CASE REPORT

Takotsubo cardiomyopathy: A case report and overview of the relevant literature

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SUMMARY

The authors present an interesting case report of 69-year-old Caucasian woman with Takotsubo cardiomyopathy. Takotsubo cardiomyopathy is a relatively recently characterized heart syndrome that probably develops due to the direct toxic effect of excessive release of catecholamines on cardiac adrenoreceptors during emotional or physical stress. Its typical features include reversible left ventricular apical dyskinesis, chest pain with ST-T changes on the ECG, minimal myocardial enzymatic release and the absence of coronary stenosis on the coronary angiogram. Early coronary angiographic examination is highly recommended as the clinical picture of this syndrome mimics acute myocardial infarction. Beta-blockers are considered to be the treatment of choice.
Key words: cardiomyopathy, apical left ventricular ballooning, echocardiography.

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CASE REPORT

A 69-year-old heavy female smoker (40 cigarettes a day) of Caucasian race, with arterial hypertension, on long-term follow-by at the Outpatient Lung Unit of our department for chronic obstructive pulmonary disease (COPD), was admitted in early June 2004 for one-week lasting intermittent pressure pain below the lower edge of the sternum, experienced on minimal exercise. A week prior to the onset of these problems, the patient had her dose of oral corticoids increased for bronchial obstruction deterioration. However, her exertional dyspnoe persisted even after the change in medication. An additional important fact in the patient′s history was increased psychological stress due to social insecurity for several weeks.

On admission, the patient was eupnoic at rest, free of cyanosis, filling of her jugular veins was not increased, lung percussion produced full, clear resonance alveolar breathing with diffuse expiratory wheezing, with audible systolic murmur of intensity 2/6 over the cardiac apex, cardiac action was regular at 60 beats/minute, blood pressure 120/80 mmHg. The ECG documented sinus rhythm with normal conduction intervals; there was evidence of 1-mm ST-segment elevations in leads II, III, aVF, V4, V5, and, partly, also in V6 associated with clear T-wave negativity (Fig. 1).

Based on ECG finding, the patient immediately underwent transthoracic echocardiography, documenting an extensive area of dyskinesis in the apical region of non-enlarged left ventricle (LV) and extending over the apical half of all LV walls (Fig. 2). An additional finding was hyperkinesis of LV basal segments; the resulting LV ejection fraction (LVEF) was decreased, being 35%. The LV walls were not hypertrophied. In the LV outflow tract, there was evident dynamic subaortic obstruction due to the systolic anterior movement of the mitral valve anterior cusp with maximal pressure gradient of 39 mmHg (Fig. 3). Mitral regurgitation of intermediate significance, directed eccentrically under the posterior cusp of the valve, was present as a result of impaired coaptation of mitral leaflets.

The patient immediately underwent selective coronary angiography with a normal finding on the epicardial coronary arteries.

A working hypothesis of Takotsubo cardiomyopathy was established based on the patient′s history and results of ECG, echocardiography and coronary angiography. The patient was placed on a monitored bed of the coronary care unit. In addition to her chronic medication including oral theophylline, methylprednisolone and N-acetylcysteine and inhaled budesonide and ipratropium, therapy was initiated with a beta-blocker, initially 10 mg metoprolol i. v. in two divided doses at 30-minute interval, with subsequent switchover to oral therapy at a dose of 25 mg b.i.d.. Therapy also included oral acetylsalicylic acid, subcutaneous enoxaparine and alprazolame to reduce psychological tension. Laboratory investigations revealed a mild elevation of cardiospecific markers with peak values of MB-creatinine kinase of 0.59 ukat/l and troponin I of 2.05 ug/l. Chest x-ray showed no signs of left-heart insufficiency, only the picture of COPD.

