Psychiatria Danubina, 2025 Vol. 37, No. 2, pp 249-253 https://doi.org/10.24869/psyd.2025.249 *Case Report*

A case of takotsubo cardiomyopathy diagnosed during first episode psychosis

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INTRODUCTION

Takotsubo cardiomyopathy (TC) is an emerging cardiovascular disease that causes acute heart failure and transient ventricular contractile dysfunction. It was first described in the literature in 1990 by Sato et al. from Japan (Watanabe et al., 2018). TC generally manifests itself with clinical symptoms similar to acute coronary syndrome (ACS). Although the incidence of TC is not clearly known, approximately 1-2% of patients presenting with ACS symptoms are diagnosed with TC (Carroll et al., 2020). Female patients constitute approximately 90% of all the cases with mean age of 65-75 and the risk of developing TC increases 5 fold in women after the age of 55 (Wittstein, 2020, 2022).

Patients present with symptoms such as chest pain, dyspnea, myocardial enzyme elevation, electrocardiographic abnormalities, etc., which generally occur following emotional or physical stress. Therefore, the disease is also known as stress-induced cardiomyopathy or broken heart syndrome (Carroll et al., 2020). Although common clinical symptoms are observed with ACS, TC has a distinct pathophysiology that does not involve acute plaque rupture or coronary obstruction. There is no precise mechanism regarding its pathophysiology, it is suggested that the main condition causing acute myocardial stunning could be sympathetic system-mediated microvascular dysfunction (Watanabe et al., 2018).

According to the International Takotsubo Registry, approximately 1/3 of patients with TC have a pre-existing psychiatric disease, also approximately 10% of the patients are diagnosed with an acute psychiatric disorder (Templin et al., 2015). Depression and anxiety disorders have the highest rates among the psychiatric disorders reported in TC to date. Apart from the presence or exacerbation of psychiatric disease, overtitration or sudden termination of psychiatric treatments can also trigger TC (Nayeri et al., 2018).

In this case report, the process of diagnosing TC in a patient with first psychotic episode is discussed. In this context, the relationship between psychiatric diseases and TC has been reviewed.

CASE REPORT

A 60-year-old female patient presented to the emergency department due to persecution, reference and somatic delusions, visual hallucinations, oral intake restriction and agitation. Psychotic symptoms had started rapidly 15 days ago and had become increasingly severe.

The patient's initial psychiatric symptoms began one year ago following the death of her husband, manifesting as sadness, apathy, anhedonia, insomnia, loss of appetite, reduced energy, anxiety and agitation. At that time, she applied to psychiatry for the first time and was diagnosed with major depressive disorder. She was prescribed escitalopram 10 mg/day and lorazepam 1 mg/day. However, she used this treatment for a short time and did not continue the medication. Her depressive symptoms intensified after she started living alone approximately 5 months later. She started taking sertraline 50 mg/day irregularly without consulting a doctor. Her psychotic symptoms, such as persecution, reference and somatic delusions and visual hallucinations occurred for the first time 15 days ago. After her psychotic symptoms were noticed by her relatives, she was quickly taken to the emergency service of a state hospital. During this hospital admission, new symptoms such as eating refusal, negativism, immobility and disorientation were also observed. Due to detection of hyponatremia (Na: 129 mmol/L (135-145 mmol/L)) in the examinations, sodium replacement was administered. After a 1-day emergency service stay, she was metabolically stable and discharged. She was admitted to our emergency department 2 days later because of ongoing psychiatric symptoms except disorientation. She was evaluated by the psychiatry consultant and diagnosed with major depressive disorder with psychotic symptoms. Sertraline 50 mg/day, aripiprazole 5 mg/day and clonazepam 1 mg/day were prescribed to her. Although her appointment in our psychiatry outpatient clinic was arranged, she vizitted diffent physicians but did not use any of the recommended treatments regularly. When she was applied to the emergency service again in a few days, zuclopenthixol acetate 50 mg/ml intramuscular (IM) and

haloperidol 5 mg/ml IM were administered to her because of treatment non-compliance and exacerbation of psychotic symptoms such as persecution, reference and somatic delusions and visual hallucinations. She was admitted to the psychiatric inpatient unit to clarify her diagnosis and reorganize her treatment. The Positive and Negative Syndrome Scale (PANSS) score during admission to the psychiatric inpatient unit was determined as 112. Late-onset first-episode psychosis was considered in the patient who had no depressive symptoms and was fully oriented. It was thought that the temporary disorientation in the past period occurred as a result of hyponatremia. She was recommended treatment with olanzapine 10 mg/day, but she refused to use the medication due to persecution delusions. Therefore, daily haloperidol 5 mg/ml IM injections were applied.

