Case report
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Toxic Myocardial Injury in a Patient with Coronary Atherosclerosis, Caused by Acute Poisoning with Gaseous Chlorine

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ABSTRACT Acute chlorine gas poisoning leads to activation of the sympathetic nervous system and, as a consequence, dysfunction of the cardiovascular system (CVS). We report a clinical case of toxic myocardial injury with gaseous chlorine. In a man with coronary artery disease and polypathy, toxic myocardial injury mimicked acute coronary syndrome (ACS) and was accompanied by a large area of left ventricular microvascular dysfunction, which did not coincide with the areas of blood supply of altered coronary arteries; the dynamics of electrocardiographic changes resembled myocardial stunning in Takotsubo syndrome (TS). The effect of chlorine on CVS, features of clinical and instrumental diagnostics and differentiation of primary / secondary CT and ACS are discussed.

Keywords: toxic myocardial injury, Takotsubo syndrome, relapse, chlorine gas, instrumental diagnostics, prognosis, coronary artery disease, myocardial infarction

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BP – blood pressure
AH – arterial hypertension
IHD – Ischemic heart disease
MI – myocardial infarction
CA – coronary artery
EDV – end diastolic volume
CAG – coronary angiography
ESV – end systolic volume
CS – cardiogenic shock
LV – left ventricle
VLC – violations of local contractility
EB – enveloping branch
ACS – acute coronary syndrome
RV – right ventricle
AIVB – anterior interventricular branch
DM – diabetes mellitus
SPPA – systolic pressure in the pulmonary artery
HF – heart failure
OFR – oxygen free radicals
CVS – cardiovascular system
TS – Takotsubo syndrome
TR – tricuspid regurgitation
EF – ejection fraction
AF – atrial fibrillation
HR – heart rate
ECG – electrocardiogram
EchoCG - echocardiography
Cl – chlorine
↓ST —depression of segment ST
↑ST — elevation of segment ST

INTRODUCTION

Chlorine-induced dysfunction of the cardiovascular system (CVS) contributes to the development of ischemic syndromes. A number of studies indicate that acute poisoning with gaseous chlorine leads to the activation of the sympathetic nervous system and, as a consequence, dysfunction of the CVS, manifested by arterial hypertension (AH), various electrocardiographic (ECG) signs of cardiac overload, heart rhythm disturbances and changes in the end part of the ventricular complex [1, 2]. A case of the development of MI and ECG changes in the terminal part of the ventricular complex in acute chlorine poisoning is described. [1]. Studies on the effects of chlorine gas on CVS are predominantly based on single case reports, autopsy data, and experimental data on animals.

The given clinical observation demonstrates the development of takotsubo-like changes in the myocardium in a patient with chlorine gas poisoning. Takotsubo syndrome (TS) (takotsubo cardiomyopathy, or apical ballooning syndrome) is characterized by acute and transient (less than 21 days) systolic and diastolic left ventricular (LV) dysfunction of unknown etiology with symptoms mimicking acute coronary syndrome (ACS) [3]; first described in 1990 by a Japanese cardiologist H. Sato et al. [4]. The American Heart Association (2006) officially named this condition "stress cardiomyopathy" [5]. However, in 2015, the European Society of Cardiology proposed to abandon "cardiomyopathy" in favor of the original term - TS, in light of recent basic and clinical research [6].

The pathophysiology of TS has a multifactorial structure, and the exact mechanism of its development is unknown [7, 8]. Presumably, excessive sympathetic activity and abnormal dynamics of catecholamines play a major role here. [9]. I.S. Wittstein et al. [10] consider this syndrome as a neurocardiogenic disorder, which is

manifested by temporary LV dysfunction due to the release of excessive amounts of catecholamines. Moreover, LV dysfunction and ECG abnormalities are usually leveled out a few weeks or months after the onset of the disease. Temporary LV dysfunction in CT may be associated with the absence of a 3-layer structure of the myocardium in the apex of the heart, uneven distribution of adrenergic receptors in the heart, and the specific effect of high plasma concentrations of adrenaline on β2-adrenergic receptors. [11]. Since most β2-adrenergic receptors are located at the apex of the LV, altered intracellular signaling may cause localized LV myocardial dysfunction. Epinephrine in high concentrations causes β2-receptor-mediated inhibition of myocardial contractility in the apex of the LV due to "switching" to G-protein-associated mechanisms of inhibition of cardiomyocyte contraction [12].

