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Reverse Takotsubo Cardiomyopathy, Flash Pulmonary Edema and Cardiac Arrest after Topical Nasal Phenylephrine and Mucosal Epinephrine Injection

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Abstract Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy, is characterized by acute reversible apical ventricular dysfunction and apical akinesis in the absence of obstructive coronary artery disease. Reverse-takotsubo is a variant form of takotsubo cardiomyopathy with basal and midventricular dysfunction and normal apical function. It is known to be more common in young patients. We present a case of a 14-year-old patient who developed reverse-takotsubo cardiomyopathy with flash pulmonary edema after topical nasal phenylephrine and iatrogenic epinephrine containing local anesthetic injection for a dental procedure. Patient experienced cardiac arrest but was resuscitated successfully and transferred to the cardiac intensive care unit. Postoperative echocardiogrpahy showed normal coronary arteries and mild left ventricular hypertrophy with uncertain correlation for the cardiac event, and the patient was discharged home with no complications.

Keywords: *reverse-takotsubo, cardiomyopathy, pulmonary edema, epinephrine, phenylephrine*

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1. Introduction

Takotsubo cardiomyopathy is characterized by transient left ventricular systolic dysfunction with apical ballooning and hyperkinesis of the basal segments. Reverse-takotsubo cardiomyopathy is a subtype, which is characterized by basal and midventricular dysfunction with preserved apical function [1]. It is known to occur more frequently in younger patients and is often stress induced or develops after iatrogenic catecholamine administration.

2. Case

A 14-year-old patient with a past medical history of borderline hypertension, high cholesterol on diet modification, eczema, allergic rhinitis, and childhood asthma presented for a dental procedure. Previous procedures included tonsillectomy with adenoidectomy and inguinal hernia repair without anesthetic complication. The patient had no significant history of any cardiac disease. No emotional or physical stressor was identified preoperatively. Patient received general anesthesia with propofol, fentanyl, and rocuronium, and nasal intubation was performed after administration of topical nasal lidocaine 3% with 0.25% phenylephrine (2-3 ml). Sevoflurane was used for maintenance. Local lidocaine 2% with 1:100.000 epinephrine 10.2 milliliters was injected by the surgeon. After few minutes patient became hypertensive to an arterial blood pressure of 240/120 mmHg and tachycardia to 130 bpm with signs of ST depression. Hypertension was treated with deepening anesthesia up to 2.5 MAC of sevoflorane and 200 mg of propofol, nitroglycerin 50 mcg bolus doses over 10 minutes (total of 200 mcg), and esmolol 50 mg to control the heart rate. Over the next 10 minutes, the patient's systolic blood pressure decreased below 80 mmHg, and he was treated with phenylephrine and ephedrine. The systolic blood pressure further decreased to below 40 mmHg with a decrease in $ETCO_2$ and no palpable pulse. Chest compression was initiated and epinephrine 100 mcg was given. Pulse returned within 1 minute after chest compression, and blood pressure was stabilized. Intraoperative transesophageal echocardiography (TEE) showed moderate left ventricular dysfunction with mild mitral regurgitation (Figure 1) and ejection fraction of 30-35%. The left ventricular apex was contracting normally, but akinesis was seen in all mid to basal segments and on the septal wall (Figure 2 and Figure 3), findings consistent with reverse-takotsubo cardiomyopathy. Left ventricular internal dimensions and wall thicknesses was within normal limits (septum: 0.6 cm, PWT: 0.6 cm, LVIDd: 4.1 cm, LVIDs: 3.5 cm, LVMI: 42g/m^2, Figure 4). Patient developed hypoxia and showed signs of flash pulmonary edema on chest x-ray and auscultation. Furosemide was given and 500cc serosanguinous fluid was suctioned from the endotracheal tube. Subsequently, the patient was transferred intubated to the cardiac intensive care unit. No inotropes were used following resuscitation. At 2 hours post transfer, the patient was

stable without any pressor support and neurologically fully intact and extubated. The patient was transferred for further workup to a tertiary children's hospital. MRI of the heart showed mid-septum moderate hypertrophy with a maximal dimension of 1.7 cm on the 4-chamber view and 1.5 cm on short axis (mid-inferior septum) view with no significant obstruction. TTE showed normal coronary arteries and mild left ventricular hypertrophy (septum: 0.7 cm, PWT: 0.85 cm, LVIDd: 4.8 cm, LVIDs: 3.4 cm, LVMI: 33g/m^2, EF 58%) with uncertain correlation for the cardiac event, and the patient was discharged home with no complications.

