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ВТОРИЧНЫЙ СИНДРОМ ТАКОЦУБО У МОЛОДОЙ ПАЦИЕНТКИ ПОСЛЕ НЕЙРОХИРУРГИЧЕСКОГО ВМЕШАТЕЛЬСТВА

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Takotsubo Syndrome in a Young Patient After a Neurosurgical Operation

Резюме

Синдром такоцубо (кардиомиопатия такоцубо, стрессиндуцированная кардиомиопатия, транзиторная кардиальная дисфункция) — клинический синдром, характеризующийся остро возникающей, обратимой систолической дисфункцией левого (реже правого) желудочка сердца, развивающийся в условиях отсутствия стенозирующего атеросклеротического поражения или тромбоза коронарных артерий. В статье приводится клинический случай развития синдрома такоцубо, развившегося после нейрохирургической операции. **Цель наблюдения:** продемонстрировать случай развития синдрома такоцубо у молодой пациентки в раннем послеоперационном периоде. **Основные положения:** пациентка 21 года находилась на стационарном лечении в отделении нейрохирургии в связи с сохраняющимся в течение года после оперативного вмешательства болевым синдромом в области левого локтевого сустава с иррадиацией в 4, 5 пальцы левой руки, нарушением функции левого локтевого сустава. Проведена декомпрессия левого локтевого нерва на уровне кубитального канала с его транспозицией. В послеоперационном периоде течение заболевания осложнилось развитием стресс-индуцированной кардиомиопатии, подтвержденной результатами лабораторного обследования, электрокардиографии, эхокардиографии, а также отсутствием атеросклеротических изменений коронарных артерий по данным коронароангиографии. **Заключение.** Ранний послеоперационный период может осложниться развитием синдрома такоцубо, в т.ч. после нейрохирургических вмешательств у пациентов молодого возраста.

Ключевые слова: *синдром апикального баллонирования, синдром такоцубо, стресс-индуцированная кардиомиопатия, сердечная недостаточность, периоперационный период, постоперационные осложнения*

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Abstract

Cardiomyopathy syndrome (stress-cardiomyopathy) is an acute reversible systolic dysfunction of left (or rare right) ventricle without stenotic atherosclerosis and/or thrombosis of coronary artery. We are presenting a case of stress-cardiomyopathy after the neurosurgery. **Aim:** The aim of this observation is to demonstrate a case of takotsubo syndrome in a young patient in the early postoperative period. **Key points:** A 21-years-old woman was hospitalized in the neurosurgery department. Hospitalization was performed due to persistent pain in the left elbow joint with irradiation to left 4 & 5 hand fingers as well as dysfunction of the left elbow joint, as a result of previous surgical intervention for a fracture one year before. Due to the lack of a positive effect from conservative therapy, it was decided to conduct a second surgical treatment. Decompression of the left ulnar nerve was performed at the level of the cubital canal with its transposition. This was complicated by the development of takotsubo syndrome in the postoperative period, confirmed by echocardiography, ECG, as well as the absence of atherosclerotic changes in the coronary artery according to coronary angiography. **Conclusion:** The early postoperative period may complicate of development of takotsubo syndrome, in the neurosurgical operations and in the young age too.

Key words: *apical ballooning syndrome, takotsubo cardiomyopathy, stress-induced cardiomyopathy, heart failure, postoperative period, postoperative comlications*

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BP — blood pressure, CAG — coronary angiography, ECG — electrocardiography, EchoCG — echocardiography, EF — ejection fraction, IVS — interventricular septum, LV — left ventricle, mPAP — mean pulmonary arterial pressure, RV — right ventricle

