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M.A. Tyapkina *[1], Ye.V. Yakovleva [1], A.A. Roschina [1], G.A. Khalmetova [1], I.V. Basov [2]

[1] — Federal State Budgetary Educational Institution of Higher Education «V. I. Razumovsky Saratov State Medical University» of the Ministry of Health of the Russian Federation, Department of Hospital Therapy, Medical Department, Saratov, Russia

[2] — State Healthcare Institution «Regional Clinical Hospital» of the city of Saratov, Cardiology Department No. 3, Saratov, Russia

Takotsubo Syndrome in a Young Man

Abstract

Takotsubo syndrome is a transient left ventricular myocardial dysfunction, which is a ballooning of the cardiac apex and the middle part, accompanied by simultaneous hyperkinesia of the basal segments of the left ventricle with no hemodynamically significant coronary artery stenosis. It is believed that catecholamines that cause the spasm of coronary arteries, myocardial stunning, and have an additional cardiotoxic effect, play a central role in the development of takotsubo syndrome. The first description of takotsubo syndrome was published 30 years ago by Japanese cardiologist H. Sato et al. and was called stress-induced cardiomyopathy. Subsequently, it turned out that not only psychoemotional but also physical factors lead to takotsubo syndrome; this fact increases the significance of this disease. Clinical signs of this syndrome are similar to acute coronary syndrome, but coronary angiography reveals no changes, and there are rapid positive echocardiographic changes. It is known that up to 90% of patients with takotsubo syndrome are postmenopausal women. This case study demonstrates development of this disease in a young man. The patient, 40 years, after psychoemotional stress, has typical clinical signs of acute coronary syndrome with ST elevation complicated by acute left ventricular failure. Examination showed no angiographic signs of coronary artery disease, normal troponins, a significant increase of N-terminal propeptide of the natriuretic hormone. It was noted that the extension of local contractility disorders, according to echocardiography, exceeds the areas of blood supply of one coronary artery, as well as the presence of a circular lesion of apical and middle LV segments. Follow-up echocardiography performed on the 3rd day from the onset of the disease revealed no hypokinesia areas, and LV ejection fraction was normalized. The discussion of this case includes the evaluation of the conformity of the signs of the disease with diagnostic criteria for takotsubo syndrome established by the European Society of Cardiology experts in 2018. Analysis of the ECG of the patient is presented, which allows early differentiation of takotsubo syndrome from anterior myocardial infarction.

Key words: *takotsubo syndrome, clinical case*

Conflict of interests

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ACS — acute coronary syndrome, ECG — electrocardiography, Echo-CG — echocardiography, TTS — takotsubo syndrome

*Contacts: Maria A. Tyapkina, e-mail: mariya-tyapkina@yandex.ru
ORCID ID: https://orcid.org/0000-0002-1860-3171

Introduction

Takotsubo syndrome (TTS) is a transient left ventricular myocardial dysfunction, which is a ballooning of the cardiac apex and the middle part, accompanied by simultaneous hyperkinesia of the basal segments of the left ventricle with no hemodynamically significant coronary artery stenosis. Translated from Japanese, "takotsubo" is an octopus trap, which is a ceramic pot with a round base and a narrow neck ("taco" is an octopus, and "tsubo" is a pot). The left ventricle acquires such a shape in systole due to the transient spherical ballooning of the apical and middle segments and hyperkinesis of the basal segments (Fig. 1).

