Severe Reversible Left Ventricular Systolic and Diastolic Dysfunction Due to Accidental Iatrogenic Epinephrine Overdose

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Catecholamine-induced cardiomyopathy due to chronic excess of endogenous catecholamines has been recognized for decades as a clinical phenomenon. In contrast, reports of myocardial dysfunction due to acute iatrogenic overdose are rare. A 35-year-old woman whose cervix uteri was inadvertently injected with 8 mg of epinephrine developed myocardial stunning that was characterized by severe hemodynamic compromise, profound, albeit transient, left ventricular systolic and diastolic dysfunction, and only modestly elevated biochemical markers of myocardial necrosis. Our case illustrates the serious consequences of medical errors that can be avoided through improved medication labeling and staff supervision.

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Key words: Echocardiography • Left ventricular dysfunction • Epinephrine • Stunning

A 35-year-old female with a past medical history significant only for an abnormal Papanicolaou smear presented to the gynecology clinic for elective loop electrosurgical excision procedure (LEEP) of the cervix. After topical anesthesia with 1% Xylocaine® Jelly, the patient's cervix was meant to have been injected with an 8 mL solution containing 1% lidocaine HCl and 1:100,000 epinephrine (Xylocaine® with epinephrine; AstraZeneca). However, unknown to the gynecologist, the patient was inadvertently injected with an 8 mL solution containing solely 1:1000 epinephrine.

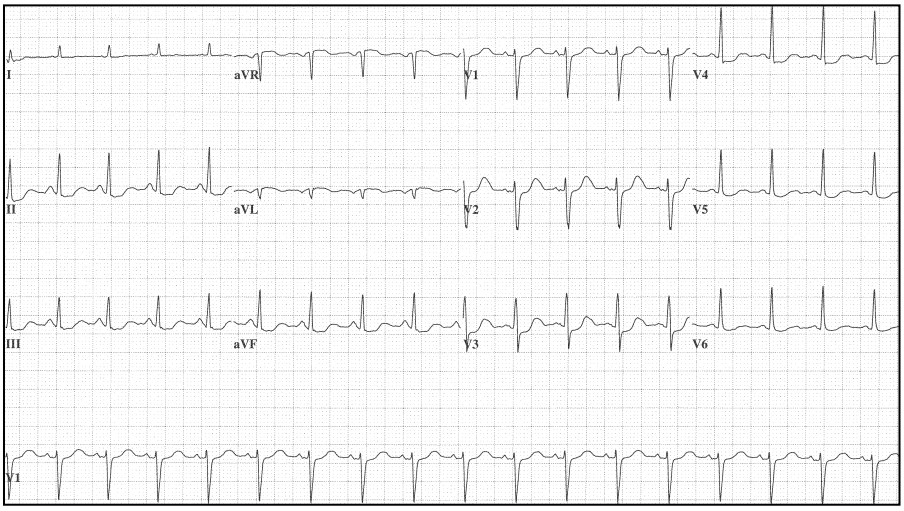

Figure 1. *Electrocardiogram obtained soon after epinephrine overdose. Note ST segment and T wave changes in leads II, III, aV_F, and $V_{3–5}$.*

Shortly afterward, the patient developed heart palpitations, chest pain, headache, fever, and abdominal pain. She also became hypotensive with a blood pressure reading of 80/50 mm Hg and developed sinus tachycardia at a rate of 120 beats/min.

Diagnosis and Treatment

Because she was initially thought to have developed an allergic reaction to Xylocaine®, she was treated with intravenous Benadryl® (50 mg; Warner-Lambert) and normal saline. Nonetheless, she required intubation for respiratory support and intravenous dopamine to sustain her blood pressure.

Findings of the electrocardiogram were significant for repolarization abnormalities in limb leads II, III, and aVF, as well as in precordial leads V3 through V5 (Figure 1). Plasma troponin I, creatine phosphokinase myocardial band (CPK-MB) mass, amount, and CPK-MB fraction peaked within 24 hours of the inadvertent epinephrine injection (Table 1).

A transthoracic echocardiogram (TTE) performed soon after resuscitation revealed normal cardiac chamber sizes. The basal and mid segments of all left ventricular (LV) walls were akinetic. However, all apical LV segments were hyperdynamic. The overall ejection fraction was severely reduced to 20%.

Spectral Doppler flow velocity pattern across the mitral valve and in the right upper pulmonary vein was suggestive of severe (grade III) LV diastolic dysfunction (Table 2). There was also mild-to-moderate mitral valve insufficiency and no pericardial effusion.

