Chronic thyrotoxic myocarditis complicated by myocardial rupture in a patient with autoimmune thyroiditis

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ABSTRACT

A case of thyrotoxic myocarditis in a 60-year-old female patient is presented. With the diagnosis of «Unstable angina» she was admitted to the intensive care unit for patients with myocardial infarction at the Yudin city clinical hospital in Moscow. Earlier, the patient had been treated with thyroxol for thyrotoxicosis, but she independently abolished the drug. She experienced pain in the chest for the first time in her life. Emergency, coronaryangiography was performed. No hemodynamically significant damage to the blood vessels of the heart was detected. Later, according to the outpatient blood test for thyroid hormones, a diagnosis was established — «severe thyrotoxicosis». The next day after hospitalization, treatment with thyroxol was started at a dose of 30 mg per day. Sinus tachycardia persisted. A reliable increase in cardiospecific enzymes was detected. The pain in the chest did not recur. Echocardiography did not reveal impairment of local or global myocardial contractility.

On the fifth day of hospital treatment the patient suddenly died of cardiac and respiratory arrest. The autopsy study revealed autoimmune thyroiditis, thyrotoxic serous-lymphocytic myocarditis, which was complicated by a rupture of the myocardium, and pericardial gemotamponade.

The difficulties of differential diagnosis of myocarditis and acute coronary syndrome and the features of treatment tactics in elderly patients with thyrotoxicosis are discussed.

Keywords: case report, thyrotoxicosis, myocarditis, myocardial rupture.

Relevance

Chronic autoimmune thyroiditis (CAT) is caused by a genetically determined defect of immune tolerance to thyroid gland antigens (TG) [1]. CAT is more common in women aged 40-50 years and is found in about 20% of elderly women [2, 3]. CAT is classified as hypertrophic or atrophic based on the anatomy and morphology. The main cyto- and histological sign of CAT is diffuse or focal lympho- or plasmacytic infiltration of the thyroid tissue, although its criteria are vague [4, 5]. Hyperthyroidism occurs in 5% of patients with hypertrophic form of CAT [6]. People who have had thyrotoxicosis, even after the radical cure, have increased mortality compared with the rest of the population, mainly from cardiovascular causes [7–9].

Myocarditis is one of the complications of CAT which is caused by toxic effects of an excess of thyroid hormones on the myocardium [10]. It also disrupts the energy-generating function of myocardiocytes and the contractile function of myofibrils [6, 11, 12]. There are cases of myocarditis occurring under the mask of acute coronary syndrome. An emergency coronary angiography is required to clarify the diagnosis [13—15].

The practice of management of patients with acute coronary syndrome involves emergency myocardial revascularization by percutaneous coronary intervention or thrombolytic therapy. This significantly reduces the incidence of early complications of myocardial infarction, in particular, myocardial ruptures at the inpatient stage of treatment [16]. Myocardial rupture as a fatal complication of myocarditis is rare. Individual cases of myocardial rupture with fulminant, giant cell, bacterial myocarditis have been described [17—19]. Descriptions of cases of myocardial rupture in thyrotoxic myocarditis were not found in the available literature, which defined the interest in this clinical observation.

Description of the case

Patient N., 60 years old, medical record № 13787, was admitted to the intensive care unit for patients with myocardial infarction of the S.S. Yudin State Clinical Hospital, Moscow, on February 15, 2017, with complains of burning pain in the chest. There was no history of coronary issues. During the last 5 years, she suffered from arterial hypertension with elevations of blood pressure up to 180/100 mmHg and was taking amlodipine 5 mg in the mornings and, occasionally, captopril. She was adapted to blood pressure 140/80 mmHg. Over the past year, blood pressure was unstable despite antihypertensive drugs therapy, but the patient did not go to a doctor.

Medical history shows that she was diagnosed with thyrotoxicosis in 2005 and was prescribed thyroxol at a dose of 10 mg per day. Four years ago, the patient self-cancelled the drug, and the level of thyroid hormones was not monitored. In the last year, she noted the appearance of unmotivated weakness not only in the evenings but also in the mornings. She had decreased exercise tolerance. She was bothered by palpitations. She visited an endocrinol-
ogist, and three days before this hospitalization, blood was taken to study the level of thyroid hormones.

More than 20 years ago, she was diagnosed with duodenal ulcer, but she could not remember the last exacerbation. Periodically she experienced heartburn and discomfort in the epigastric region which occurred after a meal.