It is believed that catecholamines that cause the spasm of coronary arteries, myocardial stunning, and have an additional cardiotoxic effect play a central role in the development of TTS. [1, 2]. The first description of TTS was published 30 years ago by Japanese cardiologist H. Sato et al. and was called stress-induced cardiomyopathy. Subsequent descriptions of this syndrome usually emphasize its association with negative psychoemotional factors, which was reflected in the description of TTS as "broken heart syndrome". Events that contribute to TTS include the death or severe illness of close ones, disasters (earthquake), financial losses, lawsuits, relocation, disputes, public speaking, suicidal attempts. The disease is much less often caused by a happy event (the so-called "happy heart syndrome"). Recent results of studying this disease show that physical factors contribute to TTS even more often than psychoemotional ones. Physical triggers include: gastrointestinal bleeding, cocaine use, electropulse therapy, overdose of insulin and beta-adrenergic agonists, surgical intervention, general anesthesia, subarachnoid hemorrhage, thyrotoxicosis, chronic obstructive pulmonary disease, acute cholecystitis, severe pain (pneumothorax or hepatic colic), stress test (dobutamine stress test), withdrawal symptoms (alcohol, opiates). Due to the large number of physical factors that can lead to acute myocardial ballooning, it was proposed to define all variants of TTS due to physical factors as secondary TTS, while the classic development of this disease due to psychoemotional stress was described as primary TTS [3].

The prevalence of TTS in the Russian Federation is unknown. The International Expert Consensus Document on TTS published in 2018 noted that the prevalence of this syndrome is 1–3% of all hospitalizations with suspected acute myocardial infarction with ST elevation; among female patients, cases of TTS can reach 5–6%. Postmenopausal women account for 90% of cases of TTS [2]. Clinical signs of TTS are similar to the symptoms of acute coronary syndrome (ACS), but coronary

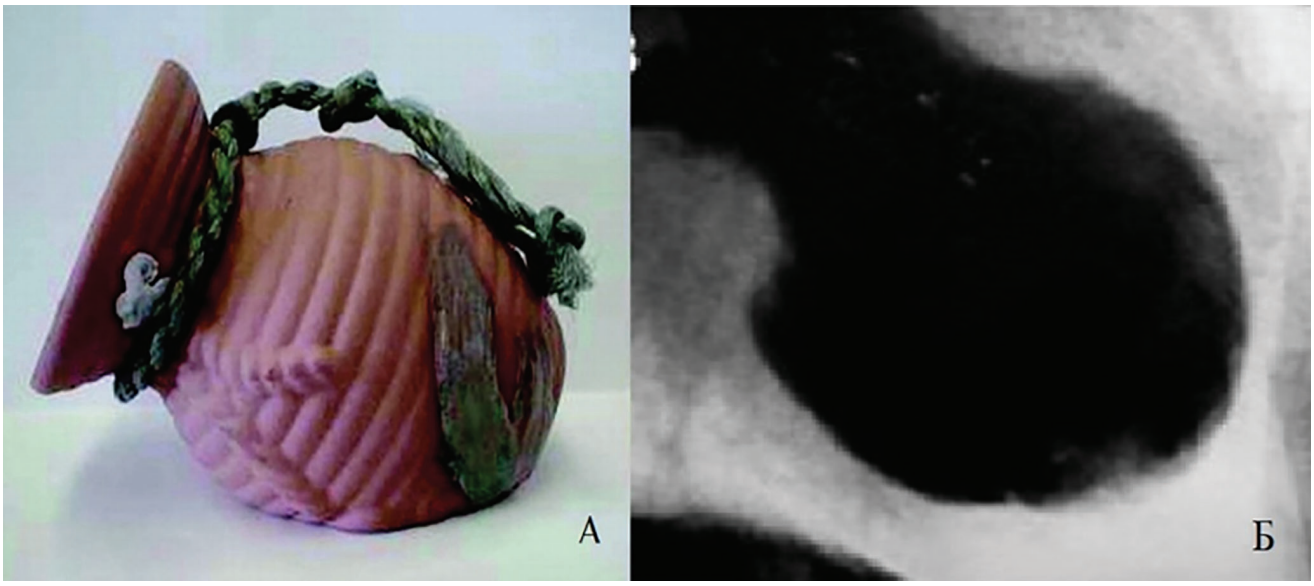

Figure 1. *A – a pot for catching octopuses (takotsubo); B – left ventriculography: apical and middle ballooning of the left ventricle in systole (adapted from [2]).*

angiography reveals no hemodynamically significant coronary artery stenosis, and rapid positive echocardiographic changes are noted. Symptoms of acute heart failure may prevail in clinical evidence, syncopal conditions and life-threatening cardiac arrhythmias are less common. The idea of favorable prognosis for TTS is not as unequivocal as it was before. It turned out that the mortality rate for TTS can reach 4–5% in the acute phase, which is comparable to the mortality rate for acute myocardial infarction with ST elevation in the case of successful revascularization [2, 3].