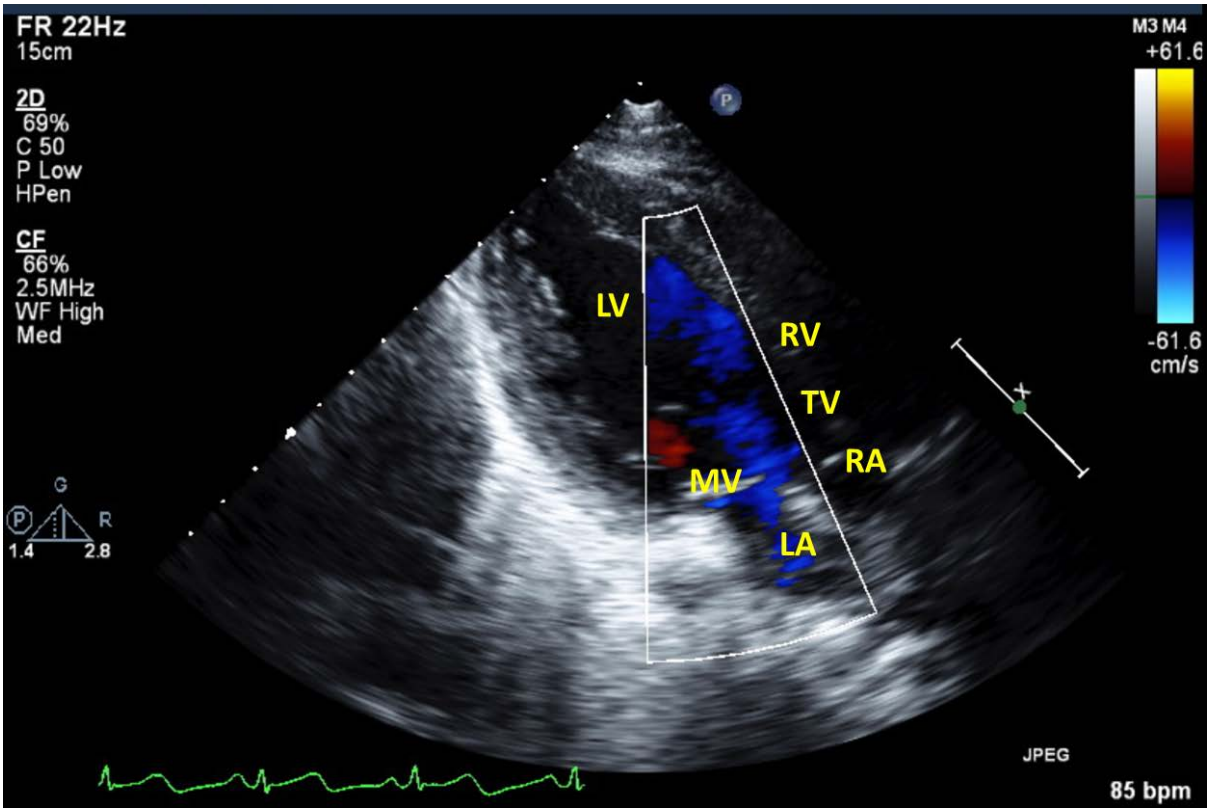

Figure 1. Mitral valve regurgitation after cardiopulmonary resuscitation

