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Case report

Takotsubo cardiomyopathy in a patient with essential thrombocythemia treated with anagrelide: Case report

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ABSTRACT

Takotsubo cardiomyopathy is a rare syndrome. Most often imitates acute coronary syndrome. It is characterized by transient wall motion abnormalities, especially in the apical segments of the left ventricule. Less frequently is possible to find transient akinesis or dyskinesis in the mid-ventricular segments of the left ventricule. Pathophysiological mechanisms are not completely clear. The main cause of stress cardiomyopathy is stress insult. But in rare cases can be takotsubo caused by other conditions. We reported rare case of takotsubo cardiomyopathy caused by high dose anagrelide therapy. Anagrelide is the most often used in patients with thrombocythemia. It belongs to phosphodiesterase III inhibitors and through specific pathways has certain effects on myocardium. It is the first case of takotsubo cardiomyopathy resulting from anagrelide therapy in the Czech Republic.

Introduction

Takotsubo cardiomyopathy is a relatively rare syndrome first described in Japan in 1990s [1]. It is sometimes called ''broken heart syndrome'', stress cardiomyopathy or transient left ventricular apical ballooning. Characteristic for this syndrome is a transient wall motion abnormality (akinesis or dyskinesis) mainly affecting the apical and less frequently the mid-ventricular segments of the left ventricle (LV). LV contraction abnormalities may imitate acute coronary syndrome, but the findings on epicardial coronary arteries are usually normal [2].

The prevalence is 1–2% of patients admitted to intensive care units with suspected acute coronary syndrome [3]. Most of the patients are postmenopausal women aged 60–76 [4].

Pathophysiological mechanisms are not completely clear. Among the possible explanations are high level of catecholamines [5], coronary spasms or microvascular dysfunction [6]. Our case illustrates that apart from emotional stress, high doses of specific drugs may be another cause of stress cardiomyopathy.

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Case report

A 61-year-old patient with a long history of essential thrombocythemia, managed with a specific combination therapy with hydroxyl-carbide and anagrelide, came for a scheduled haematology check-up. During the examination, the patient suddenly developed general weakness, accompanied with sudden breathlessness and stinging pain in the left precordium. The attending haematologist, based on the combination of clinical symptoms and the previous therapy, suspected that the patient with continuously progressing thrombocythemia (not responding even to increased anagrelide doses in the course of the recent six months) might have pulmonary embolism. The patient was with stable haemodynamic and ventilation parameters referred to an intermediary care cardiology unit for admission and further evaluation.

At the time of admission, the patient continued to report strong stinging pain in the left hemithorax. The initial ECG showed 1 mm ST-segment elevations with peaked T waves in the V2-6 leads (Fig. 1). The admission echocardiogram revealed an extensive wall motion abnormality with apical akinesis and generalized hypokinesis of the midventricular segments (Fig. 2). Systolic function of the LV was moderately reduced, with the Simpson biplane EF of 39%.

Because of suspicion of sub-acute anterior ST-elevation myocardial infarction the patient underwent an urgent coronarographic examination. However, there were no significant findings on epicardial coronary arteries (Figs. 3 and 4). Finally, left-side ventriculography was performed, showing the typical image of takotsubo cardiomyopathy (Fig. 5). The laboratory examination revealed mild elevation of troponin I (TnI 1.06 μg/l, normal ≤ 0.03 μg/l).

Interestingly, despite detailed medical history including a focused history of a stress insult in the patient's surroundings, no triggering stress factor was found. Based on that, the most probable cause of the stress cardiomyopathy remained the high-dose anagrelide therapy. As agreed with the attending haematologist, the anagrelide therapy was replaced with dual antiplatelet therapy using the combination of acetylsalicylic acid and clopidogrel. The symptoms resolved after discontinuation of treatment with anagrelide, with normalization of TnI levels, and the patient was dismissed in stable condition. A control echocardiography examination three months later showed an improvement of LV EF (from 39% to 50%) with partial resolution of the wall motion abnormalities of the apex and mid-wall segments.