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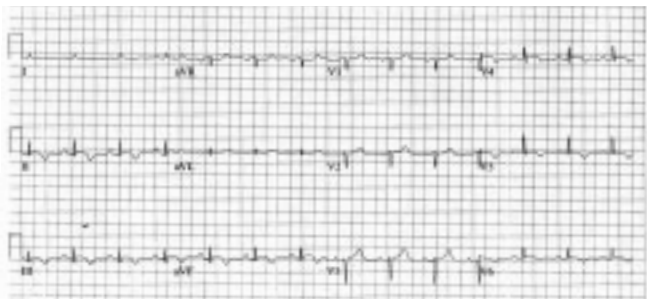

Fig. 1. ECG finding on admission
One-mm ST-segment elevations are present in leads II, III, aVF, V4, V5, and, partly, in V6 along with T-wave negativity.

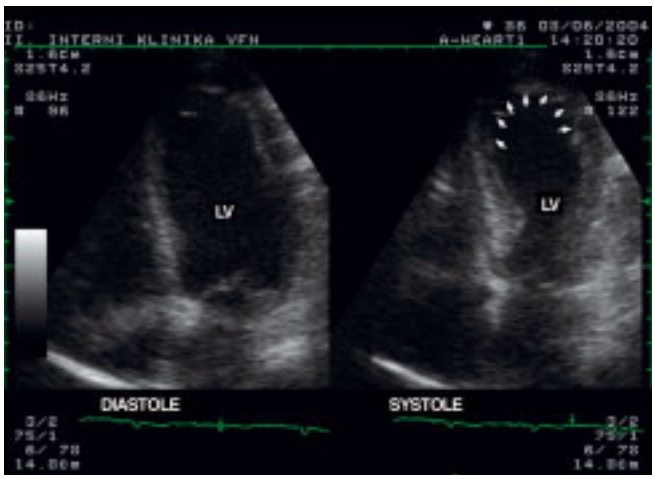

Fig. 2. Echocardiographic finding on the day of admission
The apical four-chamber view shows marked apical dyskinesis (arrows).
LV - left ventricle

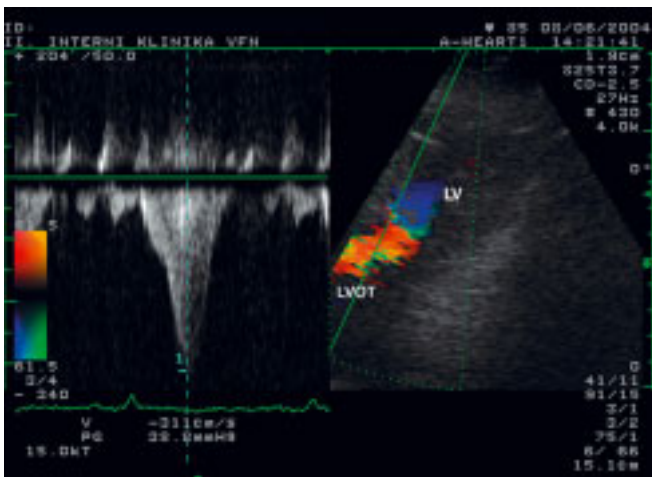

Fig.3. Echocardiographic finding on the day of admission
The left panel includes a continuous-wave Doppler recording of accelerated blood flow in the left ventricular outflow tract at the site of dynamic subaortic obstruction with a maximal pressure gradient of 39 mmHg.
LV – left ventricle, LVOT – left ventricular outflow tract

Given her circulatory stability, the patient was transferred, on her second day of hospitalization, to standard-care ward with telemetric monitoring. She continued to receive the above medication plus the angiotensin-converting enzyme inhibitor perindopril at an initial dose of 2 mg daily. Therapy with acetylsalicylic acid and enoxaparin was discontinued. Virology performed to exclude the possibility of myocarditis was negative, as were laboratory markers of inflammation. No significant arrhythmias were registered throughout the hospitalization. Echocardiography performed on day 2 of hospitalization documented improvement of LVEF to 44%. While at rest, the dynamic LV outflow tract obstruction was no longer present, it did reappear immediately during Valsalva maneuver; mitral regurgitation was significantly reduced. Complete remission of the dynamic obstruction was documented by echocardiography after one-week hospitalization, when there was also virtually normal global systolic LV function with LVEF of 55% in the presence of minor area of apical akinesis. Clinically, the patient stopped complaining of chest tightness on exertion already on therapy initiation, and the problem did not recur even after completion of bedrest at five days of hospitalization. Exertional dyspnoe persisted as did the auscultatory finding of bronchitis, whose remission required two-week intensive bronchodilator and expectatory therapy. On the ECG, there was remission of ST-segment elevations over the first week, followed by T-wave normalization over the next 3 weeks. The patient was discharged to receive home care after 3 weeks of hospitalization, only complaining of mild exertional dyspnoe. Follow-up by echocardiography at one month after the onset of problems demonstrated completely normal kinetics of all LV segments in the presence of normal global systolic LV function with LVEF of 67% (Fig. 4), absence of either resting or provoked dynamic subaortic obstruction (Fig. 5), and minimal mitral regurgitation.