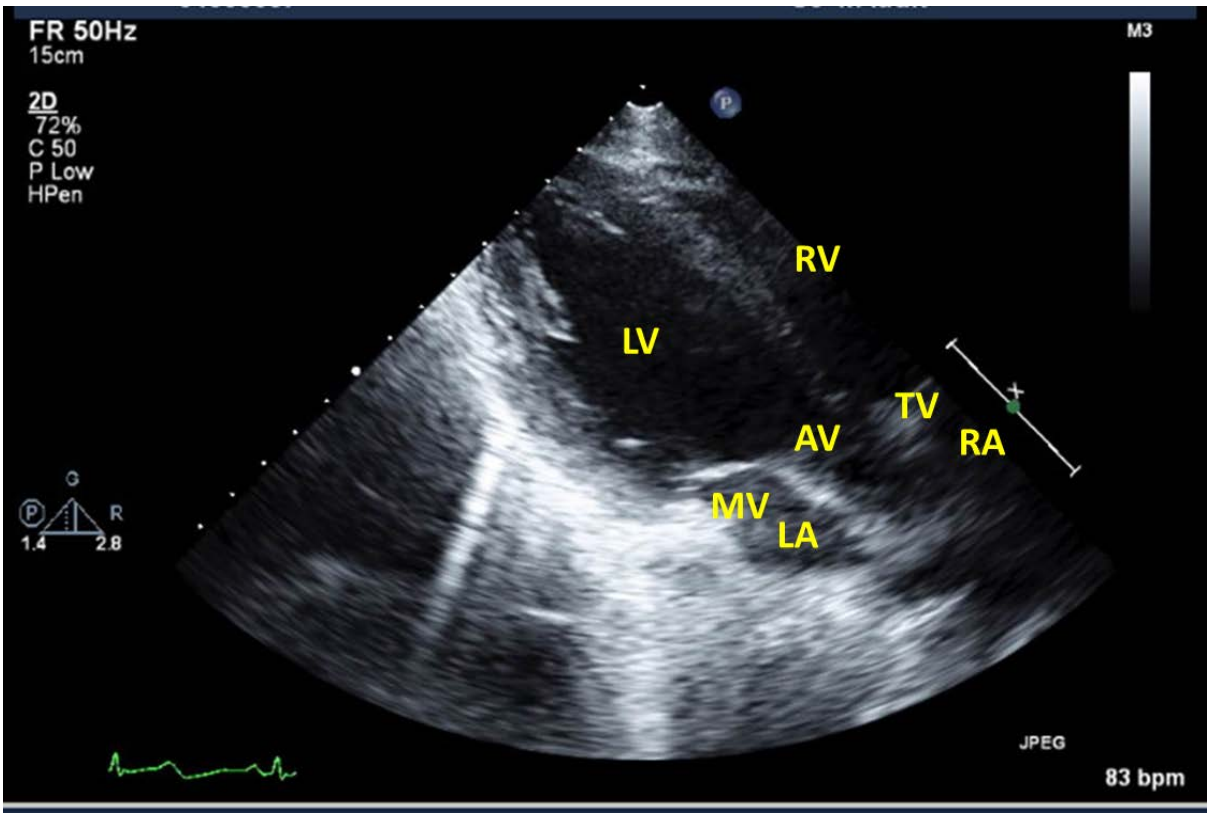

Figure 2. Reverse takotsubo - Basal and midventricular dysfunction of the left ventricle in diastole