Takotsubo cardiomyopathy (stress-induced cardiomyopathy, apical ballooning syndrome, ampulla cardiomyopathy, broken heart syndrome) is a clinical syndrome characterized by acute, reversible systolic dysfunction of the left (rarely right) ventricle (LV, RV) of the heart, which develops in the absence of stenosing atherosclerotic lesions of coronary arteries and resolves spontaneously within a few days or weeks [1, 2]. Experts of the European Society of Cardiology (ESC) recently recommended using the definition "takotsubo syndrome", avoiding the term "cardiomyopathy" [1, 3, 4]. Takotsubo syndrome was first described by Sato et al. in 1990 [5]. Translated from Japanese, Tako-Tsubo is a pot-shaped octopus trap. The left ventricle of the heart acquires a similar shape in this pathology; its basal segments contract during relative hypokinesis or dyskinesis of the apical segments [1]. This disease is caused by physical or psychological overexertion (primary takotsubo syndrome). If the disease develops with underlying severe non-cardiac pathology or surgical treatment, it is considered as a secondary takotsubo syndrome. Usually, patients with takotsubo syndrome are admitted to the hospital with a referral diagnosis of acute coronary syndrome. The incidence of takotsubo syndrome is approximately 0.00006 % of the population, approximately 1–2 % of patients with ST-elevation myocardial infarction [6]. Takotsubo syndrome occurs more often in women (80–90 %) than in men; the average age of patients is 61–76 years [1]. Cases of this condition in young patients are rare.

Clinical case

A female patient, 21, was routinely admitted to the neurosurgical department with complaints of recurring pain in the area of the left elbow joint radiating to the 4th and 5th fingers of the left hand and joint dysfunction. Twelve months before this hospitalization, surgical treatment was performed for a fracture of radius, a month later the abovementioned complaints appeared.

Due to no effect of conservative therapy, a decision was made to perform surgery — decompression of the left ulnar nerve at the level of the cubital canal with its transposition. Three years prior to this hospitalization, the patient was diagnosed with chronic gastritis, multinodular goiter, and hypothyroidism. She constantly took levothyroxine sodium 25 μg/day. The patient had no cardiovascular risk factors or bad habits.

On admission to the neurosurgical department, the patient's condition was satisfactory. Regular body type, body mass index (BMI) 27 kg/m^2. No signs of edematous syndrome were found. On auscultation: vesicular breathing in the lungs, with no side breath sounds. Clear heart tones, regular rhythm with a heart rate (HR) 80 bpm. Blood pressure (BP) 110/70 mm Hg. After a successful surgical intervention under general anesthesia, the patient was transferred to the intensive care unit for follow-up. After 10 hours of the postoperative period, the patient complained of shortness of breath, pressing pain in the chest for more than 20 minutes, palpitations, and decrease in blood pressure down to 80/40 mm Hg.

An electrocardiogram (ECG) revealed ST segment elevation in leads I, aVL, as well as ST depression in leads III, aVF, V1–V5 (Fig. 1).

Echocardiography (EchoCG) revealed normal LV wall thickness, areas of impaired local contractility of the LV myocardium in the form of dyskinesia of the anterior wall, interventricular septum (IVS), lateral and inferior walls at the apical and middle levels; decreased LV ejection fraction (EF) to 29 % according to Simpson, as well

