

Case Report

The Sudden Death of a Pregnant Woman With Takotsubo Cardiomyopathy Following a Legal Abortion: A Case Report



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ABSTRACT

Background: Takotsubo cardiomyopathy (TCM) is characterized by left ventricular dysfunction and apical ballooning due to physical or mental stress in the absence of coronary artery disease. This transient heart disorder is rare in pregnancy. It may affect women of reproductive age.

Case Presentation: The case was a 38-year-old woman in the first trimester of pregnancy with a history of TCM diagnosis one year ago, admitted to the hospital for a legal abortion. At the time of hospitalization, echo cardiography, echo cardiography, and clinical tests results were normal; however, due to stressful factors, such as the cancellation of the dilation & curettage (D&C) procedure, despite being transferred to the operating room (due to the absence of a gynecologist), receiving misoprostol for two consecutive days, the prolongation of surgery time, as well as the absence of a psychiatrist to reduce stress during the operation, suffered from recurrent TCM and eventually expired. In the autopsy, the cause of death was a massive pulmonary embolism.

Conclusion: In pregnant women, there is a possibility of TCM recurrence due to changes in hormonal levels and emotional and physical stress caused by pregnancy. Therefore, when performing a surgical procedure such as D&C, a team consisting of gynecologists, cardiologists, and psychiatrists should be present to avoid dangerous complications such as sudden death.

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1. Introduction

Takotsubo cardiomyopathy (TCM) is similar to acute coronary syndrome. However, in the absence of coronary artery stenosis in angiography and with left ventricular dysfunction, it manifests itself as variable wall abnormalities (transient left ventricular apical ballooning in ventriculography or echo cardiography). It was first named takotsubo in Japan due to the similarity of the left ventricle (LV) to the Japanese octopus trap or fishing pot. It is also called “stress cardiomyopathy” or “broken heart syndrome” (because it is usually caused by acute emotional stress). There are several diagnostic criteria for TCM. One of the most important diagnostic criteria is the modified Mayo Clinic [1]: Suspicion of AMI based on precordial pain and ST elevation observed on the acute-phase ECG, transient hypokinesia or akinesia of the middle and apical regions of the LV and functional hyperkinesia of the basal region, observed on ventriculography or echo cardiography, normal coronary arteries confirmed by arteriography (luminal narrowing of less than 50% in all the coronary arteries) in the first 24 h after the onset of symptoms, and absence of recent significant head injury, intracranial hemorrhage, suspicion of pheochromocytoma, myocarditis, or hypertrophic cardiomyopathy.

The etiology of TCM is unknown, but one of the essential etiologies proposed is the effect of catecholamines. However, due to its higher prevalence in women than men, studies have suggested the role of hormones such as estrogen and its reduction due to its higher prevalence in postmenopausal women [2, 3]. Risk factors for TCM include emotional stress, physical stress, psycho-social stress, and anxiety. Elimination of physical or emotional stress leads to a rapid decrease in TCM symptoms, although in cases such as acute heart failure and cardiac shock, hospitalization in the cardiac intensive care unit and even invasive procedures such as intra-aortic balloon pump and cardiopulmonary bypass are required. Considering a complex balance between the environment and biological factors such as hormone levels [4, 5], TCM has the possibility of recurrence in pregnancy, and it is important to distinguish it from peripartum cardiomyopathy [6-8].

2. Case Presentation

The case was a 38-year-old white pregnant woman with a known case of TCM visited the hospital for a legal abortion. The patient's vital signs were standard in the tenth week of pregnancy, with a fetal heart rate of 170

in the ultrasound examination. One year ago, she had referred to teaching hospital complaining of shortness of breath and chest pain similar to angina pectoris. Due to inverted T waves on the electrocardiogram (ECG), she was admitted to the CCU with suspected myocardial infarction. Levels of cardiac enzymes, creatine kinase-MB, and troponin T were relatively high. Due to persistent shortness of breath and chest pain, the patient underwent emergency angiography. There was no stenosis in the coronary arteries. Echo cardiography showed an ejection fraction (EF) of 35% with dyskinesia, and the LV showed apical ballooning during systole and hyper contractility of the basal segments (Figure 1).

