% of the normal value), residual volume – 3.03 l (163% of the predicted value), and total lung capacity – 5.84 l (109% of the predicted value). Five years earlier, the patient had been diagnosed with hyperthyroidism in the course of Graves-Basedow disease. Since then she had been treated in her local outpatient clinic. She had received thiamazole for an unspecified period of time. She claimed to have stopped the treatment several months earlier due to euthyrosis. Thyroid-stimulating hormone level measured in serum on admission was normal, 0.63 µU/ml (the reference range, 0.25–5.0). The patient's brother died of myocardial infarction at the age of 60. The woman had last menses 8 years ago. Her current problems were preceded by a highly stressful situation brought about by financial problems resulting from her inability to pay off credit installments. On admission, her condition was moderately severe. Wheezes and dry rales could be heard over the lungs. A heart rate increased to 110/min. Arterial blood pressure was 110/70 mmHg.

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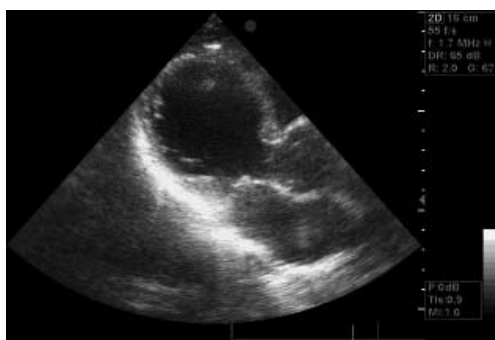
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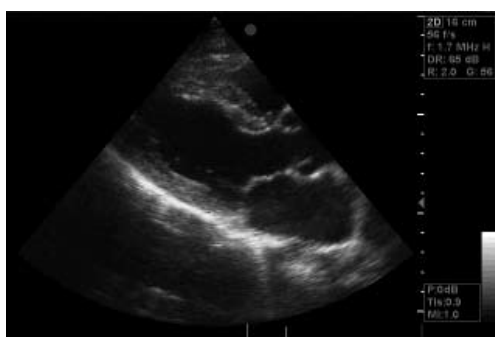
**FIGURE 1** Baseline echocardiography showing an image resembling a Japanese octopus trap typical of takotsubo cardiomyopathy (parasternal long axis view)



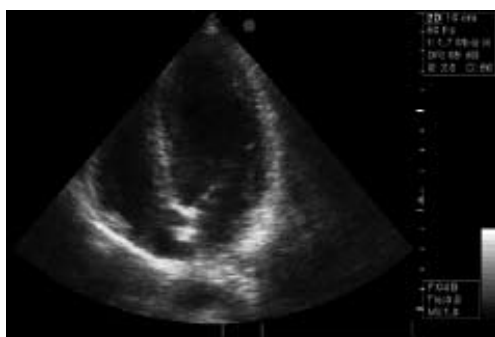
**FIGURE 2** The baseline echocardiographic apical four-chamber view



**FIGURE 3** A follow-up echocardiography (parasternal long axis view). Resolution of the earlier contractility disorders of the left ventricular apical region can be seen along with the correct left ventricular geometry



**FIGURE 4** A follow-up echocardiography (apical four-chamber view) showing resolution of the earlier contractility disorders



The baseline ECG showed sinus rhythm of about 100/min, disrupted by ventricular ectopic beats as well as small ST-segment elevation of 0.5 mm in the precordial leads V<sub>4</sub>–V<sub>6</sub>. Laboratory tests carried out on admission revealed a normal complete blood count, serum creatinine and electrolyte levels. Arterial blood gas analysis showed pH values of 7.47, oxygen partial pressure of 61.7 mmHg, oxygen saturation of 93.1%, carbon dioxide partial pressure of 35 mmHg, base deficit of 1.5 mEq/l, and standard carbohydrate concentration of 27.7 mEq/l. On admission to the ICCU, troponin I (Tn-I) concentration was 0.14 µg/l, with the cutoff value for myocardial infarction of 0.7 µg/l. D-dimer level was 509 ng/ml (the reference range <500 ng/ml),

which excluded with high probability pulmonary embolism.

Echocardiography was urgently performed and showed akinesis of the apical and mid-ventricular segments, hyperkinesis of the left ventricular parabasal segments, and the left ventricular ejection fraction (LVEF) of 35% – the symptoms indicative of takotsubo cardiomyopathy. Left ventricular end-diastolic diameter was 53 mm, the left atrial diameter was 35 mm, the right ventricle was 25 mm, whereas the ascending aorta diameter was 36 mm. The diastolic thickness of the interventricular septum was 9 mm, whereas that of the posterior wall of the left ventricle was 11 mm. The Doppler echocardiographic examination revealed mild mitral insufficiency and insignificant aortic regurgitation. Images in parasternal long axis and apical four-chamber views are presented in **FIGURES 1 and 2**.

The patient received clopidogrel, acetylsalicylic acid, enoxaparin, nitroglycerin, and furosemide. Her condition improved, dyspnea intensity fell and abnormal lung sounds normalized. However, tachycardia up to 100/min persisted and the decision was taken to administer a low-dose β-adrenolytic, 12.5 mg metoprolol. During follow-up examination after 6 hours Tn-I was 1.37 µg/l, whereas the ECG showed ST-segment elevation of 1 mm in leads V<sub>4</sub>–V<sub>6</sub>. The patient was transferred to the Department of Cardiology at the public hospital no. 4 in Lublin, where coronary angiography was urgently performed showing no significant lesions in the major coronary arteries. After evaluation the patient returned to the ICCU of the Department of Internal Diseases. Her condition stabilized and dyspnea subsided.