According to the diagnostic criteria proposed by the Mayo Clinic (Minnesota, USA), with classical CT, there is no atherosclerotic coronary artery disease (CA) [13, 14]. At the same time, cases of concomitant ischemic heart disease (IHD) have been reported in patients with TS [15, 16]. According to the International TS Registry, 15–61% of patients with apical ballooning syndrome are diagnosed with coronary artery disease [17]. Thus, TS and IHD should not be mutually exclusive.

Although TS is less common in men, their mortality rate is 3 times higher than in women due to cardiovascular and cerebrovascular complications [18].

Recovery of LV contraction occurs rapidly (within 48 hours) or gradually (within 1–2 to 6 weeks). During the period of systolic function recovery, complications may develop: acute heart failure (HF), systemic thromboembolism, LV outflow tract obstruction, arrhythmias, intramyocardial hemorrhage and ventricular wall rupture, among which the highest frequency is systolic heart failure (12–45%), outflow tract obstruction LV (14-25%) and arrhythmias (5–15%) [3, 6, 18]. Cardiogenic shock (CS) develops in 10% of patients and has a poor prognosis [19]. Takotsubo syndrome is considered as a syndrome of acquired long QT interval with a risk of developing malignant arrhythmias. Paroxysmal or persistent atrial fibrillation (AF) was recorded for the first time in 4.7%, sinus node dysfunction - in 1.3%, and AV block - in 2.9% of patients with TS, probably due to neurovegetative imbalance, catecholamine stress and increased vagus tone [20, 21].

TS is a reversible, but also recurrent process. The average relapse rate is 2 to 4% per year. Relapse may occur between 4 days and 10 years. [21]. The reversible nature of apical ballooning syndrome has given rise to the belief that it is a benign disease. Nevertheless, according to the registry data, the incidence of nosocomial complications and mortality is comparable to those in OC [17, 18]. Nosocomial mortality reaches 5%. With long-term follow-up (3-5 years), mortality rates range from 5% to 17% [19]. Predictors of hospital mortality are: age over 70 years, male sex, apical bloating, physical stress, grade III – IV Killip, LV baseline ejection fraction (EF) less than 40%, and diabetes mellitus (DM). Predictors of long-term mortality are male gender, Killip III – IV stage. and DM [22].

Secondary TS has been described in MI [23], recurrent pulmonary embolism [24], COVID-19 [25] and arterial hypertension (AH) [26], chemotherapy in patients with malignant melanoma [27]. Endocrine, neurological, pulmonological, gastroenterological and psychiatric diseases, surgical interventions can serve as triggers for the occurrence of TS [28, 29], as well as acute poisoning with various toxic substances, including carbon monoxide [30], chloroquine [31], when ingested by fungicides, herbicides, etc. [32]. We present a clinical case of the development of toxic myocardial damage, similar to TS, provoked by inhalation of chlorine in a man with concomitant ischemic heart disease and polypathy.

Clinical observation

Patient B., 59 years old, 09/05/2019, was urgently hospitalized in the toxicological intensive care unit of the N.V. Sklifosovsky Research Institute for Emergency Medicine after cleaning work in the pool, carried out with a concentrated solution of chlorine, with loss of consciousness and complaints of lack of air, weakness, cough, dizziness. From the anamnesis: the patient is suffering from hypertension for a long time (on antihypertensive therapy: felodip, irbesartan, bisoprolol, indapamide, moxonidine), about 3 years - type 2 diabetes, on insulin therapy: levemir 10 U 2 times a day and Gluconorm plus 2.5 mg / 500 mg once). Two years ago, after a stressful situation, a similar condition developed, MI was diagnosed. However, ECG and echocardiographic (EchoCG) signs of myocardial infarction disappeared after 2 months, and the diagnosis of myocardial infarction was removed by a cardiologist. Heredity is burdened by the father (4 MI). Bad habits: quit smoking 2 years ago. St. praesens: clear consciousness, serious condition. Hypersthenic constitution. Height: 186 cm, weight: 109 kg, body mass index: 37.5 kg / m2. Hyperemia of the skin of the face and chest. High humidity skin, no cyanosis. Peripheral lymph nodes