During a follow-up by a cardiologist seven months later, she denied chest pain, palpitations, or shortness of breath. During that visit, a repeated echo cardiogram was performed. The echo cardiography showed improvement in apical wall motion disorder, LV systolic dysfunction, and normal findings in auscultation of heart sounds with EF=55%. The patient was diagnosed with TCM based on these results. She had no history of allergy to a particular substance, surgery, smoking, or drug addiction. At the beginning of hospitalization, her vital signs were typical, and no abnormalities were reported in the clinical examination and echo cardiography EF=55%, heart sounds, and heart muscle movements were reported as usual. The patient was prepared for the second-day dilation & curettage (D&C) and tubal ligation. On the second day of hospitalization, the general condition was good. The patient received the first dose of micro misoprostol at 5:00 AM and a second dose at 8:00 AM, followed by dyspnea and angina tests at 8:30 AM. The symptoms were transient. At 11 AM., she was ready for a D&C. However, due to the absence of a gynecologist, the operation was canceled though the patient had been transferred to the operating room. Finally, on the third day, the patient underwent general anesthesia, and abortion was performed by D&C. Then, during the operation to close the fallopian tubes, the patient suddenly suffered a severe drop in blood pressure. In emergency echo cardiography, dyskinesia, ventricular apical ballooning during systole, and a reduction of EF to 30% were reported. Then, the patient developed refractory ventricular fibrillation and expired, despite cardiopulmonary resuscitation. The body underwent an autopsy to determine the cause of death.

3. Results

The body had a weight of 60 kg and a body height of 165 cm. Rigor mortis was present and equal throughout. Livor mortis was posterior and fixed, except for areas exposed to pressure. The sutured surgical incision was evident in the lower abdomen. The scalp was reflected normal, indicating no hemorrhage. The brain weighed 1100 g and there was an externally unremarkable CT scan. There were symmetrical and normal anatomic landmarks on brain CT. Multiple coronal cerebra, cerebellum, and brainstem sections showed no significant natural disease processes. A standard Y-shaped thoracoabdominal incision was used to open the body. All viscera showed appropriate anatomic relationships. There was no hemorrhage in the strap muscles of the anterior neck. The thyroid cartilage and hyoid bone were intact. The cervical spine had no injury. The 260-g heart was in its usual site (middle mediastinum). Heart surface fat was expected, and the thickness of the muscular walls and the appearance of the valves were reported as expected. No significant stenosis was observed in the coronary artery examination. The LV had a 1.8-cm thickness (ranged 1-1.8 cm), while the right ventricle (RV) had a 0.3-cm thickness (ranged 0.25-0.3 cm). The valves were normal, with delicate cusps and leaflets. The foramen ovale was closed. The coronary circulation had left dominance. There was no associated underlying atherosclerotic plaque. The combined weight of the lungs was 950 g (average lung weight for females=740 g). The lung parenchyma was dark

red, and foamy fluid exuded from the cut surface. The bronchi was normal. Extensive embolism was evident in the pulmonary vessels (Figure 2). In examining the vessels in the calf of both legs, the results showed no thrombosis. The esophagus and stomach were normal in appearance without any evidence of ulcers or varices. The stomach was empty, without evidence of any pills or other non-food materials. The pancreas showed a normal lobular cut surface with evidence of autolysis. The duodenum, ileum, jejunum, and colon were all grossly normal without evidence of abnormal vasculature or diverticula. The liver weighed 1500 g, and the cut surface revealed a normal liver with fat changes. The spleen was large, weighing 250 g, and the cut surface was a normal-appearing white and red pulp. No abnormally large lymph nodes were noted. The right kidney weighed 150 g and the left weighed 160 g. The renal capsules were easily stripped off, and the cortical surfaces were smooth and pale. The cortices are delineated from the renal medullae. The renal vessels were patent. The urinary bladder contained approximately 100 mL of urine. The mucosa was unremarkable. A soft uterus with a dimension of 12×4×8 cm was evident. There was a hematoma in the incision site on the inner surface of the uterus. The uterus was free from the products of conception. The ovaries were healthy. Tubal ligation was performed. A toxicology and pathology sample from the heart, lung, and liver sections were prepared and the results of laboratory and pathology studies on them were normal. Ultimately, the cause of death was pulmonary embolism (PE) due to TCM.