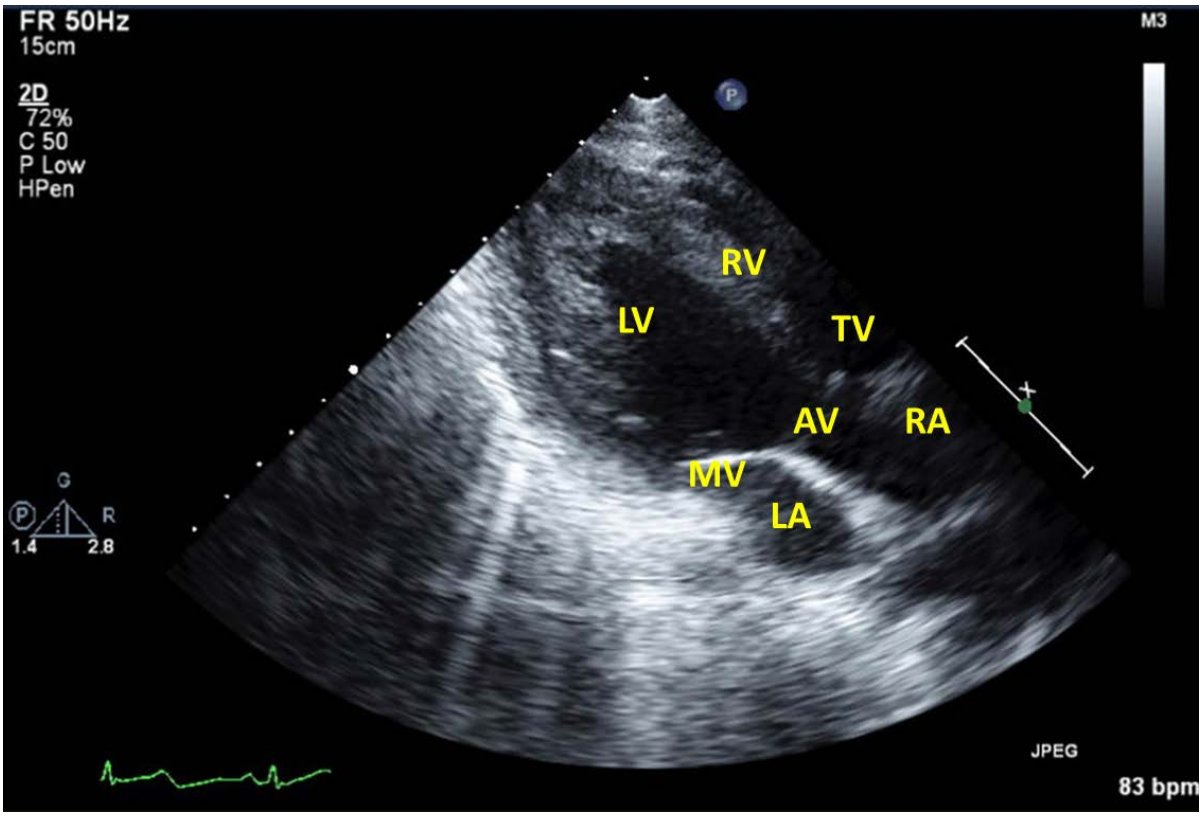

Figure 3. Reverse takotsubo - Basal and midventricular dysfunction of the left ventricle in systole.

