



Clinical Communications: Adults

REVERSE TAKOTSUBO CARDIOMYOPATHY IN THE SETTING OF ANAPHYLAXIS TREATED WITH HIGH-DOSE INTRAVENOUS EPINEPHRINE

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Abstract—Background: Takotsubo cardiomyopathy is seen, though rarely, in anaphylaxis treated with epinephrine. Stress cardiomyopathy is most likely to occur in middle-aged women. The underlying etiology is believed to be related to catecholamine release in periods of intense stress. Catecholamines administered exogenously, and those secreted by neuroendocrine tumors (e.g., pheochromocytoma) or during anaphylaxis have been reported to cause apical ballooning syndrome, or takotsubo syndrome. However, reverse takotsubo stress cardiomyopathy is rarely seen or reported in anaphylaxis treated with epinephrine. **Objectives:** To report a case illustrating that high-dose intravenous epinephrine can trigger stress cardiomyopathy, and that the risk is heightened with inappropriate dosing in the treatment of anaphylaxis. **Case Report:** We report a rare case of iatrogenic reverse takotsubo syndrome in a young woman who was inappropriately treated with high-dose intravenous epinephrine for mild anaphylaxis. **Conclusion:** Inappropriately high doses of intravenous epinephrine can trigger stress cardiomyopathy. Emergency physicians should be familiar with the diagnosis, grading, and appropriate treatments of anaphylaxis to avoid this unnecessary complication. © 2012 Elsevier Inc.

Keywords—iatrogenic cardiomyopathy; reverse takotsubo; acute coronary syndrome; anaphylaxis; epinephrine

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INTRODUCTION

Apical ballooning syndrome (ABS), or takotsubo syndrome, initially described in Japan, is characterized by transient wall motion abnormalities involving the apical segment (1). Recently, several variants have been described, including a reverse type in which the wall motion abnormalities are seen at the base while the apex is hyperdynamic (2). Stress cardiomyopathy is most likely to occur in middle-aged women (1). The underlying etiology is believed to be related to catecholamine release in periods of intense stress. There are a few case reports that link catecholamines, either administered exogenously or secreted by neuroendocrine tumors (e.g., pheochromocytoma) or during anaphylaxis, to ABS (3–8). However, reverse takotsubo stress cardiomyopathy is rarely seen in anaphylaxis treated with epinephrine (6). We report a rare case of iatrogenic reverse takotsubo syndrome seen in a young woman who was inappropriately treated with high-dose intravenous epinephrine for mild anaphylaxis.

CASE REPORT

A 44-year-old woman developed wheezing and chest tightness a few seconds after the administration of intravenous (i.v.) contrast for elective outpatient computed