DISCUSSION

Takotsubo cardiomyopathy was first described by Satohe et al. (1) and Dote et al. (2) in the early 1990s. Takotsubo is the Japanese term for a special fisherman′s container (“tsubo”) used to catch the octopus (“tako”). The shape of the container with a narrow neck and a circular bottom closely resembles to the ventriculogram of the LV in Takotsubo cardiomyopathy. Alternative terms used in the literature include ampulla cardiomyopathy or transient left ventricular apical ballooning. While most cases were originally identified in Japan, there have been reports describing the condition also in individuals of other than Asian origin (3); hence, the disease is not race-related.

Takotsubo cardiomyopathy is characterized by 1) acutely occurring and reversible LV apical impaired kinetics in terms of apical balloon-like dyskinesis, with basal LV segment hypercontractility; 2) chest pain; 3) ECG changes of the ST segment and T-waves, typically ST-segment elevations in leads II, III, aVF and V2-V5; 4) minimal increase in the levels of cardiospecific markers; and 5) absence of significant coronary stenosis demonstrated by coronary angiography (4). The etiology and pathogenesis of the disease remains poorly understood. Original case reports suggested multiple vasospasms with subsequent development of stunned myocardium (1, 2). A multicentric study by Tsuchihashi et al. included retrospective analysis of 88 patients hospitalized on the basis of clinical problems and ECG finding with suspected acute myocardial infarction, in whom the diagnosis of Takotsubo cardiomyopathy was later established based on the above criteria (5). In Tsuchihashi′s paper, provoked vasospasm was only documented in 21% of patients. As a result, multiple epicardial coronary arterial vasospasms do not seem to be the main cause for the development of this type of cardiomyopathy. The intraventricular pressure gradient resulting from dynamic subaortic obstruction was present in 18% of patients. Most patients were women over 60 years of age. A

puzzling fact was the finding that the onset of the disease was preceded, in 70% of patients, by a stressful situation, emotional or physical such as stroke, epileptic seizure, bronchial asthma exacerbation, surgery, or strenuous physical activity. Consequently, psychological and physical stress was identified as the very likely triggers of the whole process. Increased sympathetic activity leads to excessive release of catecholamines acting directly on the myocardium, and resulting in hyperactivation of beta-adrenergic receptors with their subsequent uncoupling and impaired myocardial contractility. The predilection involvement of LV apical area can be explained by several facts (5). The three-layer structure of the myocardium is not present in the ventricular apex, with loss of elasticity readily occurring in the region due to excess expansion. In addition, the cardiac apex is the borderline zone (locus minoris) of areas supplied by major coronary arteries, with the highest density of adrenoreceptors (6).