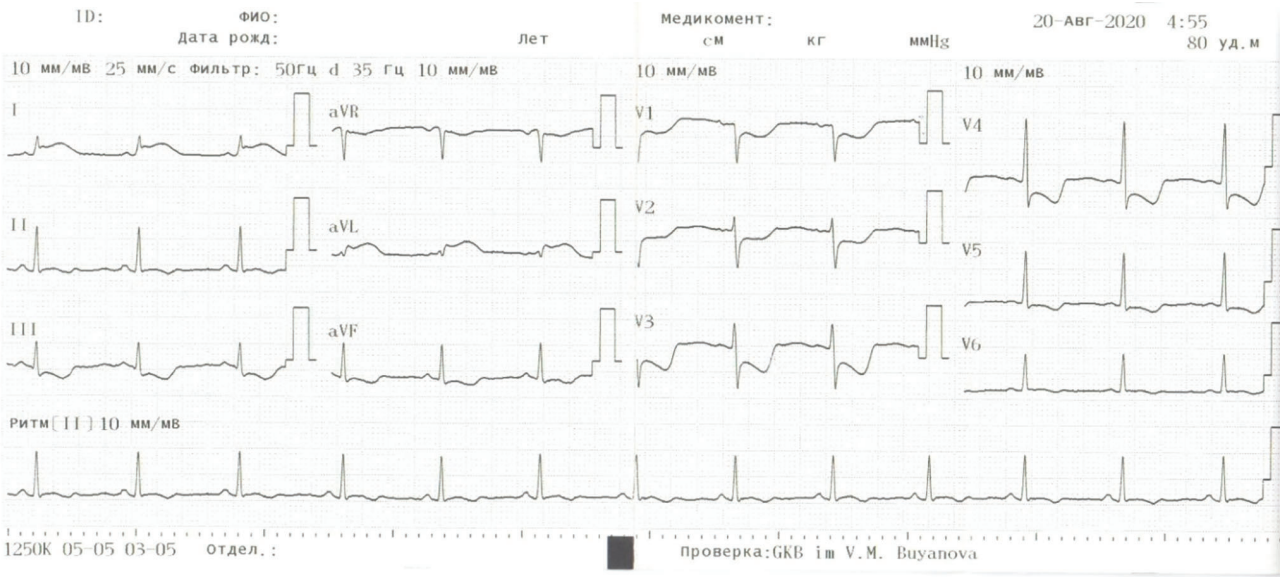

Figure 1. *ECG of the patient 10 hours after surgery: ST segment depression and negative T wave in leads III, avF, V1-5, ST elevation in leads I, avL*

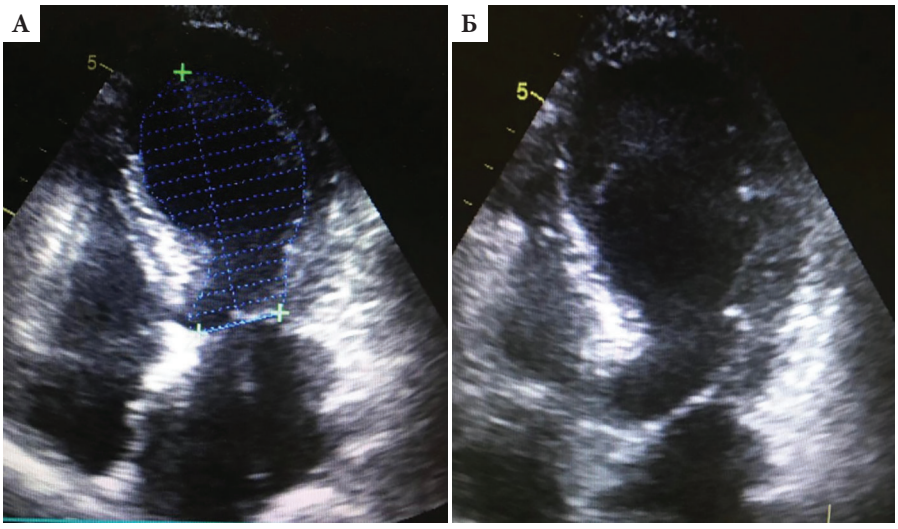

Figure 2. *Echocardiography of a patient in the postoperative period, after the onset of pain in the chest, apex ballooning, B-mode, systole: А — apical 4-chamber position, Б — apical 5-chamber position*

as signs of moderate pulmonary hypertension: mean pulmonary artery pressure (mPAP) 46 mm Hg. (Figure 2).

Laboratory tests revealed increased troponin level up to 0.71 μg/L (normal 0–0.1 μg/L), increased level of N-terminal precursor of brain natriuretic peptide — 3,280 ng/L (normal 12–133 ng/L), increased levels of cholesterol up to 5.4 mmol/L, low-density lipoprotein cholesterol up to 3.28 mmol/L, fibrinogen up to 5.01 g/L, D-dimer up to 1,231 μg/L, ESR up to 46 mm/h, with no clinically significant changes in other parameters.

Coronary angiography (CAG) revealed no atherosclerotic changes, no thrombosis of coronary arteries, as well as no plaque rupture or intimal dissection (Fig. 3).

Considering the signs of moderate pulmonary hypertension (mPAP 46 mm Hg) found during EchoCG and increased D-dimer, the patient underwent ultrasound dopplerography of the veins of lower extremities and angiopulmonography, which revealed no signs of venous thrombosis or pulmonary embolism.