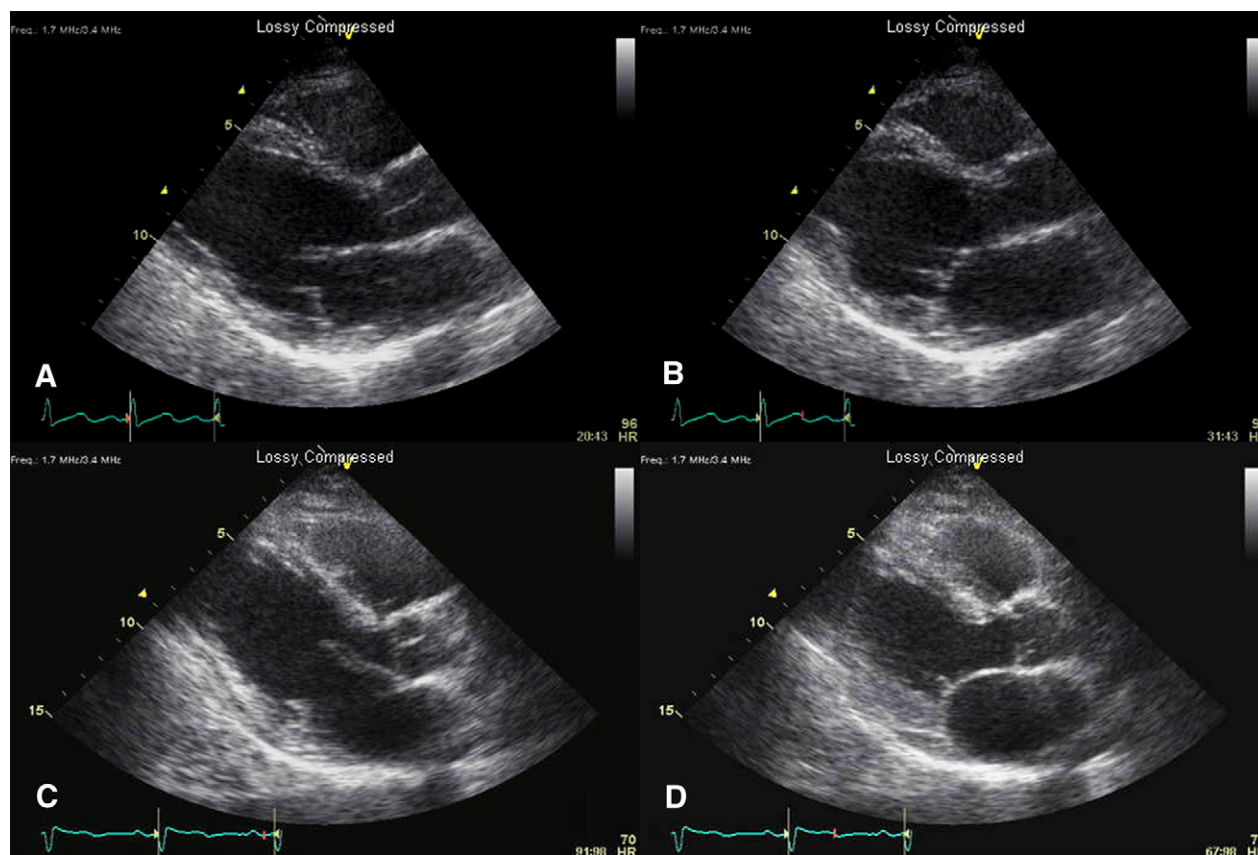


Figure 1. Two-dimensional echocardiogram, parasternal long-axis view, showing the anteroapical and posterolateral walls of the left ventricle. (A,B) End-diastolic and mid-systolic frames at the time of presentation showing an akinesis of the basal segments. (C,D) End-diastolic and mid-systolic frames on hospital day 4 showing a normalization of the segmental wall motion abnormalities.

tomography (CT) scan of the abdomen and pelvis. Her medical history included hypertension and a neurogenic bladder. She was subsequently given albuterol and oxygen, with no relief. Due to the ongoing chest discomfort and respiratory distress, the patient was given 1 mg (1:1000) of epinephrine intravenously. Immediately after this injection, she began experiencing severe chest tightness and respiratory distress, developed a headache, became diaphoretic, and experienced a transient loss of consciousness lasting a few seconds.

She was transferred to a tertiary care center. Upon arrival in the Emergency Department, her vital signs were: blood pressure 80/71 mm Hg, pulse 82 beats/min, respiratory rate 18 breaths/min, temperature 37°C, and oxygen saturation 100% on room air. She was given boluses of normal saline that increased her blood pressure to 100/73 mm Hg, and was treated with dexamethasone and antihistamines. Two hours later, the patient still had chest tightness and shortness of breath, began coughing up blood-tinged sputum, and became tachycardic to 110 beats/min. The chest auscultation was significant for crackles in both lung fields. Other physical findings re-

vealed cold extremities, but no rash. A chest radiograph revealed interstitial edema at both lung bases. An electrocardiogram showed normal sinus rhythm at 80 beats/min with non-specific ST-segment changes. She had a creatinine kinase-MB level of 2.9 ng/mL (reference ranges provided parenthetically) (≤ 5 ng/mL) and troponin I level of 0.56 ng/mL (≤ 0.05 ng/mL). Bedside echocardiography revealed hypokinesis of the mid and basal segments of the anterior, anteroapical, anterolateral, inferolateral, inferior, and inferoseptal walls. The apical segments were hyperdynamic and the ejection fraction was about 35% (Figure 1, Video 1). She received intravenous furosemide and her symptoms improved.

The patient continued to complain of non-specific left-sided chest discomfort, and her cardiac enzymes peaked on hospital day 2, with a creatinine kinase-MB level of 13.4 ng/mL (≤ 5 ng/mL) and troponin I level of 3.23 ng/mL (≤ 0.05 ng/mL). On hospital day 4, the patient was asymptomatic. A repeat two-dimensional echocardiogram revealed an ejection fraction of 50% with only minimal regional wall motion abnormalities (Figure 1, Video 2). A Persantine (Boehringer-Ingelheim,