Clinical Case

Here we describe a case study of TTS in a young man. Patient G., 40 years, became seriously ill early morning on 01.10.2019 when he felt sudden intense tearing retrosternal pain (feeling of "a stake driven into the chest") irradiating in the right shoulder and accompanied by a feeling of death anxiety, panic, trembling, and cold sweat. Along with the pain, he felt suffocation, which intensified in the supine position. He had suffered psychoemotional stress (quarreled with his wife) the night before. Due to persisting pain syndrome and shortness of breath at rest 5 hours from the onset of symptoms, the patient sought medical attention. Electrocardiogram (ECG) revealed ST elevation was in leads I, II, AVL, V2–V6 with maximum elevation in V2–V3, and high, pointed T waves in V2–V3 (Fig. 2).

Physical examination: skin of normal color and moisture, orthopnea position, respiratory rate 25 per minute, blood pressure 150 and 90 mm Hg, heart rate 80 per minute. Taking into account the typical attack of angina and ECG data, the emergency physician diagnosed him with "ACS with ST elevation"; the patient was hospitalized at the central regional hospital. Repeated sublingual administration of nitroglycerin had no effect. Pain and dyspnea were managed by intravenous administration of narcotic analgesics. Thrombolytic treatment with alteplase was performed at a dose of 100 mg (15 mg IV push, then 50 mg drip for 30 minutes, and 35 mg during the following hour). Anticoagulant treatment with enoxaparin (intravenous bolus injection 30 mg), double antiplatelet therapy (loading doses of acetylsalicylic acid (250 mg) and ticagrelor (180 mg), β blockers (metoprolol succinate 25 mg per day), statins (atorvastatin 80 mg per day), inhibitors angiotensin converting enzyme (ACE) (zofenopril 15 mg per day). Despite positive clinical changes, ECG after