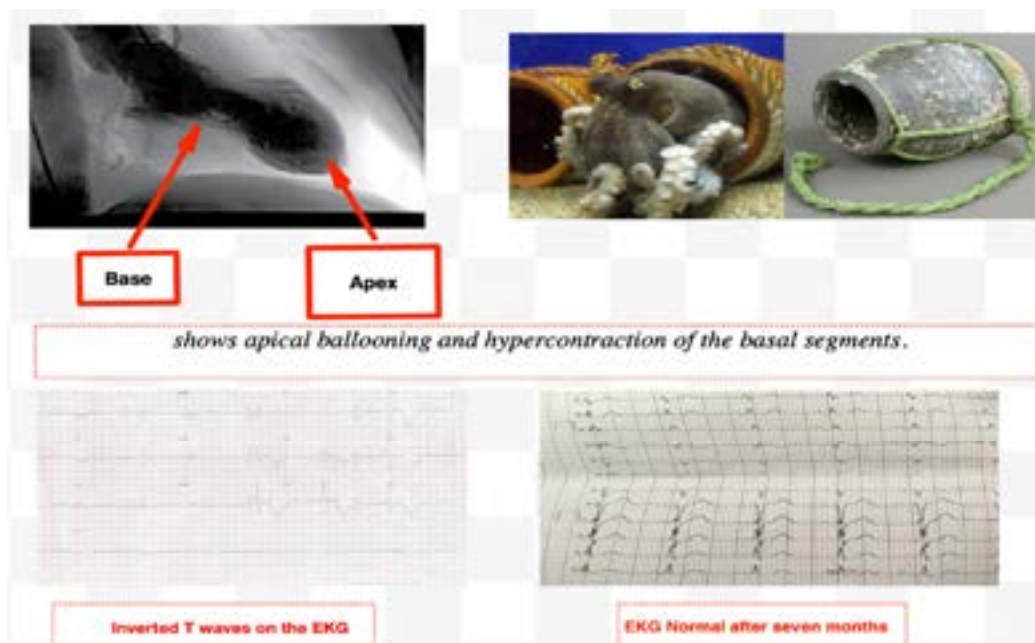


Figure 1. Echocardiography and ECG results

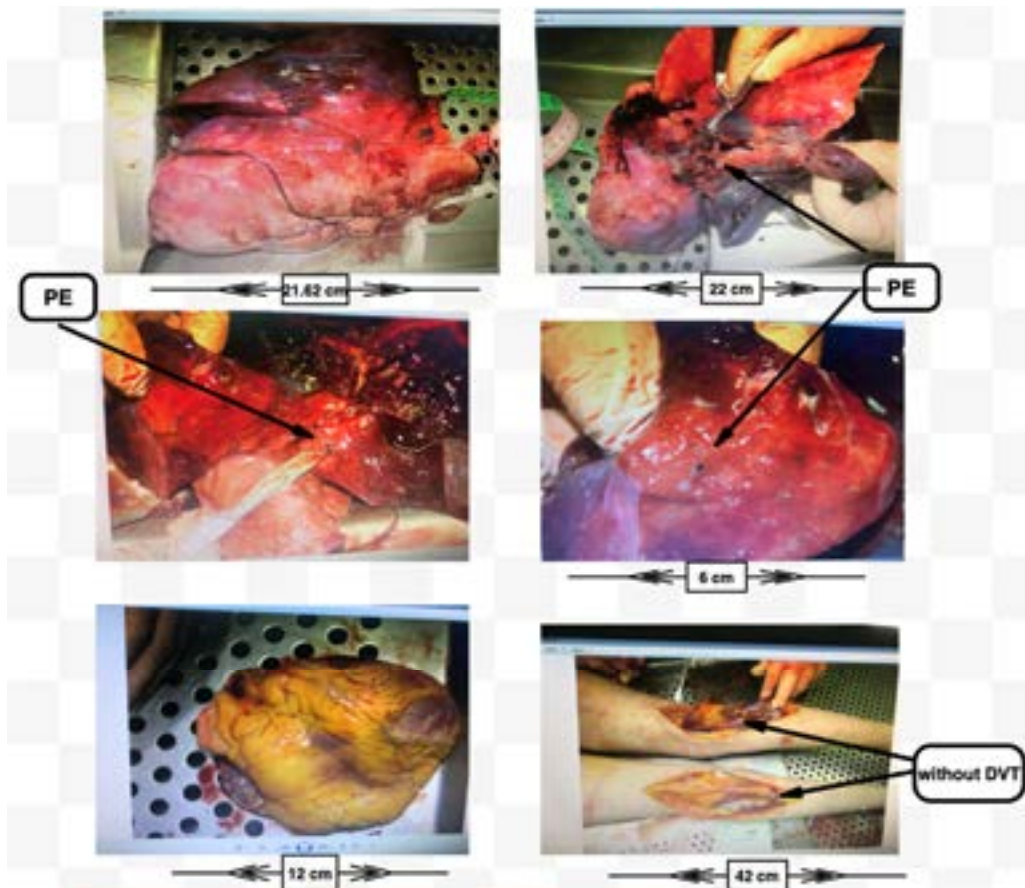


Figure 2. Pulmonary embolism without deep vein thrombosis (DVT)

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4. Discussion

The TCM diagnosis is challenging, since it is similar to an acute coronary syndrome due to changes in the ECG and the low elevation of cardiac enzymes, leading to hypotension and cardiac shock. However, the main difference between TCM and acute coronary syndrome is that TCM is prevalent in women. It does not have the risk factors related to acute coronary syndrome, and coronary angiography results do not show any significant coronary artery stenosis [9-11]. Echo cardiography results shows the rapid recovery from TCM, which indicates that TCM is transient [12]. Coronary artery spasm may be suggested, but in TCM, there are cases of RV hypokinesis as well as hypokinesis in the LV apex, which does not correspond to the place of coronary arteries as a result of coronary artery spasm [13]. Interestingly, the TCM was first introduced as cardiomyopathy by Neff et al. by examining the results of myocardial biopsy [14, 15]. Moreover, although myocarditis was previously proposed as an exclusion criterion for this syndrome, it is now introduced as a primary part of the TCM's pathogenesis,

and only viral myocarditis is accepted as an exclusion criterion [16-18]. Therefore, the underlying pathogenic mechanism of TCM is complicated; the physicians who take care of patients recovering from TCM, especially pregnant women, should have a correct understanding of the cause of this disorder and that the recovery process is often slow and is not complete. What still needs to be resolved about TCM is that its recurrence is unpredictable; thus, doctors' recommendations are currently limited in this field [19].

The TCM is a rare disease, especially in pregnant women, which is life-threatening and should be considered a cardiac emergency in these women because of symptoms such as angina pectoris, palpitations, and diaphoresis, as well as left heart failure such as stenosis. It mimics paroxysmal nocturnal dyspnea, orthopnea, dyspnea, as well as myocardial infarction, peripartum cardiomyopathy, acute myocarditis, and dilated cardiomyopathy [6, 9]. Deciding on the time and method of delivery or legal abortion in these patients is very important. Considering that TCM is one of the causes of sud-