are not enlarged, no peripheral edemas. Multiple keratomas over the entire surface of the body. Above the lungs, weakened vesicular breathing, dry wheezing, single moist fine bubbling rales in the lower parts are heard. Respiratory rate - 26/ min. The blood oxygen saturation (SPO2) level is 97%. The area of the heart is not changed. Muffled heart sounds, arrhythmic due to extrasystoles. Blood pressure (BP) 200/100 mm Hg, heart rate (HR) 111 per minute. Peripheral pulsation is preserved. The abdomen is of normal shape, participates in breathing, soft, painless. The liver and spleen are not palpable. The kidney area is not changed. The kidneys are not palpable, the tapping symptom on both sides is negative. Stool and urine output are not disturbed. ECG on admission: sinus tachycardia, heart rate 133 / min, PQ - 0.12 s, QRS - 0.10 s, QTc (according to the Framingham formula) - 0.405 s, LV myocardial hypertrophy, ST segment elevation by 1 mm in the hole III, aVF, V1 – V3, 1 mm ST segment depression in lead I, aVL, V4 – V6, QS in lead V1–V2.

In the clinical analysis of blood upon admission: hemoglobin 170.0 g / l, erythrocytes 5.581012 / l, hematocrit 51.9%, leukocytosis (leukocytes 15.99109 / l), neutrophilia (neutrophils 6.4109 / l), eosinophilia (eosinophils 0.43 109 / l). Total protein 67.13 g / L, cholesterol 4.86 mmol / L, total bilirubin 24.75 μmol / L, direct bilirubin 4.01 μmol / L, indirect bilirubin 20.74 μmol / L, creatinine 110.77 μmol / l, alanine aminotransferase (ALT) 50.51 U / L, aspartate aminotransferase (AST) 35.77 U / L, gamma-glutamyl transferase (GGTP) 80.24 U / L, alkaline phosphatase 90.71 U / L, lactate dehydrogenase (LDH) 323 72 U / l, glucose 6.72 mmol / l, glycated hemoglobin 8.5%, urea 11.25 mmol / l, uric acid 522 mmol / l, potassium 3.63 mmol / l, sodium 140.50 mmol / l. Troponin I (2nd day of poisoning) - 1,400 mcg / l, after 6 hours - 1,000 mcg / l. General analysis of urine without significant changes.

Chest X-ray: pulmonary fields without fresh focal and infiltrative shadows. The pulmonary pattern is enhanced by a pronounced vascular component against the background of pneumosclerosis. Severe hypoventilation of the inferior medial on both sides. The roots of the lungs are weakly structured, compacted, expanded. The diaphragm is clear, usually located on the right, slightly raised on the left. The shadow of the mediastinum is displaced to the right due to atypical styling. The shadow of the heart is expanded in diameter due to the left sections. The aorta is calcified. Hydropneumothorax not identified.

On the next day, an intense pain syndrome developed behind the sternum, in connection with which the patient was transferred to cardiac intensive care with a diagnosis of ACS.

On the ECG (Fig. 1) in cardiac intensive care (2nd day of poisoning): deep negative T waves appeared in leads V1 – V6, PQ - 0.12 s, QRS - 0.10 s, QTc (according to Bazett's formula) - 0.493 c, ST segment elevation is preserved by 1 mm in lead III, aVF, by 0.5 mm in lead V1 – V2 and its depression by 0.5 mm in holes. I, aVL, QS in the V1 – V2 lead. Troponin I - 1,700 mcg / l, after 6 hours - 1,400 mcg / l.

