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Takotsubo Cardiomyopathy Induced by Very Low-Dose Epinephrine Contained in Local Anesthetics: A Case Report

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Study Design A
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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 78-year-old
Final Diagnosis: Takotsubo cardiomyopathy
Symptoms: Tachycardia
Medication: —
Clinical Procedure: —
Specialty: Anesthesiology • Cardiology

Objective: Diagnostic/therapeutic accidents

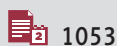
Background: Takotsubo cardiomyopathy is a reversible left ventricular dysfunction triggered by emotional or physical stress. Perioperatively, takotsubo cardiomyopathy is sometimes induced by various psychological factors, such as stress from surgery, and non-psychological factors, such as epinephrine misinjection. This report describes a case of takotsubo cardiomyopathy induced by the administration of very low-dose epinephrine contained in a local anesthetic.

Case Report: A 78-year-old woman with mycosis in the maxillary sinus was scheduled to undergo endoscopic sinus surgery. After the submucosal injection of 3 mL of local anesthetic (lidocaine, 0.5%; epinephrine, 1: 200 000) immediately before the incision, her heart rate and blood pressure reached 135 beats per min and 254/185 mmHg, respectively, inducing ventricular tachycardia. After receiving 50 mg of lidocaine, her cardiac rhythm resumed a normal sinus rhythm, without cardioversion. As her hemodynamics stabilized, the surgical procedure began as planned. Postoperative electrocardiography, echocardiography, and coronary arteriography demonstrated takotsubo cardiomyopathy. Subsequently, her cardiac movement gradually improved, and she was discharged from the hospital on postoperative day 9.

Conclusions: To the best of our knowledge, this is the first reported case in which a very small amount of epinephrine (0.015 mg) induced takotsubo cardiomyopathy. Therefore, epinephrine should be used cautiously, especially in the nasal mucosa, vaginal mucosa, and uterus, where blood flow is relatively high. If unexpected hemodynamic alterations and ST-segment abnormalities occur after epinephrine administration, asymptomatic takotsubo cardiomyopathy should be considered.

Keywords: Anesthesia, Local • Epinephrine • Heart Failure • Intraoperative Complications • Lidocaine • Takotsubo Cardiomyopathy

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Background

Takotsubo cardiomyopathy (TCM) is characterized by reversible left ventricular dysfunction, with distinctive regional wall motion abnormalities, and it is stimulated by emotional or physical stress, giving it the name “stress-induced cardiomyopathy” [1]. Typically, TCM is triggered by a major emotional stressor or a serious medical illness; sometimes, even the stress from surgery can trigger TCM [2].

Many cases of TCM have occurred during surgery. One of the non-psychological factors of TCM is the use of epinephrine [3]. This type of TCM is known as “epinephrine-induced TCM” (Ei-TCM). In this report, we describe a case of TCM induced by the administration of very low-dose epinephrine contained in local anesthetics.

Case Report

A 78-year-old woman with mycosis in the maxillary sinus was scheduled to undergo endoscopic sinus surgery. Her medical history included hypertension and hyperlipidemia. Her preoperative examinations, including laboratory examinations, chest X-ray, electrocardiography (ECG), and spirometry, were normal.

Anesthesia was induced with propofol and remifentanyl without any problem. **Figure 1** illustrates the patient’s anesthetic record. After 3 mL of local anesthetics (lidocaine, 0.5%; epinephrine, 1: 200 000) was injected submucosally immediately before the incision, the patient’s blood pressure increased to 254/185 mmHg, inducing ventricular tachycardia (135 beats per minute, data not shown). Hence, 50 mg of lidocaine was administered intravenously. Consequently, the patient’s cardiac rhythm returned to a normal sinus rhythm, without cardioversion. The ECG revealed slight ST-segment elevation in the limb lead II (data not shown). However, as her hemodynamics stabilized, and an arterial blood gas analysis did not detect lactic acidosis, the surgery proceeded as planned.