The "catecholamine" theory of development of Takotsubo cardiomyopathy is supported by several other findings. Using radionuclide techniques, Owy et al. compared myocardial perfusion and functional sympathetic innervation in their patients (7). Impaired sympathetic innervation in the apical region was obvious and associated with dyskinesis, while myocardial perfusion was not severely impaired even in acute phases of the disease. Cardiac adrenoreceptor activation as the primary cause of this clinical syndrome is also suggested by observations from an animal experiment whereby emotional stress in rats induced transient reversible contraction impairment involving the LV apex, which could be terminated by the administration of amosulalol, an adrenoreceptor inhibitor (4). The beneficial effect of beta-blocker therapy has also been reported in man (8). Invaluable data emerged from a study by Abeho et al., who consecutively identified 17 individuals with Takotsubo cardiomyopathy. Focal coronary artery vasospasm was only reported in a single patient; no marked microcirculatory impairment was documented by intracoronary Doppler examination combined with contrast echocardiography (9). Serology and endomyocardial biopsy did not reveal signs of acute myocarditis in any of the patients. Just as in the study by Tsuchihashi et al. (5), emotional or physical stress was identified as the trigger in most patients (94% of individuals).

Intraventricular subaortic dynamic obstruction of the LV outflow tract, present in some individuals (18% in the study of Tsuchihashi et al, 15% in the report of Desmet et al., none in the study by Abe et al.), is currently considered as a secondary factor occurring due to basal LV segments hypercontractility and not as the primary cause of the development of apical dyskinesis. Still, one may speculate about its role in perpetrating apical dyskinesis due to potentiation of high systolic ventricular wall tension (3).

LV apical regional dyskinesis usually resolves within several days to weeks (3). The course of the disease is usually uncomplicated; however, there have been reports of thrombus formation in the LV apex (10), development of cardiogenic shock requiring mechanical circulatory support (11) and fatal ventricular wall rupture (12). Takotsubo cardiomyopathy could thus be another cause of sudden cardiac death; hence the recommendation of close bedside monitoring of these patients in a coronary care unit with regular follow-up by echocardiography.

We believe the case reported by us fully meets the criteria of Takotsubo cardiomyopathy. To the best of our knowledge, this is the first case reported in the Czech relevant literature. In the differential diagnosis of this disease, the clear priority is to rule out acute myocardial infarction, as management of both entities is different and, particularly, administration of thrombolytic therapy to a patient with Takotsubo cardiomyopathy could appreciably raise the risk of LV wall rupture, present in this syndrome (11). It is therefore critical to perform selective coronary angiography to exclude significant coronary artery disease. Of equal importance is echocardiography documenting the typical morphological finding on the LV; alternatively, ventriculography can be performed during catheterization. The drugs of choice, because of the assumed mechanism of onset of the disease, i. e., emotional or physical stress due to myocardial stunning, and because of the beneficial effect documented in the literature, are beta-blockers. In our view, anxiolytics are a class of drugs appropriate in patients with a clearly expressed psychological component. Consistent monitoring of patients, at least over the first days of hospitalization, is imperative considering the potential risks of the disease.

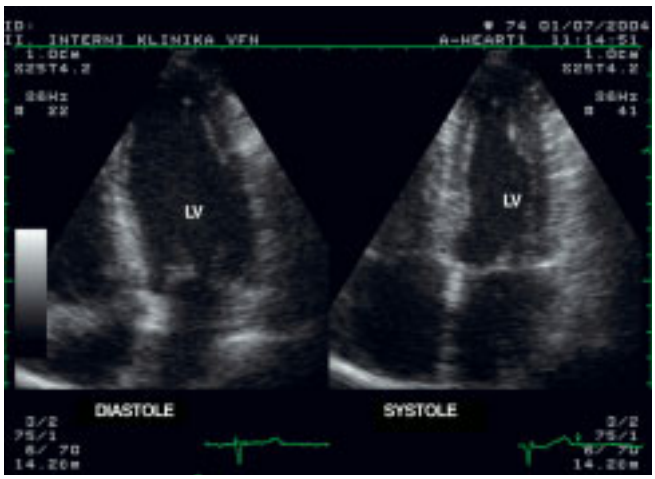

Fig.4. Echocardiographic finding at 1 month
The apical four-chamber view shows normal kinetics of all LV segments.
LV – left ventricle