She has been diagnosed with rheumatoid arthritis and has been stable for a long time without any treatment. She is an active smoker of 40 cigarettes/day and has a habit of consuming alcohol at the social drinking level. She does not use any addictive substances.

Laboratory examinations revealed hypokalemia (K: 2.92 mmol/L (3.5-5.1 mmol/L)). The patient was consulted to nephrology and intravenous potassium replacement was administered. Leukocytes and bacteria were detected in the complete urine analysis. A single dose of fosfomycin sachet was administered for urinary tract infection. Electrocardiography (ECG) was performed because of chest pain and dyspnea. In the ECG, significant T wave negativity was detected between leads V3-V5 (Figure 1). High-sensitive cardiac troponin I (hs-cTnI): 604.5 ng/L (14-42.9 ng/L), creatine kinase-MB (CK-MB): 15.7 ng/mL (0.6-6.3 ng/mL), myoglobin: 222.3 ng/mL (17.4-105.7 ng/mL), total cholesterol: 203 mg/dL (125-200 mg/dL), HDL: 57 mg/dL (30-63mg/dL), LDL: 126.2 mg/dL (66-129mg/dL) and triglyceride: 99 mg/dL (44-150 mg/dL) were detected. She was consulted to cardiology with a preliminary diagnosis of ACS. In transthoracic echocardiography (TTE), left ventricular ejection fraction (LEVF) was determined as 45% and apical hypokinesis was observed. With the recommendation of cardiology, she was administered acetylsalicylic acid 300 mg 1*1 and enoxaparin 0.6 ml 2*1 subcutaneously. In the coronary angiography of the patient, whose control cardiac enzymes tended to decrease but were still above the reference range limit, the left anterior descending artery (LAD) with mid-plaque, the circumflex artery (Cx) with plaque and tortuous distal part, and the right coronary artery (RCA) with a widespread plaque formation were found. The apex was hypokinetic and had the apperance of balooning on ventriculography (Figure 2a and 2b). She was diagnosed with non-obstructive coronary artery disease and TC. She underwent acetylsalicylic acid 100 mg/day, atorvastatin 20 mg/day, metoprolol 50 mg/day and ramipril 5 mg/day treatment. Her cardiac enzymes decreased to the reference range within one week.

