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# Primary Takotsubo Syndrome as a Complication of Bladder Cancer Treatment in a 62-Year-Old Woman

## Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

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**Conflict of interest:** None declared

**Patient:** Female, 62-year-old  
**Final Diagnosis:** Takotsubo syndrome  
**Symptoms:** Chest pain  
**Medication:** —  
**Clinical Procedure:** Coronarography  
**Specialty:** Cardiology • Oncology

**Objective:** Unknown etiology

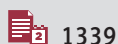
**Background:** The main causes for takotsubo syndrome (TS) in oncological patients are stress related to cancer diagnosis and treatment, pain in the course of the disease, treatment complications, and paraneoplastic syndromes.

**Case Report:** An obese 62-year-old female patient, with a 3-day history of chest pain, was admitted to the hospital with a suspected acute coronary event. She had been diagnosed with high-grade bladder cancer 6 months before. After the transurethral electroresection of the tumor 5 months before and subsequent chemotherapy (gemcitabine and cisplatin), the patient was qualified for the next cancer surgery. On admission, the patient remained without chest pain. The ECG record demonstrated inverted T waves in the leads from above the anterior and lateral wall. The coronarography demonstrated minor atherosclerotic changes in the coronary arteries. The left ventriculography presented akinesis of the apex and the apical and mid-segment of the anterior wall, and the ejection fraction (EF) was 38%. Takotsubo syndrome was diagnosed. Laboratory testing revealed elevated concentration of troponin and N-terminal pro-B-type natriuretic peptide. The subsequent ECG records demonstrated deeply inverted T waves and numerous ventricular premature beats and increased QTc (528 ms). A control echocardiography showed improved left ventricular contractive function (EF – 47%). On the 4<sup>th</sup> day of hospitalization, the patient was discharged and referred for further oncological treatment.

**Conclusions:** The diagnosis of TS in oncology patients is difficult, especially in the presence of atherosclerotic lesions in coronary arteries. Takotsubo syndrome in cancer patients delays the next stages of oncological treatment, which worsens the prognosis of these patients.

**Keywords:** Medical Oncology • Neoplasms, Second Primary • Takotsubo Cardiomyopathy • Urinary Bladder Neoplasms

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## Background

Takotsubo syndrome (TS) is a transient, stress-induced functional impairment of the left ventricle. The clinical symptoms, ischemic changes on the electrocardiogram, and increased concentration of cardiac enzymes are similar to those of myocardial infarction; however, cardiac catheterization does not demonstrate a significant coronary stenosis. A long-term prognosis is relatively good for TS, but in the acute phase of the disease, severe complications, such as cardiogenic shock, sudden cardiac arrest, or cardiac rupture, may occur [1-3].

The sole fact of diagnosis and further treatment are highly stressful for patients with cancer, which particularly expose them to TS. Due to various possible causes of myocardial damage in cancer patients, the differential diagnosis is very difficult, especially in the presence of atherosclerotic lesions in the coronary arteries. Moreover, the occurrence of Takotsubo causes a temporary delay in subsequent stages of oncological treatment, which further worsens the prognosis of patients. Here, we present the case of a female patient aged 62, in whom TS was diagnosed during the oncological treatment of bladder cancer.

## Case Report

An obese female patient, aged 62, with a 3-day medical history of chest pain, was transferred to the Department of Invasive Cardiology by a district hospital as she was suspected to have had an acute coronary event. On the day of admission, the patient experienced retrosternal chest pain at rest for around 1 hour. She had the habit of smoking tobacco and had chronic arterial hypertension, hypothyroidism, and inflammatory arthritis. Six months before admission, the patient had been diagnosed with a high-grade urothelial bladder cancer. After the transurethral electroresection of the tumor 5 months before admission and the following chemotherapy (gemcitabine and cisplatin), the patient had been qualified for a further cancer surgery.

On admission to the clinic, she remained hemodynamically stable, with no chest pain, and had a systemic arterial pressure of 110/80 mmHg. The ECG record demonstrated a normal sinus rhythm of 96/min with singular ventricular and supraventricular beats, as well as inverted T waves in the leads from above the anterior and lateral wall.