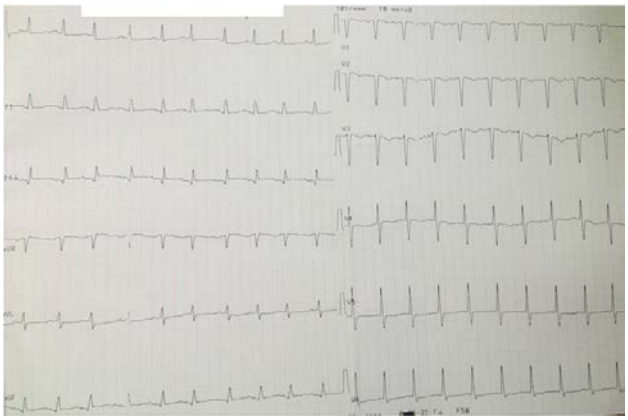

Fig. 1. Electrocardiogram on the 2nd day of poisoning

EchoCG: moderate expansion of the ascending aorta (42 mm), LV myocardial hypertrophy (interventricular septum - 12 mm, at the basal level - 14 mm, posterior wall - 11 mm), LV myocardium mass - 242 g, end-diastolic volume (EDV) - 185 ml, end systolic volume (ESV) - 124 ml, LVEF - 33–34%, the right atrium is enlarged (EDV 52 ml), the right ventricle (RV) is enlarged (size - 30 mm, free wall thickness - 5 mm); local contractility disorders (LLS) along the inferior, posterior, anterior, anterior septal walls, LV apex (9-10 segments), LV type I diastolic dysfunction, systolic pressure over the pulmonary artery (PAP) - 47 mm Hg. Tricuspid regurgitation (TR) 1st stage.

Coronary angiography (CAG): type of blood supply - left, pronounced calcification of the coronary artery, the circumflex branch (CB) - is occluded in the distal third with the formation of "bridge" collaterals. The distal channel is filled along intra- and intersystem collaterals. The right coronary artery is 2 mm in diameter, 70% stenotic in the middle third. No percutaneous coronary intervention performed.

A day later, the condition improved: no pain, shortness of breath and tachycardia; tolerated physical activity within the department satisfactorily; ECG (3rd day of poisoning): sinus rhythm, heart rate 76 per minute, ST segment in lead V1 – V3 on the isoline, ↑ST remains at 1 mm in holes III, aVF, ST segment depression by 0.5 mm in lead I, aVL, otherwise without negative dynamics. For 5 days, the instability of blood pressure remained (fluctuations 120/80 - 180/100 mm Hg).

Myocardial scintigraphy with 99mTc-technetril, 400 MBq/v (6th day of poisoning): the myocardium of a slightly increased LV (EDV - 167 ml) is visualized with a significant focal decrease in perfusion of the basal half of the LV diaphragmatic wall, hypoakinesis of the apex with a transition to the antero-septal wall and posterior. Signs of minor subendocardial focal changes. Signs of ischemia of the diaphragmatic wall of the LV and the lateral wall of the RV. RV is enlarged, EDV - 196 ml.

ECG on the 6th day of poisoning (Fig. 2): deep negative T waves persist in leads I, II, aVL, V1 – V6, ST segment elevation by 1 mm in lead III, aVF, its depression by 1 mm in holes. I, aVL, V5-V6, PQ - 0.16 s, QRS - 0.10 s, QTc (according to Bazett's formula) - 0.524 s.