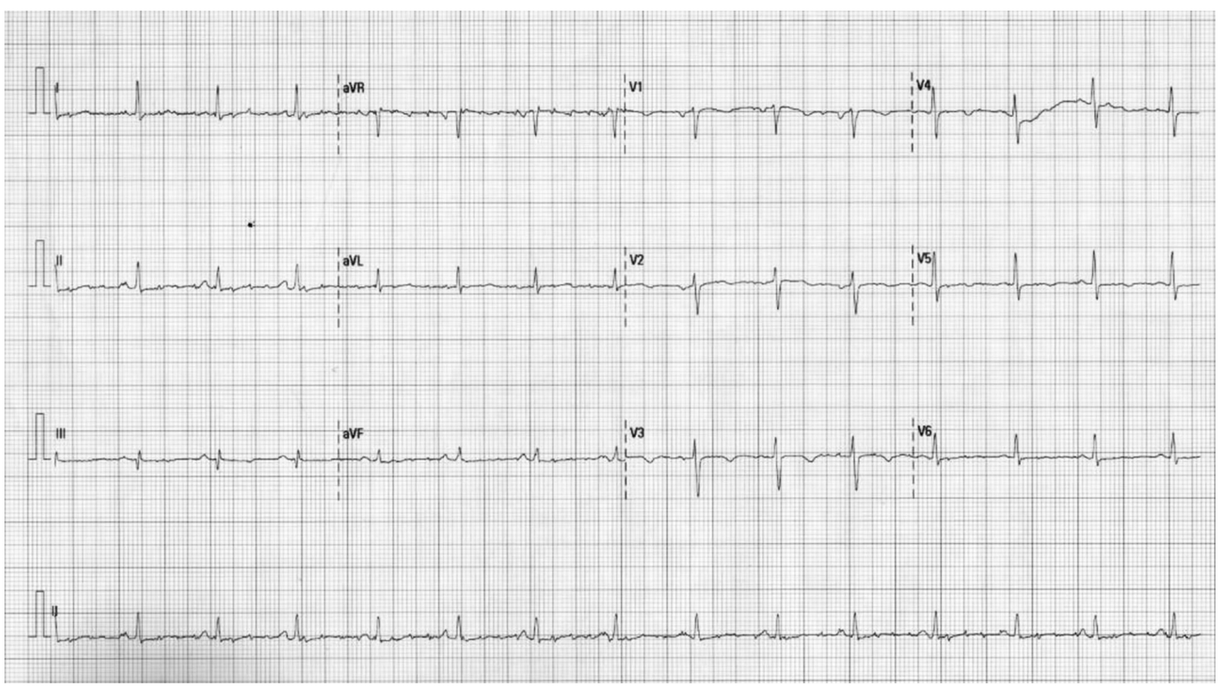

Figure 1

Figure 2.a

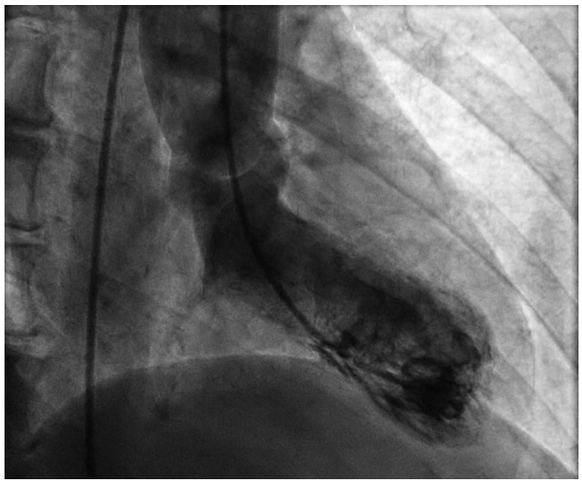

Figure 2.b

Brain magnetic resonance imaging (MRI) was performed and MRI revealed punctate infarction areas in the right cerebral hemisphere and old bleeding areas in the cerebellar hemisphere. In neurology consultation, continuation of acetylsalicylic acid 100 mg/day treatment was recommended.

On the 4th day of hospitalization, one more dose of zuclopenthixol acetate 50 mg/ml IM was administered to her. After her medical condition became stable, the patient's family requested the patient's transfer to continue psychiatric treatment in a different city where they lived. On the 10th day of her hospitalization, she was diagnosed with schizophreniform disorder and was referred to another hospital under the medication of olanzapine 5 mg/day and haloperidol 1 mg/ml solution 30 drops/day.

DISCUSSION

After the patient was admitted to our psychiatric clinic, we evaluated the patient in detail in terms of psychiatric diagnoses based on the information obtained from the patient and her relatives. There were no depressive symptoms or cognitive impairments in her examination at the time of admission. Therefore, the diagnoses of major depressive disorder with psychotic symptoms and delirium were excluded. No symptoms that could be related to prolonged or complicated grief were observed. She was diagnosed with schizophreniform disorder due to the absence of a long prodrome period, acute onset, accompanying transient confusion, good premorbid functionality and the fact that psychotic symptoms had continued for approximately 1.5 months. It was considered that the initial transient disorientation could be related to the electrolyte imbalance observed at that time or to the schizophreniform disorder itself.

In the first study examining the relationship between TC and psychiatric diseases, pre-existing psychiatric disease was detected in 37% of those with TC. Among these diseases, mood disorders are in the first and anxiety disorders are in the second place. Only 4% of the patients with TC who had pre-existing psychiatric illness were included in the diagnostic category of schizophrenia spectrum and other psychotic disorders (Nayeri et al., 2018). In a study comparing patients with TC and ACS, mood disorders and anxiety disorders were detected at higher rates in TC (Pozzi et al., 2022). In the studies conducted after the Hanshin-Awaji Earthquake, an increase in cardiovascular events was observed after intense stress exposure. In the first month after the earthquake, 16 patients who did not have premorbid ischemic heart disease were diagnosed with TC. The incidence of TC after the earthquake was roughly 24 times higher than before (Kušević et al., 2021). The exaggerated release of neuropeptides that originate from the limbic cortex and effect the myocardium after physical or emotional stressor could be responsible for the clinical symptoms observed in TC (Ben Ammar et al., 2021). Therefore, a heart-brain interaction has been proposed to play a crucial role in development of TC and premorbid psychiatric illness could be an important predisposing risk factor (Pozzi et al., 2022). In a recent systematic review, which included suicidality, grief, personality disorders, etc., as well as major psychiatric diseases, psychiatric conditions were reported in 77% of patients with TC during the index hospitalization (Carroll et al., 2020). In a report of four cases, loss experiences through death or separation from someone close were the most prevelant emotional triggers (Jenab et al., 2017). The prevalence of psychiatric disease is higher in women than