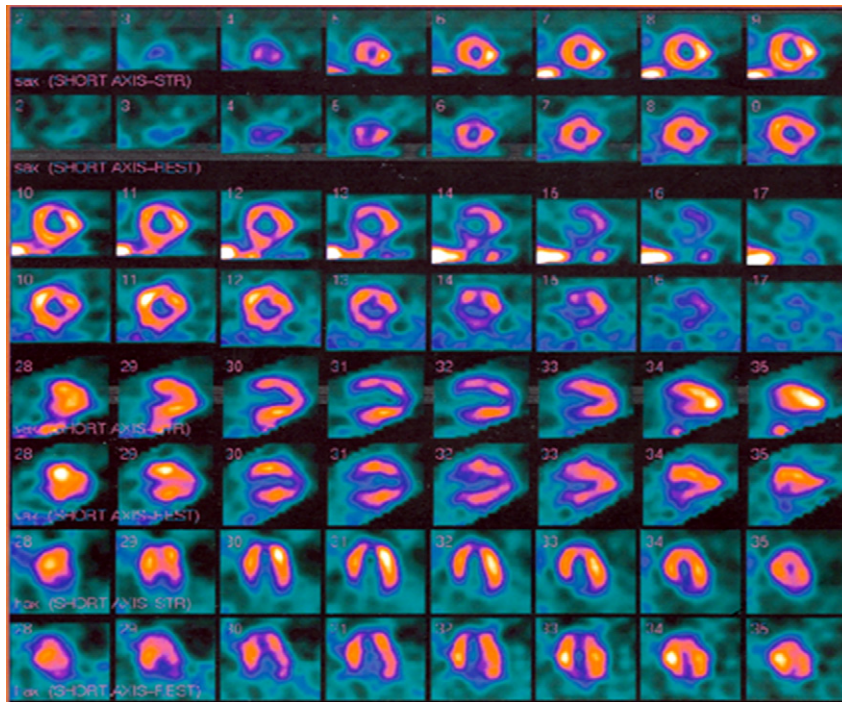


Figure 2. Persantine (Boehringer-Ingelheim, Ridgefield, CT) and rest myocardial perfusion computed tomography scan showing no evidence of ischemia during Persantine infusion.

Ridgefield, CT) thallium stress test demonstrated no evidence of ischemia, mild generalized hypokinesia, and a left ventricle ejection fraction of 54% (Figure 2). The patient was discharged home and was instructed to follow-up with Cardiology as an outpatient.

At 3-week follow-up, she continued to be asymptomatic. A CT coronary calcium score was zero. Stress echocardiography testing was performed that showed normal resting wall motion, ejection fraction, and an appropriate augmentation of all left ventricular segments at peak exercise (Video 3). The patient was scheduled for an elective cardiac catheterization, which showed no evidence of coronary artery disease.

DISCUSSION

There are few explanations for acute coronary syndrome (ACS) after anaphylactic reaction in patients receiving epinephrine. Stress cardiomyopathy (including takotsubo and reverse takotsubo syndrome), allergic myocardial infarction (also known as Kounis syndrome [KS]), and hypersensitive myocarditis (HM) are possible etiologies (3).

Stress cardiomyopathy usually affects middle-aged women during emotional stress. The syndrome is characterized by ACS with or without elevation in cardiac enzymes, reversible apical or basal ventricular dysfunction, and the presence of normal coronaries. In our case, a reverse takotsubo cardiomyopathy pattern was noticed on presentation. There are only a few case reports of stress

cardiomyopathy due to epinephrine injection, and very few reports of the reverse takotsubo type (4). A case has been reported of ABS post-anaphylaxis when epinephrine was not given. In anaphylaxis, the renin-angiotensin-aldosterone system is activated and histamine is released, leading to catecholamine release (9). It is very difficult to identify the real cause of myocardial stunning in our patient, which could be from the anaphylaxis and/or the treatment with epinephrine. However, the high dose of epinephrine is the most probable cause because the initial allergic reaction to contrast was not severe. Regardless of the etiology, the underlying mechanism is the same, catecholamine-induced stunning and microvascular dysfunction.

During anaphylaxis, histamine and a variety of other cytokines are released by mast cells, macrophages, and T lymphocytes, leading to coronary vasospasm, a process known as Kounis syndrome (10). There are currently two types of KS. The first is observed in patients with no cardiovascular risk factors and healthy coronaries, as in our case. The second involves patients with established coronary artery disease (11). This syndrome can occur in association with stress cardiomyopathy, as the two syndromes often share common inflammatory mediators (3,12). Hypersensitive myocarditis (HM) is a hypersensitive reaction that involves the heart. Clinically, it is very difficult to differentiate it from KS, as both present with ACS and normal coronary arteries. The main difference between the two entities is the presence of eosinophils,

atypical lymphocytes, and giant cells on myocardial biopsy in HM but not in KS (1).

There are no universally accepted clinical criteria for the diagnosis of anaphylaxis. For this reason, there is controversy around the dose and route of administration of epinephrine in anaphylaxis. According to the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network, anaphylaxis is likely to be present when two organs are affected after exposure to an allergen (13). Some reports suggest that in cases of mild anaphylaxis, only intramuscular (i.m.) epinephrine should be used early (14). Due to the higher incidence of cardiovascular complications, i.v. epinephrine should be reserved for patients with severe hypotension who do not respond to the i.m. dose, or those in cardiac arrest (14,15). On the other hand, others believe that the route of epinephrine administration is not the issue if a four-step clinical scale is followed (4,16). Whereas grade 1 involves cutaneous-mucous signs and should not be treated, grade 2 is associated with cardiovascular or respiratory signs, for which titrated i.v. boluses of epinephrine (0.01–0.02 mg) may be required. In Grade 3, the hallmark is cardiovascular collapse, and titrated i.v. boluses of epinephrine (0.1–0.2 mg) are required. Finally, grade 4 represents cardiac arrest, for which a high dose of i.v. epinephrine is needed (16).

CONCLUSION

Regardless of the optimal route of epinephrine therapy, the delivered dose was too high in this case of grade 2 anaphylaxis. Physicians should be well aware of the route and dose protocols of epinephrine, especially for grades 1 and 2 anaphylaxis. Our case report should alert physicians to the risk of stress cardiomyopathy with inappropriate dosing of epinephrine during the treatment of anaphylaxis.

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SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.jemermed.2011.09.032](https://doi.org/10.1016/j.jemermed.2011.09.032).

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