A follow-up echocardiography performed a week later revealed improved LV function with LVEF of about 50%, improvement in left ventricular geometry and resolution of reduced apical and mid-ventricular contractility (**FIGURES 3 and 4**). An ECG performed prior to discharge from the hospital showed regular sinus rhythm of 80/min, ST segment elevation of 0.5 mm in leads II, III, VF and V<sub>2</sub>–V<sub>6</sub>, and inverse T waves in leads II, III, VF and V<sub>2</sub>–V<sub>6</sub>. The patient was discharged home in a good general condition.

The patient was instructed to take 75 mg of aspirin, sustained-release metoprolol, inhaled ipratropium bromide, and budesonide. She remained under the care of the outpatient cardiology clinic. An echocardiographic examination performed a month later revealed no regional wall motion abnormalities; the ejection fraction was 60%. The patient reported physical weakness, easy fatigability and weight loss. Signs of hyperthyroidism were identified again and confirmed by the determination of hormone levels. Thiamazole treatment was administered on an outpatient basis and the patient was referred to the outpatient endocrinology clinic.

**DISCUSSION** Transient left ventricular apical ballooning may occur even in 2% of patients

with suspected acute ST segment elevation myocardial infarction. The clinical presentation typically involves chest pain similar to that in patients with acute coronary syndrome. Dyspnea as the only clinical manifestation of the disease has also been reported.<sup>2</sup> The patient described here presented only with rest dyspnea, which given a history of COPD and auscultatory findings could indicate exacerbation of COPD symptoms. Despite rapid decrease in ejection fraction to 35%, the arterial blood pressure was not reduced below 100/70 mmHg; however, compensatory tachycardia to 110/min and ventricular dysrhythmia were observed. Prior to hospitalization the patient had not measured her blood pressure or took antihypertensive medication. Given a rapid decrease in LVEF, even with the recommended blood pressure values observed, the reduction in mean blood pressure could have exceeded 30 mmHg, which would meet one of the criteria for cardiogenic shock; however, catecholamine administration was not necessary.

The ECG findings in takotsubo cardiomyopathy involve transient ST-segment elevation, occurring more commonly in leads V<sub>4</sub>–V<sub>6</sub> than in leads V<sub>1</sub>–V<sub>3</sub>, with subsequent T-wave inversion.<sup>3</sup> Transient Q waves and ventricular dysrhythmias have also been reported.<sup>4</sup> The ECG findings in the patient were typical, yet in the baseline ECG tracing the ST-segment elevation was hardly visible and it did not meet the criterion of 1 mm necessary to recognize ST-segment elevation acute coronary syndrome; that is why the patient was not immediately referred to the catheterization laboratory. Other findings typical of takotsubo cardiomyopathy included increased troponin levels (but usually not very high) as well as no pathology in coronary angiography. It has also been reported that coronary angiography performed in patients with transient left ventricular apical ballooning shows non-stenotic atherosclerotic lesions, minimal microcirculatory impairment and mild vascular spasm.

Characteristic echocardiographic findings in takotsubo cardiomyopathy include transient akinesis or dyskinesis of apical and medial segments, normokinesis of parbasal segments, and decreased global systolic left ventricular function. Therefore it is of vital importance to perform echocardiography in patients whose medical history may be suggestive of that disease.

Takotsubo cardiomyopathy is a quite frequent disorder in postmenopausal women and it is usually preceded by high emotional stress.<sup>5</sup> The patient described here was 59 years old, had her last menses 8 years earlier and experienced a highly stressful situation prior to symptom onset.

The etiology of transient left ventricular apical ballooning has not been fully understood so far. Potential causes involve racial and ethnic factors, hormonal disorders, genetic factors, or transient stress or vasospasm-induced catecholamine disorders.<sup>6</sup> Transient disorders of thyroid hormone secretion have been reported.<sup>7</sup> Cases of thyroid

diseases, particularly those leading to hyperthyroidism, have also been described in patients with takotsubo cardiomyopathy.<sup>8</sup> In our case, the patient has been treated for hyperthyroidism in the course of Graves-Basedow disease. Several months prior to admission, thyreostatic therapy was administered and during hospital stay she was euthyroid. Within one month of treatment, however, typical clinical signs of hyperthyroidism developed. A plausible association between thyroid disease and cardiomyopathy is not clear; most probably it is associated with catecholamines. To date, only a few reports have been published. The authors have described the occurrence of takotsubo cardiomyopathy in patients with COPD or bronchial asthma.<sup>9–12</sup> There was insufficient amount of data to establish a causal relationship between both diseases, although the cases described (including our case) may support the concept that combines the transient myocardial stunning with transient apical ballooning with the effect of catecholamines, including subjects receiving catecholamine therapy. It is not clear whether apical ballooning is induced by decreased arterial blood saturation, which occurred in the case described.

The diagnosis of takotsubo cardiomyopathy is not always straightforward. The diagnosis may be even more difficult in a patient with a history of COPD, dyspnea prevailing the clinical presentation, auscultatory findings suggestive of bronchial spasm, and minor ECG alterations. In order to establish the proper diagnosis, it is particularly important to analyze ECG tracings meticulously, determine troponin concentration, and perform echocardiography as early as possible.

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# Duszność jako dominujący objaw kliniczny u pacjentki z kardiomiopatią takotsubo leczonej z powodu przewlekłej obturacyjnej choroby płuc i nadczynności tarczycy

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### SŁOWA KLUCZOWE

kardiomiopatia  
takotsubo, nadczyn-  
ność tarczycy,  
przewlekła obturacyj-  
na choroba płuc

### STRESZCZENIE

Omówiono przypadek chorej z rozpoznaną przewlekłą obturacyjną chorobą płuc leczonej z powodu nadczynności tarczycy, u której kardiomiopatia takotsubo przebiegała z dominującą w obrazie klinicznym dusznością spoczynkową.

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