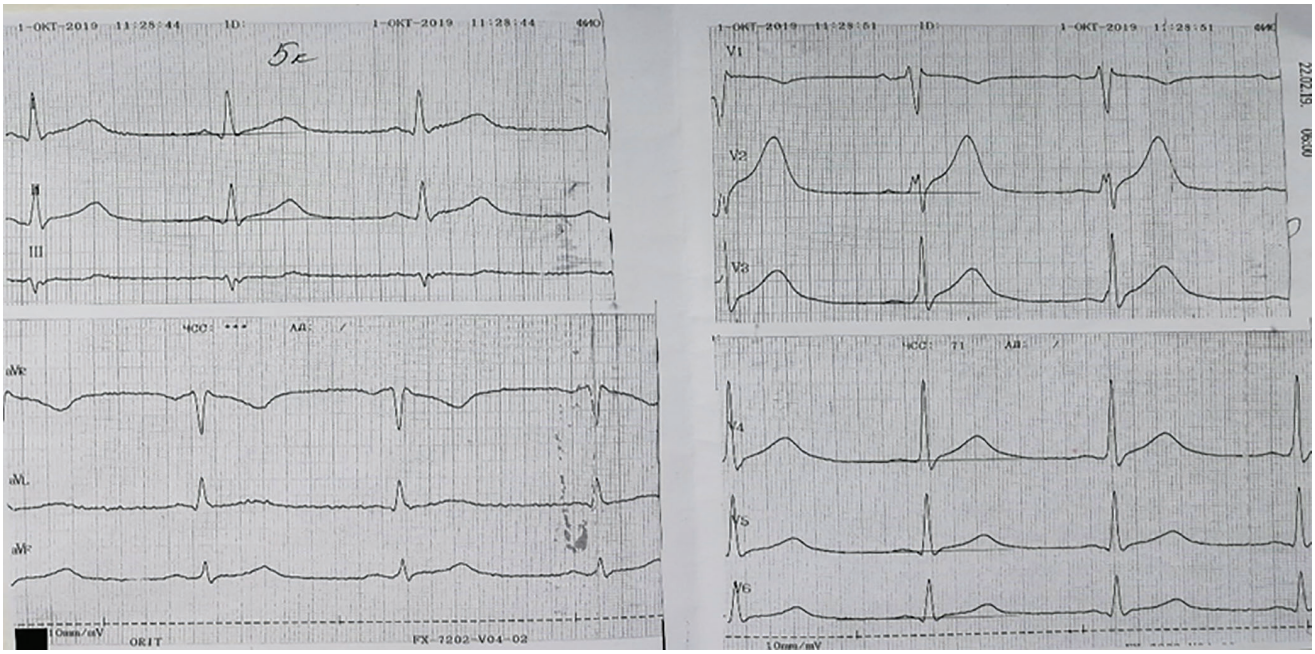

Figure 2. *On ECG: ST elevation in leads I, II, AVL, V2–V6 with maximum elevation in V2–V3, ST depression in AVR, high, pointed T waves in V2–V3, incomplete right bundle branch block (QRS 0.10 s), QTc 0.42 s*

thrombolysis showed persistent ST elevation and a high T wave; no ECG changes typical for effective thrombolysis were observed within two hours. Thirteen hours after the onset of the disease, the patient was transported in the Regional Clinical Hospital (Saratov) for coronary angiography and percutaneous coronary intervention.

The patient complained of general weakness on admission. Medical history showed that the patient had previously handled physical activity satisfactorily; he had never complained of retrosternal pain and shortness of breath. Cardiovascular risk factors for this patient included a long history of smoking: he had been smoking 10 cigarettes per day for 20 years (smoking index is 10 pack-years). Blood pressure did not exceed 120 and 80 mm Hg. No family history of early development of cardiovascular diseases. Serum glucose and cholesterol were not controlled before. On admission, the patient's condition was assessed as moderately severe. Skin was of normal color and moisture. Body mass index 23 kg/m^2, waist 70 cm. Blood pressure 105 and 70 mm Hg, heart rate 75 per minute. During auscultation, heart rhythm was regular, weak S1 at the apex is noted (S1/S2 ratio 1:1), no pathological murmurs detected. Respiratory rate was 18 per minute, harsh breathing in lungs, no rales. Oxygen saturation 98%. No abnormalities were found in other organs and systems.

ECG recorded 13 hours after the onset of the disease revealed that the abovementioned changes persisted with the same intensity. Echocardiography (Echo-CG) revealed an extensive abnormal local contractility, which significantly exceeded the area of blood supply of one coronary artery. Apical hypokinesia, circular lesion of apical (anterior, septal, lower, lateral) and middle (anterior, anterior septal, lower septal, lower, lower lateral, anterolateral) segments, of three basal (anterior, anterior septal, lower septal) segments of left ventricle were found. Therefore, local contractility disorders were identified in 14 LV segments out of 17; only 3 basal segments had no hypokinesia: lower, lower lateral and anterolateral. There was also decreased global contractility of the left ventricle (ejection fraction 39% (according to Simpson method)), slightly increased systolic pressure in the pulmonary artery (35 mm Hg), increased final systolic dimension of the left ventricle (4.0 mm, normal up to 3.7 mm). Emergency selective right and left coronary angiography (01.10.2019) performed 14 hours after the onset of the disease revealed coronary arteries with no angiographical changes (Fig. 3).