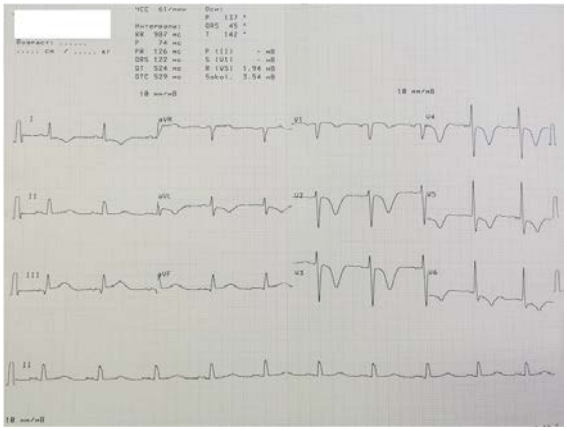

Fig. 2. Electrocardiogram on the 6th day of poisoning

With control echocardiography (8th day of poisoning): hypoakinesis persists along the lower wall of the LV at the basal and middle levels with the transition to the posterior wall of the LV, mainly at the middle level, improved kinetics at the apex, anterior septal region of the LV - moderate hypokinesis (compared with hypoakinesis) 4 apical segments, hypokinesis of the anterior segment at the middle level, restoration of the kinetics of the anterior septal and septal segments at the middle level. LVEF - 39%, EDV - 183 ml, CSR - 113 ml, SDA - 28 mm Hg. TR 1st Art.

Therapy was carried out with beta-blockers (bisoprolol 5 mg / day), antiplatelet agents (acetylsalicylic acid 100 mg / day and ticagrelor 180 mg / day), statins (rosuvastatin 20 mg / day), angiotensin II receptor antagonists (losartan 100 mg / day), calcium channel blockers (amlodipine 5 mg / day), diuretics (spironolactone 50 mg / day, torasemide 10 mg / day) and hypoglycemic drugs.

Against the background of the treatment, anginal pain did not recur, the blood pressure stabilized at the level of 120–130 / 70–80 mm Hg, the symptoms of heart failure were not pronounced, and therefore the motor regimen was expanded. On the ECG (9th day of poisoning), negative T waves in the hole are preserved. I, II, aVL, V1 – V6, ST segment elevation by 1 mm in lead III, aVF, its depression by 1 mm in lead I, aVL, V5 – V6. The patient was discharged on the 9th day at an urgent request in a satisfactory condition without pain and shortness of breath.

The results of the obtained clinical, instrumental and laboratory data indicate a transient myocardial dysfunction, identical to the TS clinic, the trigger of which was the toxic effect of chlorine gas.

DISCUSSION

TS is rarely diagnosed, its pathogenesis is not clear, and the risk of death during its development is not fully assessed. The reversibility of cardiac dysfunction made it possible to consider classic TS as a benign, transient, "self-healing" state with an emotional / physical trigger, intact CAs and without corresponding complications. [33]. However, in some patients after 6–12 months, the clinical and echocardiographic consequences of this syndrome persist [22], and the rates of hospital and long-term mortality exceed the mortality of patients with STEMI [21]. According to T. Stiermaier et al. [20], predictive factors for the risk of death are: male gender, diabetes mellitus and Killip III – IV stage. Elevated levels of natriuretic peptide and leukocyte counts have also been associated with a high rate of nosocomial complications (cardiac death, grade III – IV Killip, persistent ventricular tachycardia / ventricular fibrillation, and atrioventricular block) [22].

The probable cause of TS is the sudden release of stress hormones and endothelin-1, which leads to catecholamine-induced generalized spasm of small coronary arteries, microcirculatory disturbances, and catecholamine-induced myocardial damage [33, 34]. Plasma catecholamine concentrations remain elevated for several days after symptom onset [10]. Microvascular function is gradually improving, this correlates with the restoration of LV function; both indicators return to normal after 1 month [35].

The high level of catecholamines, apparently, is due to hyperactivation of the hypothalamic-pituitary-adrenal system in response to an exogenous trigger [28], indicating a potential interaction of the heart and brain in the pathophysiology of TS [36]. An excess of catecholamines leads to a cardiotoxic effect: stunning, myocardial necrosis [8], changes in cardiomyocytes and coronary perfusion [37], and rapid stimulation of adrenergic receptors enhances cardiac inotropy and chronotropy with resultant ischemia. Histological examination of the myocardium reveals areas of necrosis, focal fibrosis, macrophage-mediated cellular inflammatory response in the myocardium and its edema [38].