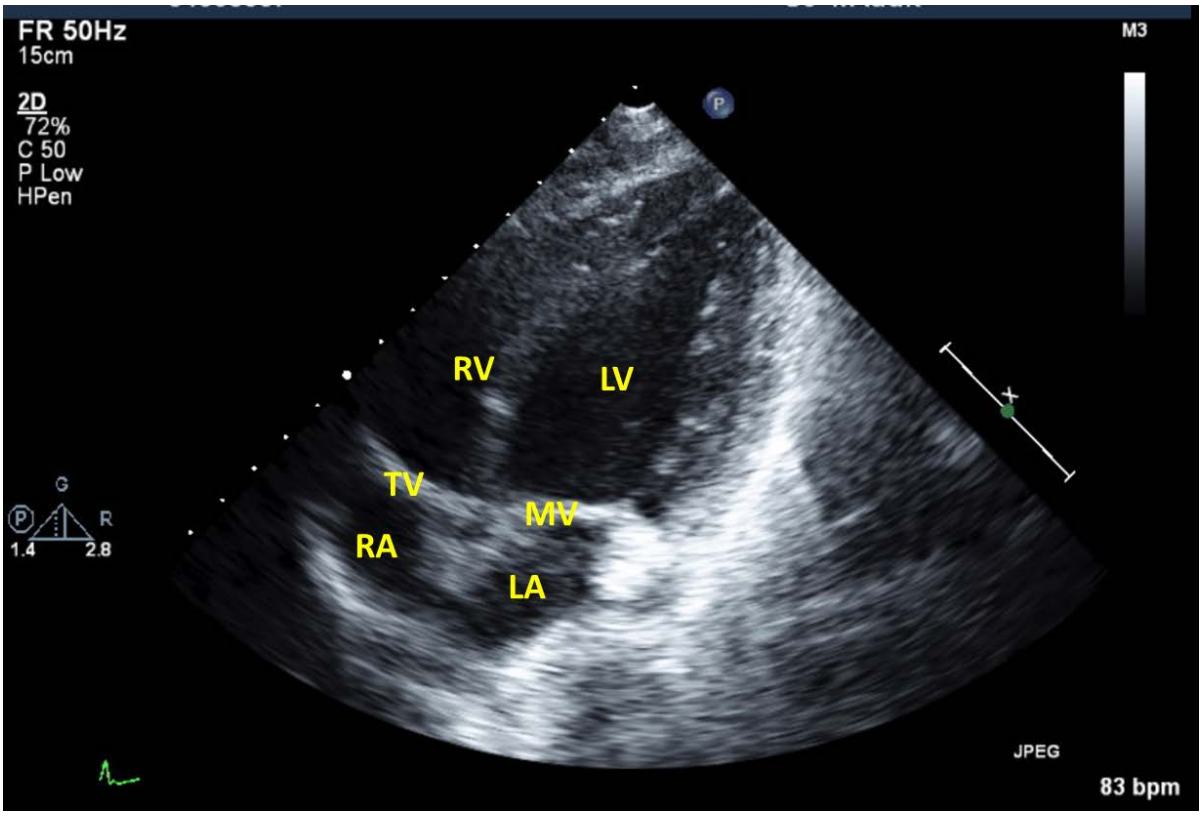

Figure 4. Apical four chamber view

3. Discussion

This case report describes a patient who experienced severe hypertension and tachycardia, most likely related to systemically absorbed topical phenylephrine and intramucosal injected epinephrine. Consequently, the catecholamine overdose and beta blocker treatment caused acute ventricular dysfunction that led to cardiogenic shock, mitral regurgitation, and pulmonary edema. The patient age group combined with the exposure to catecholamine is consistent with the pathophysiology commonly seen in takotsubo cardiomyopathy.

Anesthesiologists use topical phenylephrine as a vasoconstrictor before nasotracheal intubation to prevent nasal mucosal bleeding. Systemic absorbtion of phenylephrine can cause arterial and venous vasoconstricton and the increase in peripheral vascular resistance can cause severe hypertension. Usually deepening anesthesia and beta blocking agent controls the severe hypertension and tachycardia in those patients. However, a high incidence of pulmonary edema has been found in patients who received phenylephrine followed by β-blocking agents, and intra-operative cardiac arrests have been reported, as well [2]. Cardiac arrest and subsequent death have been reported after the use of topical phenylephrine in a 4-year-old, 9-year-old, and 26-year-old patient. All of the patients were treated with β-blocking agents to control the hypertension and tachycardia. Alpha-adrenergic stimulation can increase peripheral vascular resistance significantly, leading to an increase in left ventricular filling pressure. To preserve cardiac output under these circumstances, increased heart rate and contractility are important compensatory mechanisms. These compensatory mechanisms can be impaired after β-blocker administration leading to increased pulmonary pressure and subsequent pulmonary edema. The β-blockers esmolol and labetalol have been associated with the development of pulmonary edema, but only labetalol use has been associated with death. In these cases, the short duration of esmolol may explain why the pulmonary edema did not progress to cardiac arrest and death [3]. Neitherless, phenylephrine and a subsequent β-blocker administration should be done with caution.

First described in 1990, Takotsubo cardiomyopathy is a transient systolic dysfunction of the apical segments or mid segments of the left ventricle that occurs in the absence of coronary artery disease. The Mayo [4] and Japanese [5] diagnosis criteria are listed in Table 1. Four variants have been reported; classical, reverse, mid-ventricular, and localized. The classical type with left ventricular apical dysfunction, is the most common. Reverse-takotsubo cardiomyopathy, which is characterized by basal and midventricular dysfunction with preserved apical function, has different clinical and biological characteristics than the classical type. Reverse-takotsubo is known to occur more frequently in younger patients[1] and is often stress induced. Patients with reverse-takotsubo cardiomyopathy also have significantly higher levels of cardiac markers, such as CK-MB and troponin, perhaps because their myocardium is affected to a greater extent than in patients with classic-takotsubo cardiomyopathy [6].