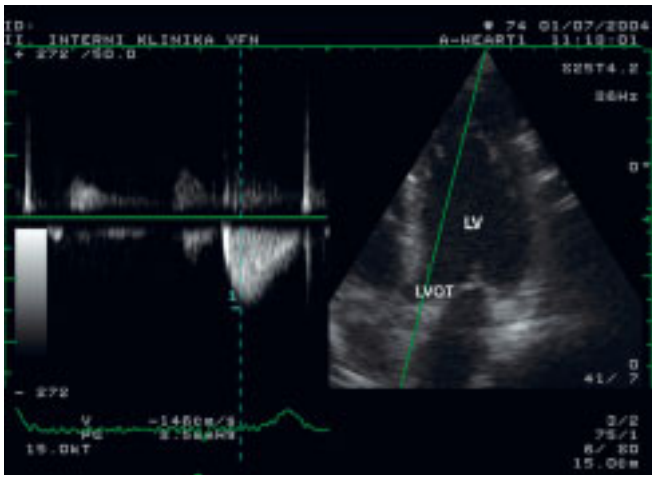

Fig.5. Echocardiographic finding at 1 month
The left panel includes a continuous-wave Doppler recording of blood flow across the left ventricular outflow tract showing normal values of this flow.
LV – left ventricle, LVOT - left ventricular outflow tract

Abbreviations

COPD - chronic obstructive pulmonary disease
ECG - electrocardiogram
EF - ejection fraction
LV - left ventricle
LVOT - left ventricular outflow tract

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Translation: René Prahl

COMMENTARY

Comments on the article by Paleček T. et al. "Takotsubo cardiomyopathy: A case report and overview of the relevant literature"

This is an interesting case report as it is the first description of so called Takotsubo cardiomyopathy (TC) in the Czech literature. The first to characterize this special condition were the Japanese authors Satoh et al. in 1990 (reference in the Paleček´s paper). While many of us have seen patients with this disease before, we were unable to classify it and would usually refer to it as a variation of hypertrophic cardiomyopathy.

Today, the disease at least has a name (although somewhat strange and making absolutely no sense to most Europeans); however, our unease and uncertainty over exact classification of TC are no smaller than they were before its identification.

The patient in the case report had a typical TC echocardiographic picture with apical dyskinesis, hyperkinesis of other myocardial regions and, also, the ECG finding (ST-segment elevation in II, III, aVF, and in precordial leads). She was typically an elderly female with chest pain developing after psychological trauma; other features consistent with literary data included the course of the disease with normalization of myocardial kinetics and mild left ventricular outflow tract obstruction.

A role in the onset of TC may be played by genetic factors, as evidenced by more recent reports (1). Coronary spasms could represent a potential pathogenic factor; however, they can only be documented on exceptional cases, and this even after pharmacological provocation. Of interest in this context are no doubt recent data of Nishikawa and coworkers (2) demonstrating a notable decrease in coronary reserve, as measured by intracoronary Doppler ultrasound, which could imply a coronary microcirculation disturbance; however, these results are inconsistent with those of earlier reports included by the authors in their list of references (Abe et al.). Likewise, Nishikawa et al. suggested the possibility of mild right ventricular involvement (3); coronary reserve improved—as did the disease as a whole—after 30 days since onset.

Mild positivity of cardiospecific enzyme is a usual, yet not constant finding. Increased levels of serum noradrenaline are increased on a regular basis (3).

TC can be distinguished from myocardial infarction by only exceptional presence of abnormal Q-waves and absence of "mirror" ST-segment depressions in contralateral leads (4). No doubt we will not dare indicate coronary angiography on the first suspicion of TC, as the degree of overlapping of clinical, electrocardiographic, laboratory, and echocardiographic features is high for both conditions.

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The prognosis of TC in most patients seems to be favorable; BNP determination does not allow identifying those with a potentially unfavorable course (5). Complications of TC may include rupture of the free wall of the left ventricle, formation of intracardiac thrombi and, possibly, severe heart failure suggestive of cardiogenic shock. While beta-blockers are the preferred medication, the condition may resolve even without therapy (3).

Future research into TC will no doubt provide further insights into this particular disease and, perhaps, some surprises. One should expect researchers to focus their attention on the etiopathogenesis of the disease and definition of the molecular-genetic basis of the entity.

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