Following the surgery, a detailed examination was conducted. **Figure 2** shows the postoperative results of the chest X-ray and time changes of the 12-lead ECG. Compared with the preoperative results, the postoperative chest X-ray demonstrated slight cardiac dilatation (**Figure 2A**), while, 1 h after surgery, the 12-lead ECG demonstrated slight ST-segment elevation in the precordial lead V2 and slight depression in leads V3 to V6 (**Figure 2B**). Moreover, an echocardiography revealed apical akinesis (data not shown). These findings can indicate acute coronary syndrome or TCM. Hence, a coronary arteriography was also performed on the same day, showing that the coronary artery had no significant stenosis (**Figure 3A**). However, a left ventricular angiography revealed akinesis from the area of the

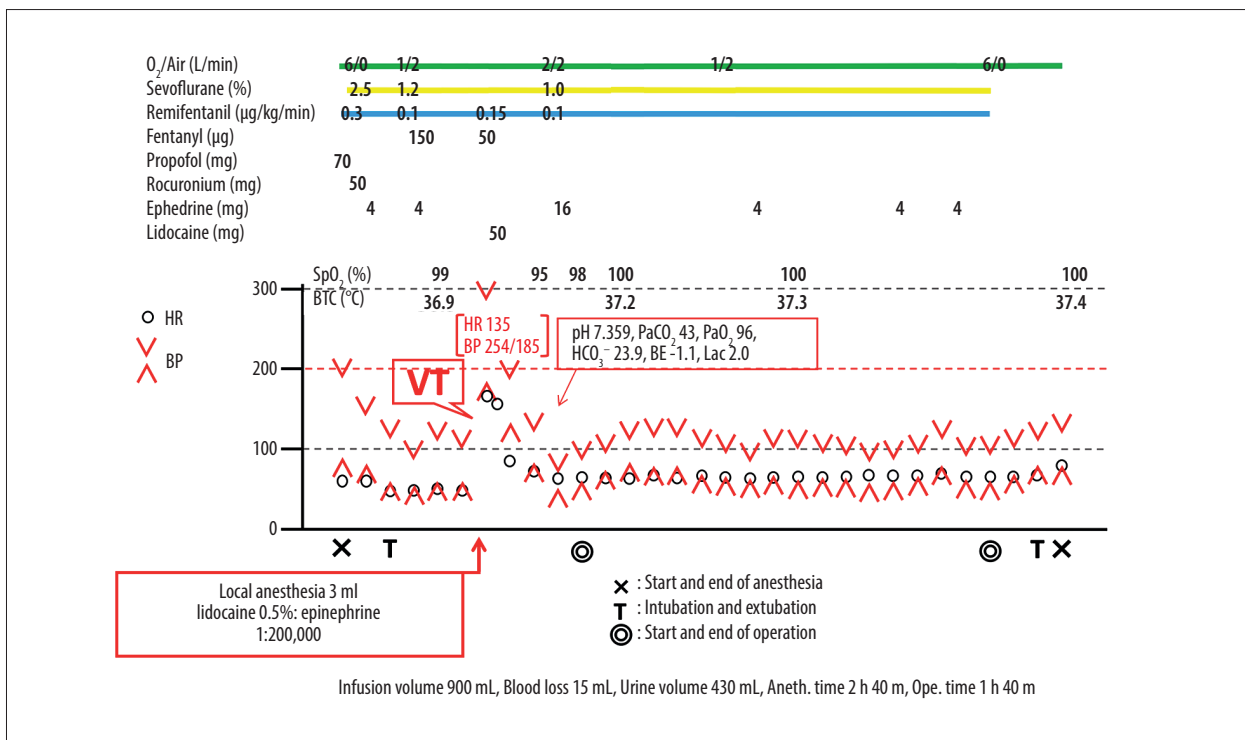


Figure 1. Anesthesia record showing ventricular tachycardia and hypertension right after local anesthesia using epinephrine-containing anesthetics.