The patient was prescribed a beta-blocker (bisoprolol at a dose of 2.5 mg a day) and acetylsalicylic acid at a dose of 75 mg a day. Forty-eight hours later, considering the satisfactory condition of the patient, complete resolution of clinical signs and normalization of blood troponin level, the patient was transferred to the neurosurgical department.

On day 6 of the postoperative period, normalization of the N-terminal precursor of brain natriuretic peptide was found, regression of the identified pathological changes was registered on ECG (Fig. 4), and EchoCG revealed restoration of LV EF and local myocardial contractility.

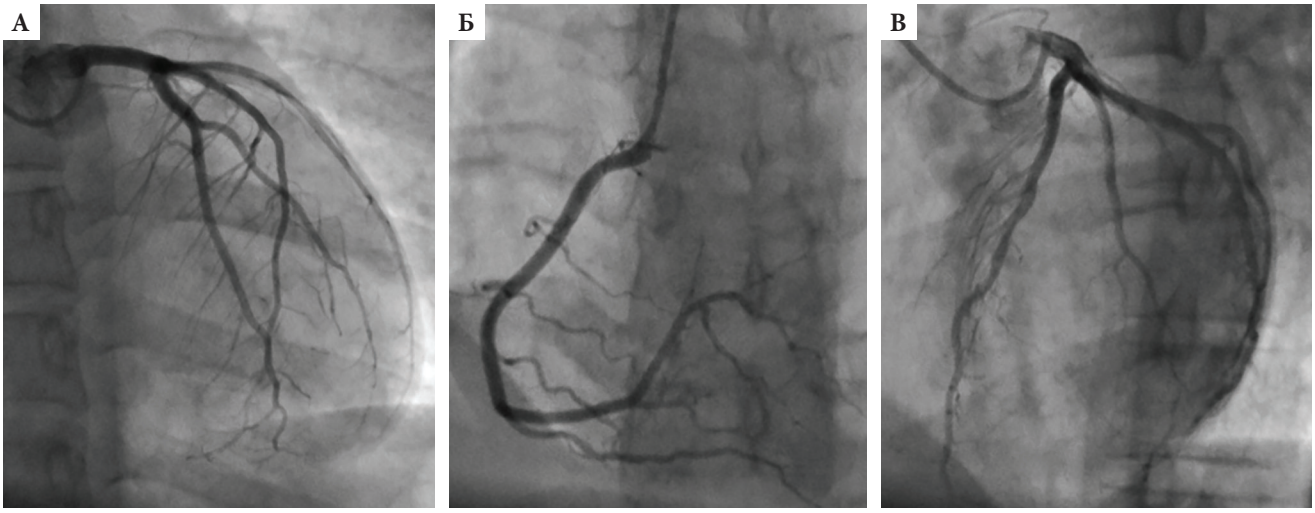

Figure 3. *Intact coronary arteries during emergency coronaroangiogramm. A. Left coronary artery: AP view, 0⁰. Б. Left coronary artery: left oblique view, 45⁰. Right coronary artery: left oblique view, 30⁰*