den cardiac death in young people, especially in those with physical and emotional stress, pregnancy and legal abortion should be considered as intense stress. TCM is still a complex entity with complex and unknown pathophysiology. Even if most young patients with TCM recover within 4-5 weeks, some patients have complications such as pulmonary edema, malignant arrhythmia, and even death. Therefore, TCM is receiving more and more attention, and doctors should be highly suspicious of TCM in young pregnant women presenting with clinical manifestations similar to other heart diseases. Murashko et al. investigated the effect of abortion at the 7-8 weeks of pregnancy on the level of sex hormones in the blood. Abortion was performed under anesthesia and with D&C. At the 7-8 weeks of pregnancy, estradiol level was increased by 4-5 times and the progesterone level by two times. Abortion reduced the progesterone level by 38% after one hour, 52% after 3 hours, and 80% after 24 hours. Estradiol concentration decreased by 58% one hour after abortion and 88% after 24 hours [20]. Considering the hormonal effects on the development of TCM, it is important to pay attention to this issue. In a study conducted after abortion, the amount of urinary secretion of adrenaline and noradrenaline increased, indicating the significant activation of the sympathetic-adrenal system. Also, the cortisol level decreased by 38% [21]. These factors can be considered during D&C, especially in the first trimester, due to the effective role of catecholamines in TCM as a trigger. Misoprostol is a proven agent for cervical ripening before a surgical abortion in the first trimester. Effective regimens are 400 µg of misoprostol vaginally for 3-4 hours, 400 µg of misoprostol orally for 8-12 hours or 400 µg of misoprostol sublingually for 2-4 hours, prior to suction curettage [22]. Misoprostol can result in cardiac arrest due to coronary vasospasm. Coronary vasospasm induced by misoprostol can be relieved with intra-arterial nitroglycerin. In a study in 2012 on the adverse effects of vaginal administration of misoprostol, angina or myocardial infarction without stenosis were reported, especially in women over 35. In practice, this risk should be considered, especially in women with risk factors for cardiovascular diseases, or when using the vaginal route. When a high cardiovascular risk is identified, it is better to warn patients about the cardiac effects of this drug, and advise them to consult a doctor or propose an alternative method if they feel chest tightness. If possible, these women should not be alone when they take misoprostol [23]. In our case, the patient received misoprostol for two consecutive days, which is a risk factor in the development of TCM.

The in-hospital mortality rate for patients with TCM is 4.2%, with a higher mortality rate for men than women (8.4% vs. 3.6%) [24]. The exact relationship mechanism between PE and TCM is unclear. However, it seems that increased catecholamine level during severe pain and pulmonary perfusion defects related to PE lead to the LV wall motion abnormalities, creating a fatal situation in the patients. It should be noted that, once TCM is suspected, PE should be considered as a potential stressor. The hypercoagulability of blood during pregnancy has been confirmed with thromboelastography, and is thought to be due to the increased production of factor VII and fibrinogen [25]. The hemostatic changes produce enhanced coagulation and formation of micro-thrombi or thrombi, and prompt diagnosis is crucial to prevent and treat PE to save the lives of pregnant women and their fetus [26]. Patients with cardiac diseases, such as coronary artery disease, atrial fibrillation, and heart failure, are at a higher risk for PE. On the other hand, PE may precipitate RV and LV dysfunction and induce acute heart failure or cardiac shock [27, 28]. In our case, the cause of death was massive PE without DVT, according to the autopsy performed and a detailed examination of the deep leg veins.

This study showed a specific case of TCM with specific conditions; a case of death in a young pregnant woman in the 10th week of pregnancy. Most of the reported cases related to this syndrome were related to elderly and menopausal women after emotional stress; the cases in pregnant women were more related to the last months of pregnancy or after delivery. It seems that in our case, factors such as the stress of pregnancy, stress of abortion surgery, unwanted change in surgery time, administration of misoprostol for two consecutive days, decrease in estrogen level, or previous history of TCM triggered the TCM. This syndrome and the coagulation disorders caused by pregnancy caused PE, which led to the exacerbation of the defective cycle and finally death. In our case, the diagnosis of TCM and stressful conditions, such as pregnancy and hospitalization for legal abortion, the prescription of vaginal misoprostol, the delay in surgery (change of schedule due to absence of a gynecologist), and the prolongation of the surgical procedure (performing D&C along with tubal ligation) created life-threatening conditions.

Removing physical or emotional stress can lead to rapid improvement in TCM symptoms, although in cases with acute heart failure and cardiac shock, hospitalization in the cardiac CCU and even invasive procedures such as intra-aortic balloon pump and cardiopulmonary bypass are required. According to the effect of environmental factors, there is need for a complex balance between the environment and biological factors such as hormone levels [6, 9, 29, 30].

5. Conclusion

Considering that massive PE caused the sudden death of the pregnant woman with TCM, we recommend the presence of a multidisciplinary team consisting of obstetrician-gynecologists, cardiologists, and psychiatrists or psychologists to manage the patients' conditions.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this work.

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Authors' contributions

The authors contributed equally to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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