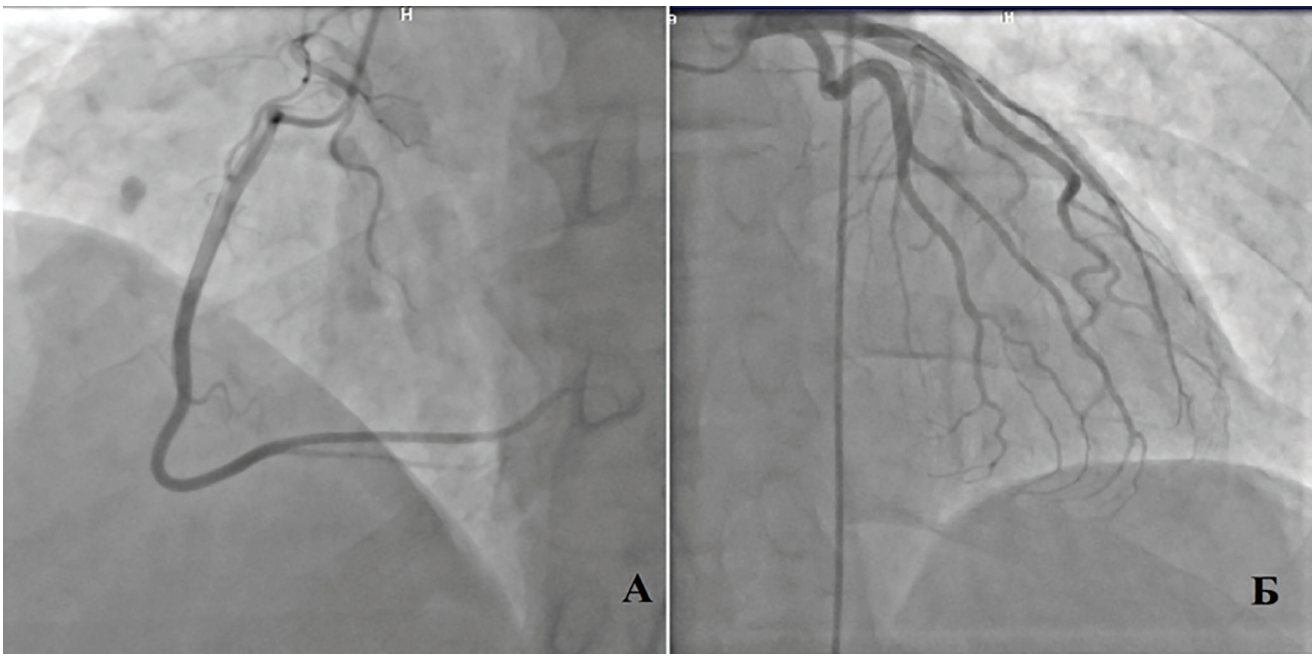

Figure 3. *Selective right (A) and left (B) coronary angiography: coronary arteries with no angiographical changes*

Triplicate test for biochemical markers of myocardial necrosis showed no abnormalities: creatine phosphokinase (CPK) 57.1–58.7–57.2 U/L (N 26–174 U/l); CPK MB 11.7–10.7–11.2 U/l (N up to 24 U/l); troponin I 0.004–0.003–0.004 ng/ml (N up to 0.05 ng/ml). Blood biochemistry revealed a significant increase of C-reactive protein to 99 mg/ml (N up to 5 mg/ml) and N-terminal propeptide of the natriuretic hormone to 536 pg/ml (N up to 125 pg/ml). No abnormal lipid or carbohydrate metabolism was detected: total cholesterol was 4.5 mmol/l, low density lipoproteins 2.8 mmol/l, high density lipoproteins 1.5 mmol/l, atherogenic index 2.2, blood glucose 5.2 mmol/l.

Treatment was continued at the hospital: double antiplatelet therapy (acetylsalicylic acid and ticagrelor), anticoagulant therapy (enoxaparin subcutaneously), β blockers (metoprolol succinate), ACE inhibitors, statins.