On the evening of February 15th, after returning home from work, she experienced burning and pressing chest pains radiating to the back at rest for the first time in her life. The patient suffered pain for 1.5 hours and did not try to manage it. Then she called the ambulance and, following a ECG registration she was hospitalized with a diagnosis of unstable angina. (Fig. 1).

The ambulance team prescribed the following treatment: ticagrelor 180 mg, accardol 250 mg, 2 doses of isocet. The pain in the chest persisted.

**Examination in the intensive care unit**

The general condition of the patient was moderately severe. The skin with normal color, warm, normal humidity. No peripheral edema. RR: 20 per min. Auscultation revealed hard breathing without wheezing. The region of the heart was unmodified, the borders of the heart were expanded to the left. Heart sounds were muffled rhythmic. A systolic murmur was heard over the projection of the apex of the heart. Strong pulse in the main and peripheral arteries. BP: 150/90 mmHg, HR: 120 bpm.

ECG did not identify a significant increase in the ST segment, there was the oblique-ascending depression in ST-segment registered by V4—V6 leads.

Taking into account the clinical presentation, laboratory diagnostic data, ECG changes (see Results of the examination), the patient’s condition was regarded as an “acute coronary syndrome” requiring emergency coronary angiography (CAG).

After obtaining the informed consent, administering neuroleptic algesia and pain relief, the patient was transferred to an X-ray room where she underwent CAG (see Results of the examination). No hemodynamically significant constriction of the coronary arteries was identified.

The dynamical study of the cardiospecific enzymes revealed changes characteristic for focal myocardial damage (see Results of the examination).

After the relief of pain, the patient’s condition did not worsen, chest pain did not recur, however, the complaints of palpitations persisted. With the prescribed treatment, blood pressure stabilized at a level of 120—130/70—80 mmHg.

Sinus tachycardia persisted on ECG, there was no convincing data for the presence of focal changes (Fig. 2).

Chest X-ray revealed left-sided encapsulated pleurisy (see Results of the examination). No signs of hypokinesia and impaired global contractility of the left ventricle were noted in echoCG (see Results of the examination).

The patient received the following treatment: amlopidine 2.5 mg in the morning, losartan 25 mg in the morning, brilint (ticagrelor) 90 mg, omeprazole 20 mg, accardol 100 mg, atorvastatin 40 mg.

On 16.02.17, the patient was transferred to the cardiology department in a stable condition, where bisoprolol (5 mg of in the morning and 2.5 mg in the evening), as well as 5 mg torasemide in the morning on an empty stomach, were added to the treatment regimen.

At an outpatient blood test, the TSH level was 0 μMU/L (decreased), T4 concentration was 41 μg% (increased), and antithyroid antibodies were not detected.

Endocrinologist diagnosis: Recurrent diffuse toxic goiter. A complicated course of thyrotoxicosis, decompensation. Thyrotoxic heart. However, the genesis of chest pain remained unclear.

From February 16, 2017, the therapy with tyrosol in a daily dose of 30 mg was prescribed with monitoring of thyroid hormone levels. On treatment, the patient suffered from general weakness and palpitations during the whole day. An abnormal Q wave appeared on the ECG in the posterior wall of the left ventricle. (Fig. 3). The cause of pain in the chest could be an exacerbation of peptic ulcer disease. Further examination was planned.

On February 20, 2017, the patient suddenly fainted, and breathing and cardiac activity ceased. Resuscitation for 30 minutes was ineffective. Biological death was declared.

**Final clinical diagnosis**

**Main disease:**
1. Coronary heart disease: atherosclerosis of the heart vessels.

2. Recurrent diffuse toxic goiter. A complicated course of thyrotoxicosis, decompensation.

**Underlying disease:** Hypertension stage III, grade 3, high risk of CVE.


**Accompanying diseases:** Duodenal ulcer, exacerbation. Chronic gastritis without exacerbation. Chronic bronchitis, exacerbation.

**Pathological diagnosis (autopsy report No. 764/438)**

**Main disease:** Autoimmune thyroiditis, hypertrophic phase; chronic thyrotoxic serous lymphocytic myocarditis, developing thyrotoxic septal cirrhosis, hyperplasia of the lymphoid tissue of the spleen.

**Complications:** Foci of necrosis of the myocardium of the left ventricle with the size of 4×3 cm with a linear rupture of the posterior wall with a length of 3 cm. Pericardial hemotamponade (300 g. blood clots). Pulmonary edema. Diagnostic coronary angiography on February 16, 2017. Chronic venous plethora of internal organs: cyanot-
Fig. 1. The results of the ECG of the patient N., conducted by the ambulance service.