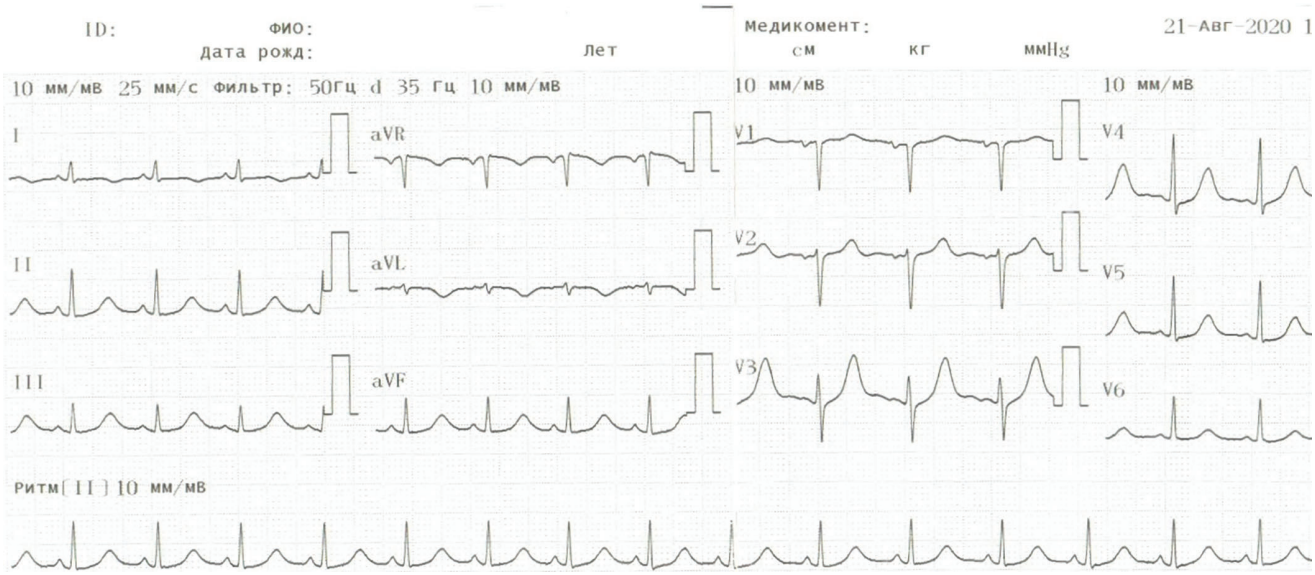

Figure 4. *ECG of the patient on the 6th day of the postoperative period. Regression of pathological changes: return of the ST segment to the isoline in leads III, avF, V1-5, I, avL, positive T wave in these leads*

Massively parallel sequencing of dried blood spots revealed no mutations in genes ACTC1, DES, FLNC, GLA, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2, PTPN11, TNNC1, TNNI3, TNNT2, TPM1, TTR[1].

Based on clinical, laboratory and instrumental results, acute myocardial infarction and myocarditis were excluded. Considering the reversibility of local contractility disorders, normalization of LVEF, N-terminal precursor of brain natriuretic peptide (NT-proBNP), troponin, regression of ECG changes, the patient was diagnosed with stress-induced cardiomyopathy (takotsubo).

The patient was discharged on day 8 in satisfactory condition under outpatient follow-up by a cardiologist.

During two years of follow-up, the patient did not experience any recurrence of symptoms.

Discussion

Immediately after neurosurgical intervention, the young patient developed a presentation of anginal pain, acute left ventricular heart failure, hypotension, ECG and laboratory signs of acute myocardial injury, impaired local contractility of the left ventricular myocardium extending beyond the blood supply zone of a certain coronary artery, systolic myocardial dysfunction in intact coronary arteries.

The described patient has all diagnostic criteria for takotsubo syndrome according to the recommendations of the Heart Failure Association of the European Society of Cardiology (ESC) 2016 [6]:

1. Transient local disorders of LV myocardial contractility that are often, but not always, preceded by a stressful trigger (emotional or physical).
2. Local impairments of contractility that go beyond the blood supply zone of one coronary artery and are manifested by circular dysfunction of the involved areas of the heart muscle.
3. Absence of atherosclerotic lesions of the coronary artery leading to myocardial infarction, including acute plaque rupture, thrombosis, coronary artery dissection, and other pathological conditions (for example, hypertrophic cardiomyopathy, viral myocarditis) that could cause transient LV dysfunction.
4. New reversible ECG changes (*ST* elevation, *ST* depression, inversed *T* wave and/or prolonged *QTc*) during the acute phase.
5. Significant increase in natriuretic peptide level (BNP or NT-proBNP) during the acute phase.
6. Relatively small increase in cardiac troponin levels compared with the area of myocardial dysfunction.
7. Recovery of myocardial function according to the results of imaging methods during follow-up [1].

In the described clinical case, the neurosurgical decompression of the left ulnar nerve at the level of the cubital canal with its transposition became a trigger for takotsubo cardiomyopathy in the patient. This suggests secondary takotsubo syndrome in this patient with another underlying (neurological) disease. With primary (caused by emotional or physical stress) takotsubo syndrome, cardiac symptoms are the reason for seeking medical help. Some cases of takotsubo syndrome are detected among patients hospitalized for other medical, surgical, gynecological and even psychiatric diseases [1]. There are cases of takotsubo syndrome in the literature in connection with such neurological pathology as stroke, subarachnoid hemorrhage, acute neuromuscular crisis, encephalitis, epileptic seizures, encephalopathy [2].