Discussion

Anagrelide is a phosphodiesterase III inhibitor used for selective reduction of thrombocyte count in patients with essential thrombocythemia or other myeloproliferative diseases [7]. Its biological halftime is very short. Therefore, the medication must be used several times a day [7].

While small doses reduce megakaryocyte size and ploidy, higher doses produce antiplatelet effects through phosphodiesterase inhibition [8].

Anagrelide, as a phosphodiesterase III inhibitor, has certain effects on the myocardium, too. Through intracellular signalling, the drug exercises a positive inotropic and chronotropic effect on the heart muscle. These effects are achieved through an increase of cyclic adenosine monophosphate (cAMP), which increases binding of catecholamines to β1-adrenergic receptors in the next part of the signalling pathway [9].

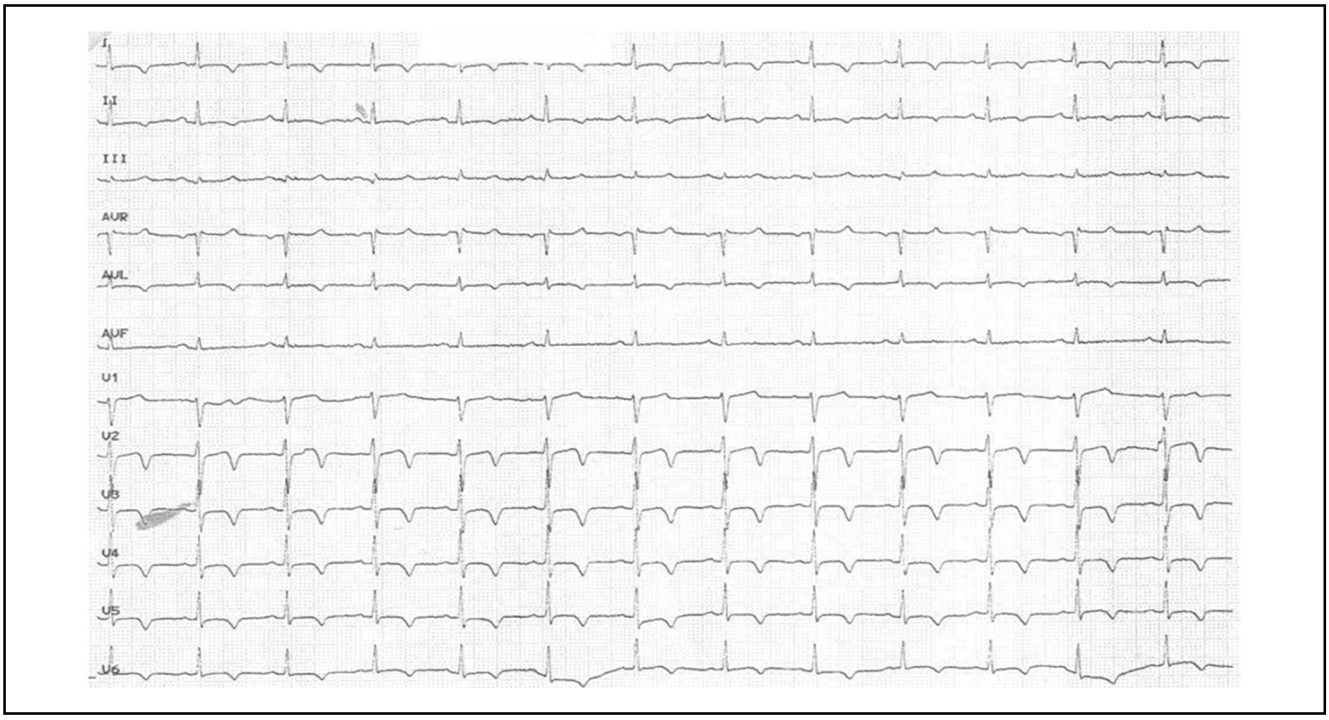

Fig. 1 – Initial ECG.

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