Fig. 2. Dynamics of the patient's N. ECG.
ic induration of the kidneys and spleen. Left-sided hydrothorax (200 ml). Edema of the brain.

Accompanying diseases: Aortic atherosclerosis (Stage 2, Grade 2, lesion area up to 50%). Chronic diffuse atrophic gastritis without exacerbation. Chronic diffuse bronchitis without exacerbation. Diffuse reticulate pneumosclerosis. Emphysema of the lungs.

Conclusion: A 60-year-old patient who suffered from autoimmune thyroiditis and developed thyrotoxic myocarditis died from a pericardial hemotamponade due to a rupture of the left ventricular myocardium (Fig. 4—8, see section ADDITIONAL INFORMATION).

Results of the examination

Coronary angiography (radial access). Innova 3100 GE instrument

Through an introducer in the radial artery, a bolus of a solution of verapamil 5 mg and heparin 5 thousand U was injected. A contrast angiography of the left coronary artery and the right coronary artery was performed using a 6 Fr BLK catheter with Visipac 370 as a contrast agent (150 ml). The trunk of the left coronary artery without significant narrowing. Left anterior descending coronary artery without hemodynamically significant narrowing. The diagonal branch: 40-45% stenosis at the mouth, no hemodynamically significant contractions further. The circumflex branch without hemodynamically significant contractions. Obtuse marginal branch without hemodynamically significant contractions. Right coronary artery without hemodynamically significant narrowing. Posterolateral branch without hemodynamically significant narrowing. Right-handed type of blood supply to the heart. Conclusion: Coronary arteries without hemodynamically significant narrowing.

Laboratory Results

**15.02.17** (time 23:33—23:36, at the admission):
— Troponin (immunochemical assay) — 0.37 ng/ml;
— creatine phosphokinase — 148 U/l;
— hemoglobin — 133 g/l; hematocrit — 41.1%; red blood cells — 4.62×10¹²/l; leukocytes — 6.81×10⁹/l (stab neutrophils — 2%, segmented — 60%, lymphocytes — 29%, monocytes — 9%); MCV — 89.0 fl; MCH — 28.9 pg; MCHC — 325.0 g/l; platelets — 258×10⁹/l;
— fibrinogen — 5.42 g/l (normal 2-4); INR — 0.98; prothrombin time — 14.3 s. (norm 15-17); Quick’s prothrombin time — 106% (norm 78-142).

**16.02.17:**
— Troponin (immunochemical assay) — 3.16 ng/ml;
— creatine phosphokinase — 542 U/l; KFK MV (activity) — 103 U/l;
— cholesterol — 2.80 mmol/l; triglycerides — 0.5 mmol/l.

**20.02.17:**
— creatine phosphokinase — 119 U/l;
— fibrinogen — 8.28 g/l; APTT — 23.1 seconds (normal 25-36); INR — 1.04; prothrombin time — 15.0 s; Quick’s prothrombin time — 97.6%;
— hemoglobin — 131 g/l; hematocrit — 38.1%; red blood cells — 4.28×10¹²/l; leukocytes — 12.3×10⁹/l; granulocytes — 33%; lymphocytes — 56%.

Radiography of the chest 17.02.17

X-ray of the chest in 2 projections (standing) on the left: the anterior sections are homogeneously darkened with a clear upper boundary at the level of the 5th rib in...
the mid-clavicular line due to fluid in the right pleural cavity. From the posterior, the darkened section is delimited by an interlobar pleura. Hyper-translucent lung fields. The lung pattern is deformed, the roots are compacted, not expanded. The diaphragm is contoured on both sides. The front sinus is darkened on the right. The median shadow is not shifted, not expanded. The heart is expanded to the left sections, the waist is smoothed, the aorta is indurated and sclerosed. Focal infiltrative changes were not detected. X-ray picture of the left-sided encapsulated hydrothorax.

**Echocardiography in B- and M-mode with Doppler analysis (17.02.17):**

**B- and M-mode.** Aorta is indurated. 3.4 cm in size. Ascending aorta — 3.7 cm. The aortic valve opening shape is correct. Opening size 1.8 cm. The mobility of the leaflets is not limited. The valve is indurated at the bases of the aortic leaflets. Mitral valve is unchanged. The movement of the leaflets is multidirectional. Tricuspid valve is unchanged. Valve pulmonary artery is unchanged. Size: left atrium — 3.6×5.3 cm; right atrium — 4.0×5.1 cm; right ventricle — 2.9 cm; interventricular septum — 1.22 cm; posterior wall — 0.93 cm; final diastolic size of the left ventricle — 4.73 cm; final systolic size of the left ventricle — 2.96 cm; final diastolic volume of the left ventricle — 104 ml; final systolic volume of the left ventricle — 34 ml; ejection fraction — 67%. No disruptions of myocardial contractility. There is no division of pericardial leaves. The lower vena cava collapse on an inhale more than 50%.