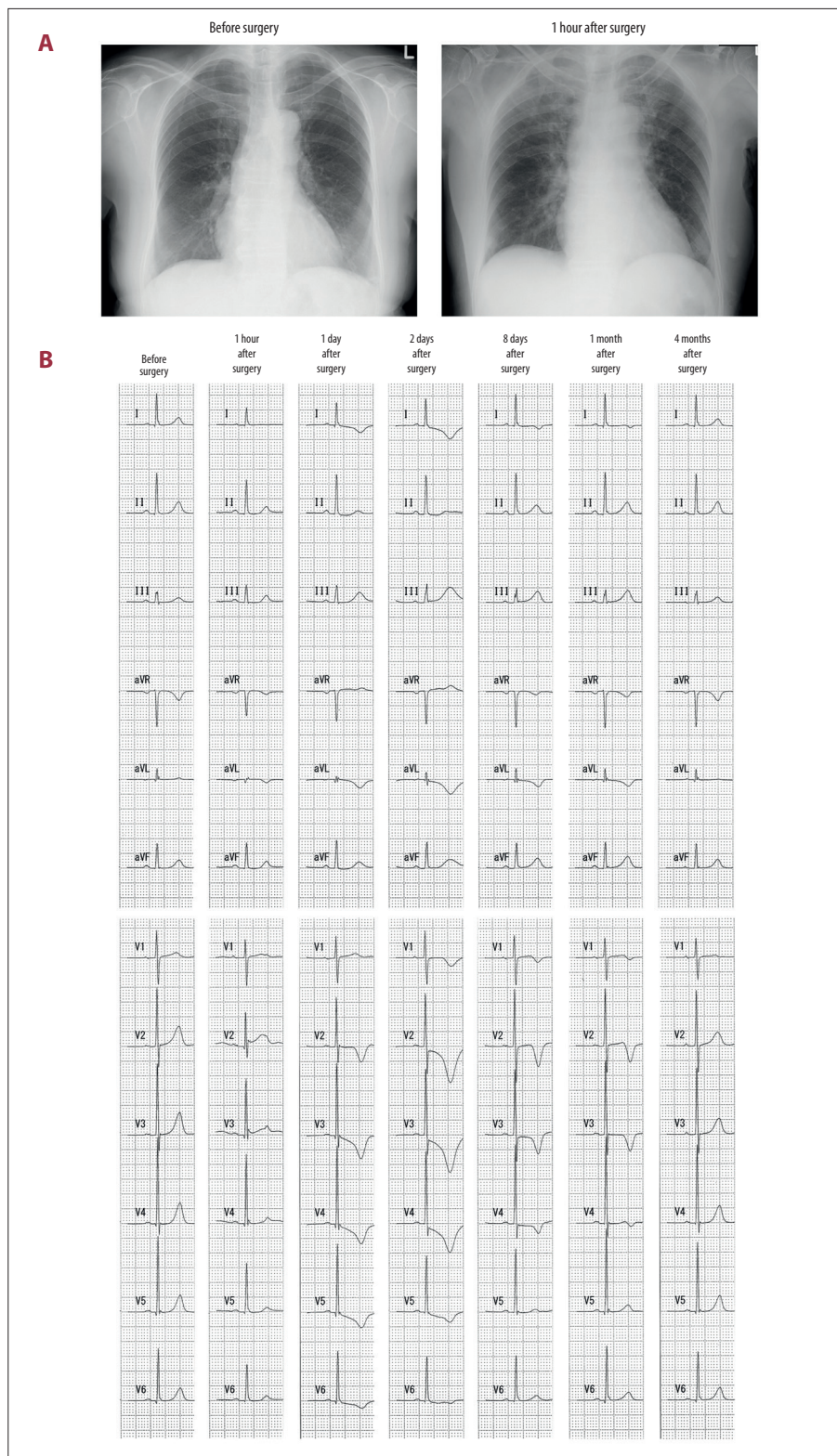


Figure 2. Time change of electrocardiography. Chest X-ray results and time changes of 12-lead electrocardiography (ECG) after surgery. **(A)** Preoperative and postoperative chest X-ray results. **(B)** The 12-lead ECG demonstrated slight ST-segment elevation in precordial lead V2 and slight depression in leads V3 to V6 at 1 h after surgery; additionally, a giant negative T wave occurred on postoperative day 2 but was resolved 4 months later.