When compared with primary TS, the secondary is characterized by frequent relapses, a high incidence of cardiogenic shock (CS), AF, hospital and long-term mortality [39]. In individuals with ST, male sex is an independent predictor of CS and mortality. CS, being a marker of TS severity, can identify the latent HF phenotype with increased vulnerability to catecholamine-mediated myocardial stunning [19]. AF in patients with TS, compared with those without arrhythmia, doubles all-cause mortality [40]. After normalization of LVEF, the risk of long-term mortality from cardiovascular diseases increases by 5 times [20]. The inflammatory theory of TS occurrence demonstrates the formation of both localized and systemic inflammatory reactions (persisting for 5 months), which may explain the development of long-term HF and a more unfavorable long-term prognosis. [41]. Thus, TS, as an acute "benign" condition, requires revision.

In the acute phase, TS is clinically indistinguishable from acute MI and may present with acute chest pain, shortness of breath, and fainting [17]; 50% patients have ST segment elevation [42], serum troponin is usually elevated, but its values are usually low compared to the extensive zone of myocardial dysfunction detected by instrumental diagnostic methods, which took place in our patient. 1–2% of patients with suspected ACS are eventually diagnosed with TS [37].

Since in the early hours of TS disease it is difficult to distinguish from myocardial infarction, a thorough diagnosis is required, aimed at differentiating these conditions. M. Inoue et al. [43] believe that ECG is informative only in differentiating TS and MI in patients with proximal lesions of the left anterior interventricular branch (AIB), and ST-T changes that persist for several weeks do not increase the risk of developing malignant ventricular arrhythmias.

TS is characterized by ST segment elevation, T wave inversion, lengthening of the QT interval, and transient Q wave [42]. According to R. Ogura et al. [44], ST segment elevation in leads V4 – V6 is specific for ST, in comparison with leads V1 – V3 in MI. The duration of ST-segment elevation is short, while T-wave inversion is long. T wave inversion persists from several days to several weeks and can be recorded in the absence of ST segment elevation. In some cases, with ST-segment elevation, deep and negative T waves may disappear and then re-register. With T wave inversion, the QT interval is extended. Q-waves are reversible and disappear over time. The mechanism of ECG changes in CT is not clear, it is assumed that repolarization disorders develop due to the effects of catecholamines. Similar ECG changes were observed during stressful events. ECG criteria for distinguishing MI without ST segment elevation from ST segment with ST segment decrease is T wave inversion in at least 6 leads (sensitivity 74%, specificity 92%) [45]. The most obvious changes are found in leads V3-6. In more than 50% of cases, non-specific ECG changes are determined,

including depression of the ST segment and sinus tachycardia. ↓ST occurs in less than 10% of patients and more than 30% with ACS, so the presence of ST segment depression may indicate ACS. Thus, the evolution of ECG abnormalities in patients with CT resembles acute myocardial stunning caused by ischemia [18].

ECG with CT can record various forms of arrhythmias [46], including sinus tachycardia, ventricular extrasystoles of the quadrigeminic type, and prolongation of the QT interval, as in our patient. However, these changes may be associated with the toxic effects of chlorine gas. Our patient's ECG had all of the above changes: T wave inversion, ST segment elevation and depression, lengthening of the QT interval, and a transient wave Q.

In a provocative test, 43% of patients with TS develop multivessel spasm of the CA and segment elevation ST. It is suggested that catecholamine-mediated endothelial stunning may be the cause of microvascular dysfunction, and the severity of the perfusion defect in TS correlates with the degree of myocardial injury. Therefore, TS is considered as a disorder at the cellular level, and not as a structural contractile disease of the myocardium, since it may be associated with impaired coronary microcirculation, accompanied by prolonged stunning of the myocardium [47].

Transthoracic echocardiography is a mandatory method for TS diagnosis [24]. TS has various morphological variants of NLS. The most typical and common variant is the defeat of the apical and middle segments with their hypo-, akinesia, up to dyskinesia, and normal, and even hyperkinetic contractility of the basal LV [48]. Anomalies of contraction of the anterior, inferior, and lateral walls of the ventricles that extend beyond the territory of the blood supply of one CA can be considered a hallmark of TS [49]. In addition, an inverted variant of PT with hypokinesia of the basal LV regions, a variant with hypokinesia predominantly of the middle regions instead of hypo-, akinesia of the apex, and a variant with lesions of both LV and RV are described. Hypokinesia, dyskinesia, wall akinesia on echocardiography, as a rule, recover after 4-8 weeks.