**Doppler analysis.** The maximum speed of aortic blood flow is 1.0 m/s. The maximum pressure gradient between the left ventricle and the aorta is 4.0 mmHg. No regurgitation on the aortic valve was detected. Mitral valve: The maximum rate of early diastolic filling of the left ventricle is 0.4 m/s. The maximum rate of filling of the left ventricle during atrial systole is 0.8 m/s. $P_g$ max $E$ 1.0 mmHg. The degree of regurgitation on the mitral valve — I. Tricuspid valve: degree of regurgitation — I — II. Pulmonary artery valve: degree of regurgitation — I.

**Conclusion.** The walls of the aorta are thickened. No zones of left ventricular hypokinesia were identified at the time of inspection. Global contractility of the left ventricle is satisfactory. A slight increase in the cavity of the left and right atria. Hypertrophy of the interventricular septum.

**Discussion**

There are cases of myocarditis developing under the guise of acute coronary syndrome described in the literature. Sometimes these patients undergo emergency coronary angiography [13-15,20].

Our patient is 60 years old, the clinical presentation of the disease which included burning and pressing chest pains radiating to the back at rest, and which developed for the first time in her life and was accompanied by an increase in the level of cardiospecific enzymes is typical of acute coronary syndrome. Therefore, an emergency coronary angiography examination 2 hours after the onset of the painful attack was justified.

Myocardial rupture, as a complication of myocarditis, is an extremely rare event. A clinical presentation similar to acute myocardial infarction (17,18) is possible.

At the time of CAG, our patient did not have blood test results for thyroid hormones made on an outpatient basis, but there was an evidence of a history of thyrotoxicosis.

Rapid administration of 150 ml of iodine-containing contrast during CAG could have caused an increase in the effects of hyperthyroidism with a sharp increase in the blood levels of thyroid hormones and catecholamines, which, in turn, could have contributed to myocardial damage with the development of its transmural damage. In addition, the effect of tachycardia that persisted in the following days on the expansion and deepening of the myocardial damage zone cannot be excluded.

**Conclusion**

In elderly patients with a long history of thyrotoxicosis, CAT may be the cause of the disease.

Thyrotoxic myocarditis may develop in case of CAT with the presentation similar to that of acute coronary syndrome.

In thyrotoxic myocarditis, administration of iodine-containing contrast agents can lead to a deepening and expansion of the myocardial lesion and cause myocardial rupture.
Supplementary Information

Supplementary materials for the article

Figure 4. Macrospecimen of the heart. The zone of myocardial necrosis (yellow-green), with a gap, the walls of the gap are infiltrated with blood. Available at color inset and on the Internet: http://doi.org/10.14341/probl9276-3297

Figure 5. Microspecimen of the heart. Marked infiltration with segmented nuclear leukocytes in the area of necrosis. Stained with hematoxylin and eosin (magn. ×100). Available at color inset and on the Internet: http://doi.org/10.14341/probl9276-3298

Figure 6. Macrospecimen of myocardium. Picture of serous-lymphocytic myocarditis with diffuse infiltration of lymphocytes, muscle fiber necrosis, pronounced interstitial edema. Stained with hematoxylin and eosin (magn. ×100). Available at color inset and on the Internet: http://doi.org/10.14341/probl9276-3299

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Fig. 4. Macrospecimen of the heart.
The zone of myocardial necrosis (yellow-green), with a gap, the walls of the gap are infiltrated with blood.
Fig. 5. Microspecimen of the heart. Marked infiltration with segmented leukocytes in the area of necrosis. Stained with hematoxylin and eosin (magn. ×100).

Fig. 6. Microspecimen of myocardium. Picture of serous-lymphocytic myocarditis with diffuse infiltration of lymphocytes, muscle fiber necrosis, pronounced interstitial edema. Stained with hematoxylin and eosin (magn. ×100).
Fig. 7. Macrospecimen of the thyroid gland with a picture of the hypertrophic phase of autoimmune thyroiditis.

Fig. 8. Microspecimen of the thyroid gland.
Diffuse-focal lymphocytic infiltration mixed with plasma cells, destruction of thyrocytes, follicular hyperplasia, focal sclerosis of the stroma of the gland. Stained with hematoxylin and eosin (magn. ×100).