The patient was subject to cardiac catheterization, which demonstrated minor atherosclerotic changes in the coronary arteries (Figures 1, 2). The left ventriculography conducted at the same time presented akinesis of the apex and the apical and mid-segment of the anterior wall, and the ejection fraction

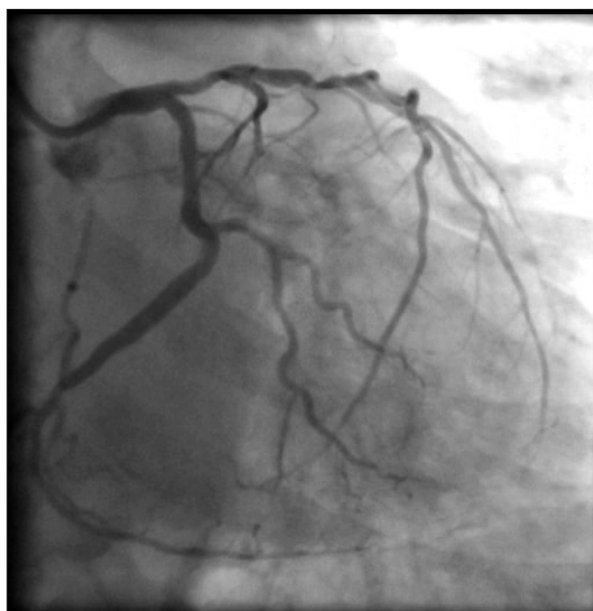


Figure 1. Coronarography of the left coronary artery.

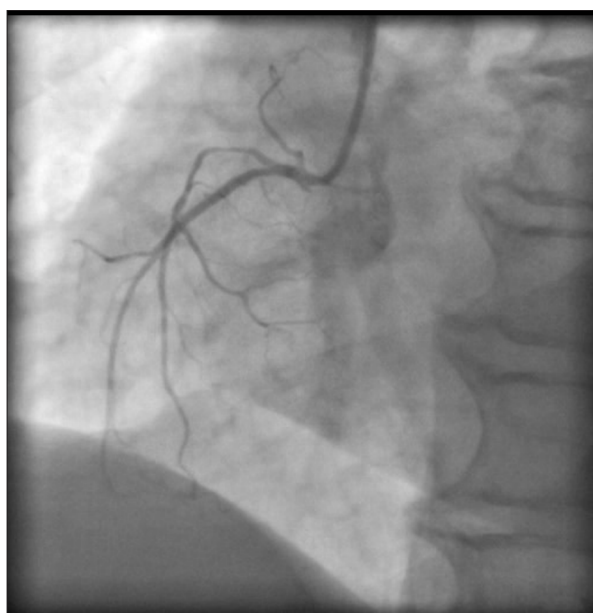
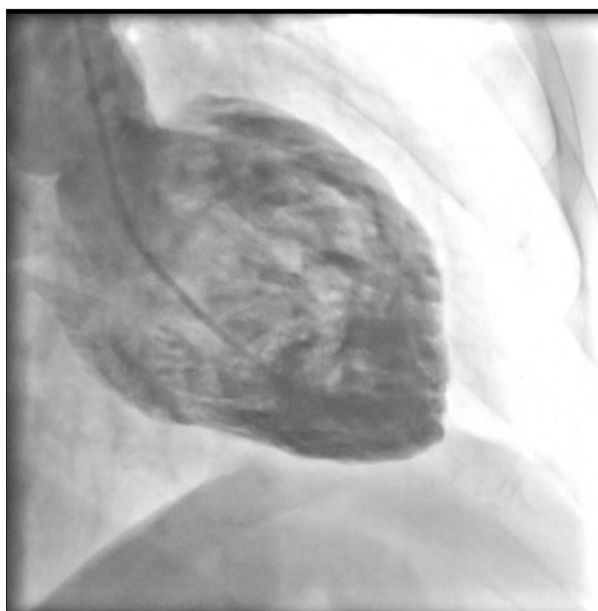


Figure 2. Coronarography of the right coronary artery.

was 38% (Figures 3, 4). The patient was initially diagnosed with TTS and was qualified for the conservative treatment of the coronary disease.

Laboratory testing revealed decreased red blood cells with a hemoglobin level of 9.3 g/dl and a markedly elevated concentration of cardiac markers such as troponin I hs – 9552 ng/l (lab standard: 0.00-15.60 ng/l), B-type natriuretic peptide (BNP – 175 pg/ml; lab standard: 0.00-100.00 pg/ml), and N-terminal pro-B-type natriuretic peptide (NT-proBNP – 2691 pg/ml; lab standard: 0.00-125.00 pg/ml).



**Figure 3.** Ventriculography – left ventricular diastole.



**Figure 4.** Ventriculography – left ventricular contraction (akinesia of the apex, apical, and mid-segments of the left ventricle wall).

The hospitalization period was devoid of complications. The retrosternal pain did not reoccur. The subsequent ECG records demonstrated deeply inverted T waves and numerous ventricular premature beats, with the QTc interval increased to 528 ms. In the echocardiographic examination, apart from the normal function of all valves, an improved left ventricular contractive function with 47% ejection fraction was observed, which confirmed the diagnosis of TTS.