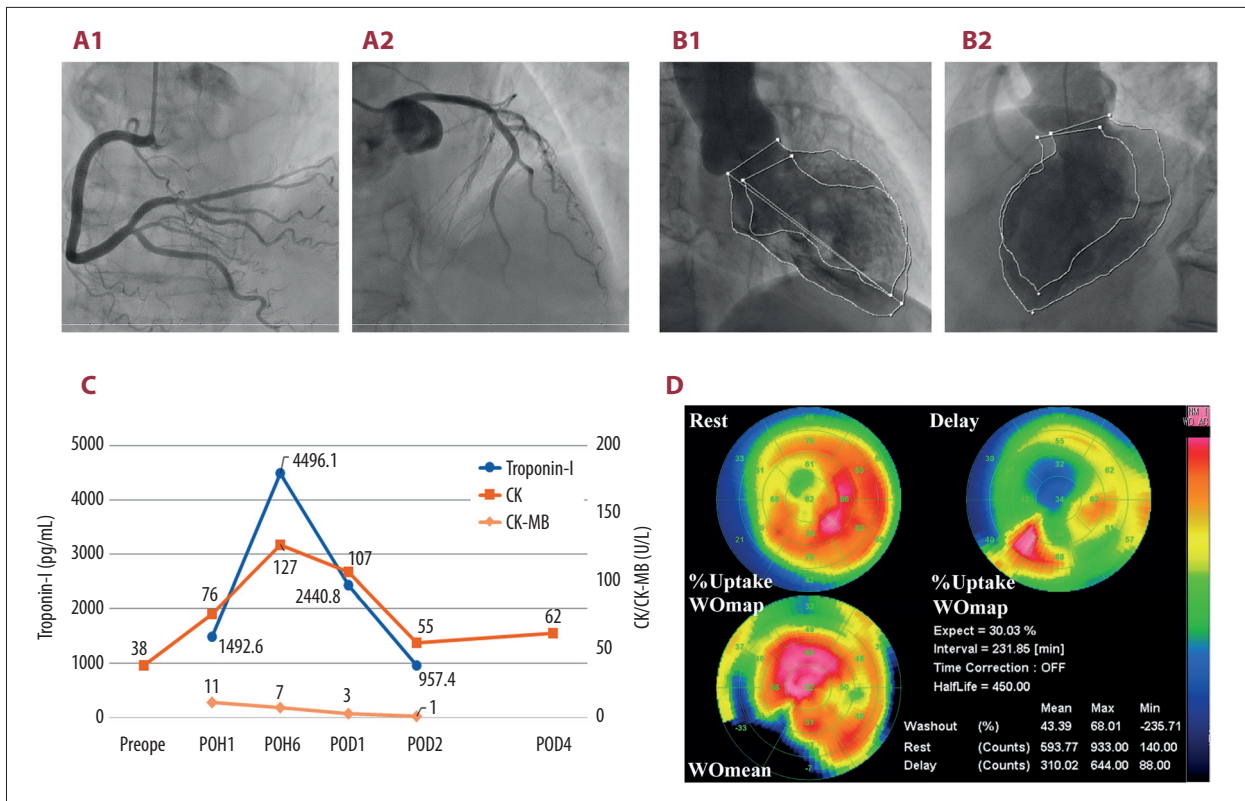


Figure 3. Postoperative examinations. (A) Postoperative coronary arteriography showed no significant stenosis in the coronary artery. (B) Left ventricular angiography revealed akinesis from the area of the apex to the left ventricle anterior wall. (C) Blood examination demonstrated normal levels of creatine kinase isozyme-MB and elevated levels of creatine kinase and troponin-I at the peak, 6 h after surgery. (D) ^{123}I -metaiodobenzylguanidine myocardial scintigraphy on postoperative day 8 shows decreased accumulation in the septum and increased accumulation in the base. POH – postoperative hour; POD – postoperative day.