in men in TC and emotional triggers are more common than physical triggers in women (Carroll et al., 2020). Not only a having a pre-existing psychiatric disorder but also exacerbations of psychiatric illnesses might trigger TC. It is also stated that rapid dose increase or overtitration of drugs such as SNRI or lithium, sudden termination of psychiatric treatment and applying ECT, could be important in etiology of TC (Nayeri et al., 2018; Zvonarev, 2019). In the literature on the relationship between antipsychotic drugs and TC, there are only 2 case reports of TC observed in patients with neuroleptic malignant syndrome (Kawabata et al., 2003; Ullah et al., 2020). In our case, social stressors such as loss of spouse, starting to live alone and the subsequent psychotic attack may have triggered TC.

Various etiologies are presumed to cause TC to date, but no consensus has been reached. In this complex pathophysiology, catecholamine-mediated microvascular dysfunction appear to play a pivotal role (Nguyen et al., 2009). Increased catecholamine levels have been determined in patients with TC. Sustained exposure to increased sympathetic system activity may result in direct toxic effects on cardiomyocytes, acute microvascular dysfunction or spasm (Pozzi et al., 2022). High epinephrine levels can also stimulate the conversion of Gs proteins to Gi proteins in β_2 adrenoceptors, resulting in an increased negative inotropic effect. The apex has the highest density of β adrenergic receptors, this anatomical distribution difference may explain the characteristic apical ballooning finding seen in TC (Oliveri et al., 2020).

Takotsubo cardiomyopathy occurs mostly in postmenopausal women older than 55 years. Because resting sympathetic system activity increases with age and older patients are exposed to greater cardiac sympathetic stimulation due to increased catecholamine release and impaired reuptake (Wittstein, 2020). Estrogen affects β_1:β_2 receptor expression ratios. Decreased β_2 receptor expression, decreased vagal tone, and decreased baroreflex activity are observed in postmenopausal women. This negative change in the protective effect may result in postmenopausal women becoming more prone to stress-triggered cardiomyopathy than men. In older women, TC can easily develop with a milder sympathetic stimulation and results in fewer cardiac complications. However, in men who have lower resting sympathetic tone than women, TC occurs with severe sympathetic stimulation and more cardiac injury emerges (Wittstein, 2022). So our patient may have become prone to TC due to physiological changes that occurred in postmenopausal period.

Patients with TC have a high prevalence of cardiovascular risk factors similar to those in ACS (Pozzi et al., 2022). As a result of the evaluation of more than 1000 patients with TC, obstructive CAD was determined in 23% of the patients and non-obstructive CAD in 41.2%. Angiographically normal coronary artery structure was detected in only 35.7% of the patients (Napp et al., 2020). In our active smoker case, non-obstructive coronary artery disease was detected, consistent with TC reports in the literature.

Although TC has long been considered to be a benign disease that recovers within days or weeks, mortality rates in the first 30-day acute period are 4-5%, similar to ACS (Pozzi et al., 2022). Pre-existing psychiatric diseases increase the risk of complications and recurrence in the acute period, but do not affect long-term mortality (Oliveri et al., 2020). The risk of hospital complications also increases in patients with acute psychiatric exacerbations. However, only 1/3 of Takotsubo patients receive psychiatric care during hospitalization, and this rate decreases to 19% during follow-up (Carroll et al., 2020). These results suggest that long-term psychiatric follow-up of our case may also be decisive for cardiac prognosis.

In this case report, a postmenopausal female patient was evaluated in terms of different factors that may play a role in the etiology of TC and her treatment was organized in a multidisciplinary manner.

CONCLUSION

There are limited studies on the relationship between TC and psychiatric diseases. In these studies, evaluations were generally made only for major psychiatric diseases. The exact effect of psychiatric diseases and psychotrops on this stress-triggered cardiomyopathy during the long term course is not yet known. In order to determine appropriate treatment approaches, awareness of TC should be increased not only among cardiologists but also among physicians of different departments.

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