Therefore, after psychoemotional stress, the patient developed typical clinical signs of ACS accompanied by acute left ventricular failure and severe vegetative manifestations. However, the absence of increased myocardial necrosis markers, coronary arteries without angiographical changes in combination with normal lipid profile, and no family history of the early development of cardiovascular diseases raised doubts over the presence of acute coronary syndrome.

Extended local contractility disorders according to Echo-CG data, exceeding the blood supply areas of one coronary artery, a circular lesion of the apical and middle segments of the left ventricle, coronary arteries without angiographical changes, and the association of symptoms with psychoemotional stress suggested the patient had TTS. This assumption corresponded with the rapid positive changes in Echo-CG parameters: on the 3rd day there were no areas of local myocardial contractility disorders, the left ventricular ejection fraction (Simpson's method) increased to 58%, normal sizes of cardiac cavities were restored, systolic pressure in the pulmonary artery normalized (25 mm Hg). ECG results on the 7th day revealed a decrease in the ST segment to the baseline and normalization of the shape and height of the T wave (Fig. 4).

Based on the obtained information, the patient was diagnosed with primary takotsubo syndrome complicated by acute left ventricular failure. Therapy was adjusted: antiplatelet agents, anticoagulants, statins were discontinued, treatment with ACE inhibitors (zofenopril 15 mg per day) and β blockers (metoprolol succinate 25 mg per day) was continued. Patient was discharged on the 7th day in satisfactory condition with recommendations to continue taking the abovementioned drugs in the same doses. During subsequent

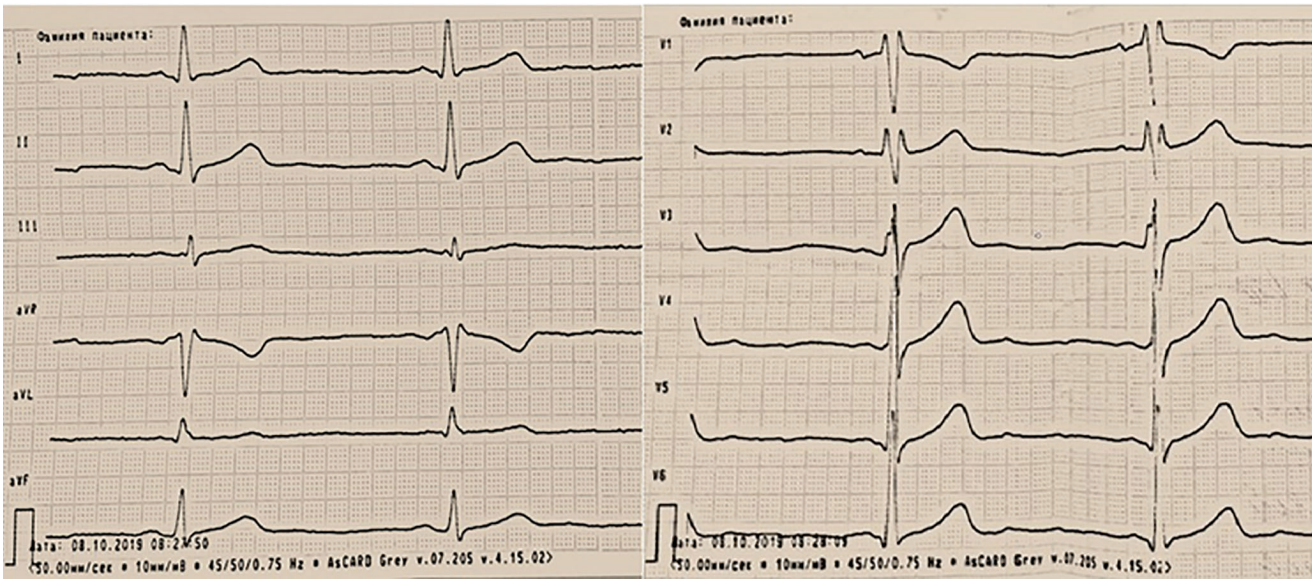

Figure 4. *ECG on day 7. ST segment at baseline, amplitude of T wave within normal range, incomplete right bundle branch block (QRS 0.10 sec), QTc 0.40 sec*

examinations a month and three months after discharge, the patient had no complaints, no retrosternal pain, and no dyspnea; he returned to his usual physical activity.