The pathophysiology of takotsubo cardiomyopathy is not well understood. Three theories may explain the mechanism. The first is vasospasm: Patients with takotsubo cardiomyopathy undergoing angiography have demonstrated severe global coronary spasm [7]. The second is coronary microvascular dysfunction: Several studies have suggested that impaired myocardial perfusion due to abnormal microvascular blood flow may play a pivotal role [8]. The third is excessive circulating endogenous or exogenous catecholamines: Takotsubo cardiomyopathy could be triggered by physical or emotional stress or by catecholaminergic states such as an endogenic catecholamine-producing tumor like pheochromocytoma. Additionally, exposure to iatrogenic catecholamines and beta-receptor agonists, used routinely during procedures and diagnostic tests, can precipitate takotsubo cardiomyopathy [9]. Also anaphylaxis treated with intravenous epinephrine has been reported to result in reverse-takotsubo [10]. Zubrinich et al. [11] showed that even when epinephrine is injected at low intravenous doses (0.1 mg x 2), it may result in the occurrence of takotsubo cardiomyopathy.

Reverse-takotsubo seems to be more common in young patients (mean age = 36 years). This may be due to the abundance of adrenoreceptors at the base of the heart in younger individuals compared with in the apex in older individuals [12]. With symptomatic treatment, left ventricular failure and cardiac function typically normalize within a few weeks. The overall mortality associated with takotsubo cardiomyopathy is very low, and, as in this case, most patients fully recover cardiac function with supportive therapy. Whether to use of β-adrenoceptor blockers in the acute phase of takotsubo cardiomyopathy is a matter of debate. Given the findings in the animal model, treatment with a combined α- and β-blocker seems rational, whereas treatment with catecholamine as an inotrope seems contraindicated after initial resuscitation. Since the underlying mechanism of takotsubo cardiomyopathy is excessive circulating catecholamines, cardiotonic agents might worsen the cardiac function. When shock occurs, intraaortic balloon pumping instead of inotropes may be useful to establish additional support for the circulation.

A guideline that was published by the New York State in 2000 advised that an initial dose of topical phenylephrine should not exceed 0.5 mg (four drops of a 0.25% solution) for adults and 20 μg/kg for children (up to 25 kg). It also advised that β-blockers and calcium-channel blockers should be avoided when vasoconstrictive agents such as phenylephrine are used [2]. After this incident described in this case report, the use of topical phenylephrine was completely abandoned from the operating room and replaced with oxymetazoline nasal spray. Oxymetazoline was reported to cause less hypertension [13].

Table 1. Diagnosis criteria for takotsubo cardiomyopathy

Mayo-Clinic criteria	Japanese criteria
1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always present.	1. Acute left ventricular apical ballooning of unknown cause. Nearly complete resolution of the apical akinesis in the majority of the patients within a month. A dynamic obstruction of the left ventricular outflow tract is also observed
2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.	2. Exclusion of significant organic stenosis or spasm of a coronary artery and acute myocardial infarction
3. New electrocardiographic abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin.	3. Exclusion of cerebrovascular disease
4. Absence of: Pheochromocytoma, Myocarditis	4. Exclusion of viral or idiopathic myocarditis
	5. Exclusion of pheochromocytoma

Upon discharge from the children's hospital the patient was diagnosed with hypertrophic cardiomyopathy (HCM). HCM must have developed after the cardiac event since the patient did not have a history of any cardiac disease preoperatively and the intraoperative TTE showed no signs of HCM. HCM during recovery from takotsubo cardiomyopathy has been reported recently by Kato et al. [14]. The transient apical hypertrophy was attributed to hypertrophic signaling in the myocardium, which was stimulated by catecholamine's and the hypertrophied myocardium gradually returned to normal as the syndrome receded. Additionally, takotsubo induced myocardial edema resulting in hypertrophic LV-apex is occasionally seen in the subacute and chronic phase of convalescence from takotsubo cardiomyopathy. Whether the LV-hypertrophy represents HCM or takotsubo-induced myocardial edema can be resolved by observing subsequent electrocardiograms for chronically persisting giant negative T-waves and R-waves in the mid-precordial leads, and by comparing old and follow-up echocardiograms [15].