apex to the left ventricle anterior wall (Figure 3B). Figure 3C shows the patient's postoperative blood examination. One hour after the surgery, the creatine kinase and creatine kinase isozyme-MB levels were normal, with a slight elevation in the troponin-I level. Because of these findings, the patient was diagnosed with TCM. At 6 h after surgery, the creatine kinase and troponin-I levels reached the peak levels, and then gradually decreased. Heparin at 5000 units/day was administered to prevent intraventricular thrombosis. On postoperative day 1, a 12-lead ECG still demonstrated an abnormal pattern, but an echocardiography detected improvement of the left ventricular wall motion. Therefore, the administration of heparin was stopped. Furthermore, the 12-lead ECG demonstrated a giant negative T wave on postoperative day 2, which finally improved 4 months after surgery (Figure 2B). On postoperative day 8, ^{123}I -metaiodobenzylguanidine myocardial scintigraphy was performed, revealing decreased accumulation in the septum and increased accumulation in the base (Figure 3D), consistent with TCM. On postoperative day 9, the patient was discharged from the hospital.

Discussion

Ei-TCM emerges immediately after epinephrine administration. It is now hypothesized that its pathogenesis consists of epinephrine inducing a switch in signal trafficking through the pleiotropic β_2 -adrenergic receptor between the canonical stimulatory G-protein-activated cardiostimulant and inhibitory G-protein-activated cardiodepressant pathways [4]. The mean left ventricular ejection fraction of Ei-TCM is approximately 40% during onset, with cardiogenic shock, lung edema, and severe arrhythmia as the common complications [5]. Nevertheless, given that cardiac function generally recovers within days or weeks, the prognosis is favorable [1].

All findings observed in this case, including the time of onset, the data of the detailed postoperative examination, and the postoperative course, were consistent with Ei-TCM. At the time of onset, our patient presented with symptoms including temporal elevation of blood pressure, ventricular tachycardia, and subsequent slight ST elevation. As the hemodynamics stabilized after the sinus rhythm returned to normal, we

proceeded with the surgery but still performed a postoperative 12-lead ECG. Therefore, when unexpected hemodynamic changes and ST segment abnormalities occur in patients after epinephrine use, the possibility of asymptomatic TCM should be considered.

Epinephrine is used perioperatively to prevent allergic reactions, such as anaphylaxis and asthma, and bleeding from the surgical site. Approximately 40 cases of Ei-TCM have been reported [6]. According to Hassan et al, Ei-TCM is mainly caused by the therapeutic use of epinephrine for anaphylaxis or the inadvertent use of high-dose epinephrine [7]. In rare cases, Ei-TCM is induced by surface anesthesia of the nasal mucosa [8] and irrigation fluid for arthroscopy [9]. The typical dose of epinephrine ranges between 0.3 mg and 1 mg [7]. In addition, a higher than 1 mg dose is significantly related to the development of complications, such as heart failure, cardiogenic shock, and pulmonary edema [7]. Interestingly, the epinephrine dose of 0.015 mg administered in our patient is the smallest among previously reported cases. Our case indicates that even a very small amount of epinephrine can induce TCM. Therefore, local anesthesia using epinephrine-containing anesthetics must be performed cautiously, and patient vital signs must be monitored carefully. In particular, the local administration of epinephrine via the nasal mucosa, vaginal mucosa, and uterus, where the blood flow is relatively abundant, has been identified in many TCM cases. Although epinephrine use is extremely effective and useful for the hemostasis of these tissues, administration of such a drug via these tissues must be performed with caution because it is highly prone to misinjection into the vessel.

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Conclusions

In conclusion, even a small amount of epinephrine, such as 0.015 mg, can induce TCM. Epinephrine must be administered cautiously, especially in the nasal mucosa, vaginal mucosa, and uterus. If unexpected hemodynamic changes and ST segment abnormalities of the ST segment occur after the use of epinephrine, clinicians should consider the possibility of asymptomatic TCM.

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Conflicts of Interest

None.