Discussion

Since the publication of the first diagnostic criteria in 2003, more than ten different diagnostic criteria for TTS based on local registers have been proposed. The best known and most common were the modified Mayo clinic criteria (USA), 2011 Approaches to the diagnosis of TTS changed as more information about the syndrome accumulated. In 2018, experts from the European Society of Cardiology developed and published a Consensus Document on TTS, which proposed international diagnostic criteria for TTS based on the most current understanding of this disease [2]. The following criteria were found in the patient described in this case study: transient disorder of LV local myocardial contractility that corresponds to the myocardial areas supplied by more than one coronary artery and often results in circular dysfunction of LV segments; previous stress factor (emotional or physical); first-time and reversible abnormalities on the ECG (elevation or depression of ST, inversion of T waves and/or increased duration of QTc); clinically significant increase in the concentration of natriuretic peptides during the acute phase of this disease. The coronary arteries were without abnormalities according to angiography. However, according to the European Consensus Document, at present, it is not a mandatory criterion for the diagnosis of TTS.

Changes in the ECG registered at the onset of the disease in this patient resemble those in cases of anterior myocardial infarction caused by occlusion of the left anterior descending artery: ST elevation in leads I, II, AVL, V2–V6 and high, pointed T waves in V2–V3. However, some characteristic features that are not typical for myocardial infarction of this localization were revealed: the biggest changes in V2–V3 with no ST elevation in V1, ST depression in AVR, no reciprocal changes in II, III, AVF. These changes in the ECG are considered to be the criteria that allow differentiating anterior myocardial infarction with ST elevation from TTS [4]. Existing differences in the ECG pattern in cases of TTS and anterior myocardial infarction suggest TTS at the onset with characteristic clinical signs and characteristic Echo-CG findings. However, reliable differential diagnosis of these conditions requires emergency coronary angiography [2].

The development of TTS in the young man in this case study is not typical for this disease since older women are more susceptible to it [2]. There is evidence in literature that the development of TTS in men is more often preceded by physical stress; higher levels of myocardial damage markers are detected, QT prolongation and ventricular arrhythmias are more frequent and are associated with higher mortality [5]. However, our patient had none of these signs: the disease was preceded by emotional stress, no increased myocardial necrosis markers were found, no heart rhythm disorders or QTc prolongation were registered.

Conclusion

In conclusion, it should be noted that if the interest of clinicians in TTS was previously primarily due to the need for differential diagnosis with ACS, today there is an understanding that TTS is an independent disease and has specific features confirmed by magnetic resonance imaging of the myocardium in T2 mode (myocardial hibernation, signs of inflammation and myocardial edema) [3]. The increasing accessibility of coronary angiography for ACS, the wide range of ideas about the variety of factors that contribute to TTS, and the ambiguity of data on the outcome prognosis require practitioners to be more informed about this disease.

Author Contribution:

M.A. Tyapkina (ORCID ID: https://orcid.org/0000-0002-1860-3171): patient management definition, examination, evaluation, diagnosis, data's analysis, development of general concept and article design, writing of the manuscript, verification of critical important intellectual content, making a final determination regarding the publication readiness of the manuscript, responsibility for all work aspects

E.V. Yakovleva (ORCID ID: https://orcid.org/0000-0001-6700-8531): patient management definition, development of general concept and article design, writing of the manuscript, verification of critical important intellectual content

A.A. Roshchina (ORCID ID: https://orcid.org/0000-0002-6312-0427): patient management definition, examination, evaluation, data's analysis, development of general concept and article design, writing of the manuscript

G.A. Halmetova: patient management definition, examination, evaluation, data's analysis, development of general concept and article design, writing of the manuscript

I.V. Basov: patient management definition, examination, evaluation, data's analysis, development of general concept and article design

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