Rapid recovery of systolic function occurs within 2 weeks and continues for the next 3 months. LVEF improves after an average of 6.5 days and reaches normal values within 6 weeks [18]. In the given clinical case, there was a positive dynamics of control echocardiography and myocardial scintigraphy after 7-8 days. In a two-week period, the T wave gradually deepens, and the LVEF is restored [18, 50]. This is due to myocardial edema found on cardiac MRI [51]. Evaluating the results of the CAG of our patient, we can assume the presence of VLC mainly in the inferior septal and inferolateral parts of the LV. However, the changes found on echocardiography and myocardial scintigraphy cover a wider area of the myocardium. The discrepancy between the VLC areas revealed by echocardiography and myocardial scintigraphy, the areas of blood supply of atherosclerotic coronary arteries, as well as the ECG picture, give grounds for diagnosing TS. Positive dynamics of control echocardiography and scintigraphy confirmed this diagnosis. Therefore, the presence of angiographically significant coronary artery disease should not be considered as a criterion for excluding TS [15, 16]. The absence of significant coronary artery stenosis does not exclude the presence of coronary artery disease due to the limitations of the CAG. According to the International Expert Consensus Document on TS [18], patients with TS with ST segment elevation are recommended to perform ventriculography, with the help of which it is possible to observe the movement of the LV wall and its relationship with coronary anatomy and pathology. However, this study is not performed in all patients, even with ACS. In this clinical case, the diagnosis of TS was delayed after the analysis of all clinical and instrumental studies, therefore, ventriculography was not performed. Intravascular CA imaging shows eccentric atherosclerotic plaques in the middle third of LAD in individuals with TS, which are not detected in CAG [52]. Several typical cases of apical ballooning syndrome with concomitant coronary artery stenosis have been described, and the area of myocardial dysfunction was wider or did not correspond to the areas of blood supply of the stenotic coronary artery [15, 18]. Our patient was diagnosed with concomitant coronary artery disease with OS occlusion in the distal third and stenosis of the right coronary artery up to 70% in the middle third, however, the area of myocardial dysfunction was much wider and did not coincide with the areas of blood supply of atherosclerotic coronary arteries, which is confirmed by CT. Было выдвинуто предположение, что анатомия коронарного русла имеет значение у пациентов с TS. When the sympathetic nervous system is activated and tachycardia develops with a decrease in diastole and an increase in myocardial contractility, hemodynamics deteriorates in patients with CA tortuosity (including myocardial bridges), which can serve as a potential pathogenic substrate in TS [53].

In many patients with suspected TS, differentiation from ACS or myocarditis cannot definitively rule out these diagnoses using EchoCG and CAG. Especially in patients with LV wall motion abnormalities that coincide with the perfusion area of the affected coronary artery, or in patients in whom wall motion abnormalities are impaired in the posterolateral segments, where myocarditis is often manifested. In these cases, an MRI of the heart provides important information for making a correct diagnosis [51].

Despite the tendency towards restoration of LV function, recurrence of TS is possible. According to the literature, the 5-year recurrence rate is 5–22%, with recurrence usually occurring between 3 weeks and 10 years [54, 55]. A significant number of relapses occur several years after the index event, regardless of age and gender [56]. At the same time, the frequency of relapses can be different, a case of the development of 6 episodes of TS in one patient has been described [57]. Localization of NLS in repeated episodes of TS may not correspond to that in the first episode [6]. Even after restoration of LVEF, structural abnormalities of the heart (e.g., abnormal patterns of LV deformity) and metabolic changes have been described [22]. Patients who have undergone TS may experience symptoms such as fatigue, shortness of breath, chest pain, palpitations, and exercise intolerance. Thus, many researchers emphasize the importance of long-term monitoring of patients with TS and the identification of effective preventive strategies. We assume that our patient 2 years ago after a stressful situation developed TS, which was safely resolved after 2 months.