LV-systolic dysfunction and wall motion abnormalities reverse rapidly, returning to normal range as early as 5 days [16]. The full recovery time varies between patients and can be as short as several days or as long as several weeks.

4. Conclusion

Appropriate use of topical vasoconstrictors like phenylephrine and local anesthetic with epinephrine is important, especially in dental or ear, nose and throat procedures. Reverse-takotsubo cardiomyopathy is a variant of the classic takotsubo cardiomyopathy with similar pathophysiological causes but more common presentation in young patients. Even a small dosage of epinephrine can lead to this temporally but severely depressed left ventricular function.

Conflicts of Interest

None.

Funding

None.

References

[1] Ramaraj R, Movahed MR. Reverse or inverted takotsubo cardiomyopathy (reverse left ventricular apical ballooning syndrome) presents at a younger age compared with the mid or apical variant and is always associated with triggering stress. Congest Heart Fail.16 (6). 284-286. November 2010.

[2] Schwalm JD, Hamstra J, Mulji A, Velianou JL. Cardiogenic shock following nasal septoplasty: a case report and review of the literature. Can J Anaesth. 55(6). 376-9. June 2008.

[3] Groudine SB1, Hollinger I, Jones J, DeBouno BA. New York State guidelines on the topical use of phenylephrine in the operating room. The Phenylephrine Advisory Committee. Anesthesiology. 92(3). 859-64. March 2000.

[4] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J. 2008 Mar; 155(3): 408-17.

[5] Kawai S, Kitabatake A, Tomoike H; Takotsubo Cardiomyopathy Group. Guidelines for diagnosis of takotsubo (ampulla) cardiomyopathy. Circ J. 71(6). 990-2. June 2007.

[6] Song BG, Chun WJ, Park YH, et al. The clinical characteristics, laboratory parameters, electrocardiographic, and echocardiographic findings of reverse or inverted takotsubo cardiomyopathy: comparison with mid or apical variant. Clin Cardiol. 34 (11). 693-699. November 2011.

[7] Nojima Y, Kotani J. Global coronary artery spasm caused takotsubo cardiomyopathy. J Am Coll Cardiol. 55 (9). e17. March 2010.

[8] Khalid N. Microcirculatory disorder hypothesis in Takotsubo cardiomyopathy. Int J Cardiol. 195. 29. September 2015.

[9] Abraham J, Mudd JO, Kapur NK, Klein K, Champion HC, Wittstein IS. Stress cardiomyopathy after intravenous administration of catecholamines and beta-receptor agonists. J Am Coll Cardiol. 53 (15). 1320-1325. April 2009.

[10] Khoueiry G, Abi Rafeh N, Azab B, et al. Reverse Takotsubo cardiomyopathy in the setting of anaphylaxis treated with high-dose intravenous epinephrine. J Emerg Med. 44(1). 96-99. January 2013.

[11] Zubrinich CM, Farouque HMO, Rochford SE, Sutherland MF. Tako-tsubo-like cardiomyopathy after EpiPen administration. Intern Med J. 38 (11). 862-865. November 2008.

[12] Patankar GR, Choi JW, Schussler JM. Reverse takotsubo cardiomyopathy: two case reports and review of the literature. J Med Case Rep. 7. 84. March 2013.

[13] Riegle EV, Gunter JB, Lusk RP, Muntz HR, Weiss KL.Comparison of vasoconstrictors for functional endoscopic sinus surgery in children. Laryngoscope. 102 (7). 820-3. July 1992.

[14] Kato T, Ban Y, Kuruma S, Ishida S, Doi C, Iura T, Terawaki H, Inoko M, Nohara R. Two cases of reversible left ventricular hypertrophy during recovery from takotsubo cardiomyopathy. Echocardiography. 30 (1). 92-94. February 2013.

[15] John E. Madias. Myocardial Apical Hypertrophy and Takotsubo Cardiomyopathy. Tex Heart Inst J. 41 (5). 568. October 2014.

[16] Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, Maron BJ. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation. 111 (4). 472-9. February 2005.