Russian researchers described three clinical cases of cardiomyopathy after induction with general anesthesia, which accounted for 0.04 % of all anesthesias performed in a year [7]. These cases, as well as the one we described, indicate the need for strict control of hemodynamic parameters in patients in the early postoperative period, performing ECG and, if necessary, EchoCG, informing anesthetists about the possibility of takotsubo syndrome,

[1] **1. Genetic testing — cardiomyopathy panel:** ACTC1 actin alpha cardiac muscle 1; DES desmin; FLNC filamin C; GLA alpha galactosidase A; LAMP2 lysosomal-associated membrane protein 2; MYBPC3 myosin binding protein C3; MYH7 myosin heavy chain 7; MYL2 myosin regulatory light chain 2; MYL3 myosin regulatory light chain 3; PLN phospholamban; PRKAG2 protein kinase AMP-activated non-catalytic subunit gamma 2; PTPN11 protein tyrosine phosphatase non-receptor type 11; TNNC1 troponin C1, slow skeletal and cardiac type; TNNI3 troponin I3, cardiac type; TNNT2 troponin T2, cardiac type; TPM1 tropomyosin 1; TTR transthyretin

2. Criteria for risk stratification of cardiac complications (including acute left ventricular failure, malignant arrhythmias, and myocardial rupture) in takotsubo syndrome [1].

Major risk factors for a poor outcome:

- age 75+;
- systolic BP < 110 mm Hg;
- pulmonary edema;
- VT, VF, syncope that cannot explained by other reasons;
- LVEF < 35%;
- pressure gradient in LV outflow tract 40 mm Hg or higher. (It would seem that its appearance, which indicates the high contractility of the intact myocardium, indicates reserves of LV systolic function as well. However, the obstruction of the outflow tract, which also develops due to the anterior systolic movement of the anterior mitral leaflet with mitral regurgitation of different severity, can result in intraventricular blood regurgitation into a stretched akinetic/dyskinetic apex and aggravation of left ventricular failure.)
- moderate or severe mitral regurgitation;
- LV apex thrombosis;
- IVS rupture;
- rupture of LV free wall.

Minor risk factors:

- age 70–75 years;
- lengthening QTc up to 500 ms or more;
- pathological Q wave;
- ST elevation for three days or more;
- LVEF 35–45%;
- presence of a physical stressor;
- BNP level 600 pg/ml or higher;
- NT-proBNP level 2,000 pg/ml or higher;
- concomitant obstructive coronary pathology;
- involvement of both ventricles.

A marker of high risk is the presence of at least **one major or two minor criteria**.

as well as the diagnostic and therapeutic approach for the management of this condition.

The risk of developing cardiac complications in takotsubo syndrome (including cardiogenic shock, malignant arrhythmias, and even myocardial rupture), which are observed in about half of patients, [3, 4] was high in this patient (Appendix 2): there were two major (systolic BP < 110 mm Hg, LVEF < 35 %) and one minor (0 NT-proBNP level of 2,000 pg/mL or higher) risk factors for a poor outcome.

The clinical presentation of takotsubo cardiomyopathy is transient, and in the described clinical case, it resolved within six days. Drug therapy at the initial stage of treatment usually includes standard therapy for systolic heart failure. Due to hypotension in this patient, no angiotensin-converting enzyme inhibitors (as well as angiotensin II receptor blockers, angiotensin /neprilysin receptor inhibitors) and no diuretics were prescribed; low doses of a beta-blocker and antiplatelet agents were recommended for four weeks.

The annual recurrence rate of takotsubo syndrome during the first few years is 2.9 % [1]. Our patient experienced no recurrence during two years of follow-up.

Conclusion

We presented a case of takotsubo cardiomyopathy in the early postoperative period after neurosurgical intervention. Such cases are extremely rare, especially in young patients. Prognosis in cases of timely diagnosis and adequate treatment is usually favorable.

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All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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