Diabetes mellitus (DM) as a risk factor for stress cardiomyopathy is present in 10–25% of patients and is associated with increased mortality [58], leads to neuroautonomous nerve remodeling and activation of vasoactive neuropeptides such as neuropeptide Y, which can lead to increased susceptibility to stress cardiomyopathy and arrhythmias [58]. Описываемый пациент страдал СД 2-го типа, прогностическая роль которого противоречива. At the same time, data are given that patients with DM and TS have a more favorable hospital and annual outcome [55], and it is assumed that autonomic dysfunction in DM may blunt the secretion of catecholamines in patients with TS. This can play a protective role in relation to the development of TS and its prognosis. [59].

There are conflicting data on the presence of a genetic predisposition to TS [60–62]. We assume that our patient has a burdened heredity, the father suffered several MIs and, possibly, one of the episodes was TS.

According to data obtained by H.M. Himmel [63], halogenated hydrocarbons and volatile anesthetics, including those containing chlorine, are capable of sensitizing the heart to catecholamines. In addition, the role of chlorine-induced CVS dysfunction is to activate sympathetic activity, oxidative stress, the development of hypoxia [1], edema and apoptotic death of cardiomyocytes, which leads to endothelial dysfunction in the systemic vasculature [56], contributing to the development of ischemic syndromes. [1, 64]. Several studies have reported that chlorine inhalation can cause sinus tachycardia, ST segment depression [14], sinus bradycardia [65], AF [66], MI [1], AG [54], cardiac arrest [67], AH [68], heart hypertrophy and heart failure [65]; autopsy revealed cardiomegaly [68].

In the presented clinical case, ST developed as a result of the toxic inhalation effect of chlorine, the mechanism of which is not fully understood. Inhalation of chlorine gas itself is a stressor. As a result of chlorine poisoning, a massive release of catecholamines into the circulatory system occurred, in addition, inhalation of chlorine gas causes hypoxia, the formation of free oxygen radicals (FOR) and an increase in sympathetic activity. FOR, formed upon contact of chlorine gas with water, damage cellular proteins, which, in turn, leads to tissue damage, and, as a consequence, to a decrease in myocardial contractility and deterioration of myocardial function. In addition, bronchospasm, which develops after irritation of the respiratory tract, causes hypoxemia, triggering myocardial ischemia. Exposure to chlorine gas increases sympathetic stimulation and myocardial oxygen demand and prevents myocardial contraction, disrupts cardiac conduction [1]. In this clinical case, we assume that the cardiotoxic effect of chlorine gas slowed down the dynamics of restoration of LV myocardial function, which is somewhat different from the typical rapidly recovering dysfunction in TS, since the cardiovascular toxic effects of chlorine can be prolonged (even for several years) [68, 69]. The clinical picture was due to the activation of the sympathetic nervous system (tendency to tachycardia and hypertension), which persisted for several days. Recovery of myocardial contractility was delayed as a result of prolonged hypercatecholaminemia. However, the pathogenesis of this condition is not completely clear; it is probably explained by the presence of prolonged circulation of toxic reagents [70].

CONCLUSION

Thus, a rare clinical case of recurrence of secondary ST, provoked by an atypical trigger, chlorine gas, is presented. The features of the clinical case are: male sex, coexistence of TS with ischemic heart disease; probable genetic predisposition to ischemic heart disease and TS; relapse mimicked ACS and was accompanied by a large area of LV microvascular dysfunction, which did not coincide with the areas of blood supply of altered coronary arteries and the dynamics of ECG signs of myocardial stunning. Hypercatecholaminemia, which developed in response to chlorine, contributed to vasoconstriction, hypertension, vulnerability of atherosclerotic plaque to rupture with moderate release of troponin I into the blood and a large area of LV microvascular dysfunction, myocardial stunning. Chlorine cardiotoxicity slowed down the recovery period of myocardial dysfunction, which differs from classical TS. Analysis of scientific literature and the given clinical case emphasize the importance of timely diagnosis of TS and its coexistence with IHD, the need for long-term outpatient follow-up and the development of preventive measures.

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