On the 4<sup>th</sup> day of hospitalization, the patient was discharged and referred for further surgical and oncological treatment. On discharge, the following were recommended: acetylsalicylic acid 75 mg/day, bisoprolol 2.5 mg/day, ramipril 1.25 mg/day, atorvastatin 20 mg/day, pantoprazole 20 mg/day, supplementation with iron and thyroid hormones, and continuation of the ongoing analgesic chronic therapy. After 4 months, the patient died from cancer.

## Discussion

TS is extremely rare in the general population, accounting for only 0.02% of hospitalization and approximately 1-2% of acute coronary events, while the incidence of TS in oncological patients is approximately 10%. Taking into account the negligible number of cancer patients who come to our clinic with TS, it seems that many cases of takotsubo syndrome in these patients are not diagnosed. Cardiac problems in cancer patients, complaints and complications resulting from the underlying disease and cardiotoxic effects of therapy may be similar to the symptoms of takotsubo syndrome. However, in view of the various possible causes of myocardial damage in cancer patients, as in the case presented here, the differential diagnosis is very difficult, especially in the presence of atherosclerotic lesions in the coronary arteries.

In oncological patients, TS may be induced by a stress factor and a physical factor associated with the neoplastic disease and its treatment. The main causes for TS in this group of patients include the stress associated with the diagnosis of the neoplastic disease, as well as the stress associated with its treatment, pain in the course of the disease, and complications of operative therapy or chemotherapy, as well as paraneoplastic syndromes [4,5]. In the discussed patient, TS was most likely caused by the stress associated with the subsequent stages of oncological therapy, previous chemotherapy, and another scheduled surgical intervention.

Diagnostics such as ECG, troponin and BNP concentrations, echocardiography, and cardiac catheterization with ventriculography are highly important for the diagnosis of TS in oncological patients. The ECG recordings are typical for TS ischemic changes such as ST elevation, negative T, or QT prolongation. The pathomechanism of these changes in TS is not fully understood. The ST-segment elevations and negative T waves observed in the early stages of the disease are presumed to be due to abnormal repolarization resulting from high catecholamine levels. Later changes, such as negative T, QT prolongation, or ventricular arrhythmias are probably the result of cardiomyocyte ischemia [6].

The greatest importance in the differential diagnosis is borne by the examinations demonstrating contractility disorders (echocardiography, ventriculography, computed tomography, and magnetic resonance). The cardiotoxic effect of chemotherapy drugs results in the global defect of left ventricular contractility, whereas segmental disorders of the systolic function, primarily in the apex area and apical segments of the left ventricle, occur in TS.

TS related to neoplastic disorders is primarily a secondary form of TS, characterized by a more severe clinical course and a more frequent occurrence of severe complications [7]. In the cases of TS in oncological patients described thus far, severe heart failure with very low left ventricular ejection fraction (10-20%), cardiogenic shock, sudden cardiac arrest secondary to ventricular tachycardia or asystole, or rupture of the left ventricular wall was commonly observed [8]. Severe complications of TS were most frequently observed during chemotherapy on infusion of the drug or shortly after the procedure [7-11].

The diagnosis of TS in our patient was somewhat difficult by the result of the coronary angiography. The patient had a borderline stenosis in the middle segment of the LAD. The change was estimated at 60% and was ultimately considered insignificant and not responsible for her left ventricular contractility disorders. In addition, the image of the left ventricle in ventriculography is characteristic of TS. In the presented patient, TS was most likely a primary, stress-induced form. It showed a benign course, and apart from the minor rhythm abnormalities, no severe complications were observed.

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Our patient's prognosis was unfavorable due to the nature and advancement of the cancer, and she died after 4 months. However, the occurrence of TS in oncological patients, particularly during chemotherapy, complicates further cancer therapy. It causes a temporary delay in subsequent stages of oncological treatment, which further worsens the prognosis of patients. If TS occurs during the administration of the chemotherapy drug, its change should be taken into account due to the risk of TS recrudescence. To reduce the risk of TS relapse, it is also recommended to use angiotensin-converting enzyme inhibitors [12]. The cancer therapy can be continued after left ventricular contractility function is restored (typically after 2-3 weeks).

## Conclusions

Because of the many possible causes of chest pain in patients with cancer, TS diagnosis is difficult, especially in the presence of atherosclerotic lesions in the coronary arteries. Takotsubo syndrome in cancer patients delays the next stages of oncological treatment, which worsens the prognosis of these patients.

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## Conflict of Interests

None.