Emergent cardiac catheterization revealed normal epicardial coronary arteries, severely decreased LV systolic function (cardiac index by Fick method of 1.5 L/min/m^2), and elevation of both left and right heart pressures (mean pulmonary capillary wedge pressure = 33 mm Hg, peak right ventricular systolic pressure = 61 mm Hg). Furthermore, systemic vascular resistance (SVR) was elevated (1700 dynes/s/cm^{-5}). Based on these hemodynamic data, a diagnosis of cardiogenic shock secondary to accidental iatrogenic epinephrine overdose was established. An intra-aortic balloon pump was used to maintain adequate blood pressure over the next several days.

A follow-up, in-hospital TTE performed 3 days after the initial episode still showed akinesis of basal and mid segments of the inferior wall and the interventricular septum. However, the basal and mid segments of the other LV walls had regained contractility. LV ejection fraction increased to about 35%. LV diastolic function improved to grade I (Table 2).

Two weeks later, the patient was

Table 1
Profile of Cardiac Markers Following Epinephrine Overdose

Hours After Epinephrine Injection	CPK-MB Mass (ng/mL)	CPK-MB Fraction (%)	Troponin I (ng/mL)
3	12.6	7.9	11
9	35.9	14.0	58
17	60.3	8.8	49
39	29.4	2.1	10
54	13.4	1.5	5
Normal Values		<5	<5

CPK-MB, creatine phosphokinase myocardial band.

Table 2
Left Ventricular Systolic and Diastolic Function Following Epinephrine Overdose

Time After Epinephrine Overdose	LVEF	Mitral Inflow		Pulmonary Venous Flow		Diastolic Function
		E/A	DT (ms)	S/D	Peak AR Wave Velocity (cm/s)	
Day 0	20%	2.0	95	<1	45	Severely abnormal
Day 3	35%	0.9	217	1	29	Mildly abnormal
Day 19	60%	1.9	178	>1	23	Normal

AR, pulmonary vein atrial reversal wave; DT, deceleration time of early diastolic mitral wave; E/A, ratio of early-to-late peak velocity of mitral diastolic inflow; LVEF, left ventricular ejection fraction; S/D, ratio of systolic-to-diastolic peak velocity of antegrade pulmonary venous flow.

asymptomatic and her outpatient TTE revealed normalization of both systolic and diastolic LV function.

The time course of transient left ventricular systolic and diastolic dysfunction in this patient is consistent with epinephrine-induced myocardial stunning.

Discussion

Epinephrine is used parenterally either alone or in combination with a local anesthetic. When used singly, such as for hemodynamic support during anaphylactic shock, it is routinely administered subcutaneously using a 1:1000 solution, which delivers 1 mg of epinephrine per mL of solution. The usual total dose of epinephrine in cases of shock is 0.3 – 0.5 mg.

This case is only the third case of catecholamine-induced reversible myocardial stunning ... and the first to document profound LV diastolic dysfunction.

In contrast, epinephrine is used at much smaller dosages when combined with a local anesthetic in an attempt to prolong the duration of the anesthesia. In such instances, epinephrine is usually delivered using dilutions of 1:100,000, which deliver 0.01 mg of epinephrine per mL of solution.

Because of a medication error, our patient, who should have received a total dose of 0.08 mg epinephrine, received instead 8 mg epinephrine, a hundred-fold overdose.

Shortly after epinephrine overdose, the patient developed heart palpitations, chest pain, headache, and abdominal pain.

Catecholamine-induced cardiomyopathy due to chronic excess of endogenous catecholamines[1] or caused by deliberate short-term experimental overdosage of catecholamines in animals[2] has been recognized for decades as a clinical phenomenon.

Common clinical conditions leading to endogenous catecholamine excess include pheochromocytoma,[3] cocaine use,[4] and subarachnoid hemorrhage.[5] In a series of 51 patients with catecholamine-secreting tumors, echocardiographic evidence of LV hypertrophy was observed in 45% of patients while the prevalence of impaired LV contractility was 24%.[6]

Two mechanisms of catecholamine-induced myocardial injury have been proposed: (1) direct toxic effect on myocytes and (2) vasomotor constriction of the coronary microcirculation causing myocardial stunning.[7] Because both mechanisms may lead to intracellular calcium overload or oxidative stress, catecholamine-induced injury may, at least in part, represent a form of myocardial stunning.[8,9]

In contrast to numerous reports of pheochromocytoma-related myocardial dysfunction,[3,6,10–12] ours is only the third case of catecholamine-induced reversible myocardial stunning due to iatrogenic overdose and the first to document not only LV systolic but also profound LV diastolic dysfunction.

Of the prior two cases reported, interestingly, one of the patients had been inadvertently injected into the cervix uteri, just as our

patient was, with a similar dosage of epinephrine.[13]

The pattern and the time course of LV dysfunction in our patient demonstrates the most salient features of acute catecholamine-induced myocardial stunning: rapid development of profound (often global) LV systolic dysfunction, significant hemodynamic compromise, a large discrepancy between the severity of LV contractile impairment and the modest rise in serum markers of myocardial necrosis (such as CPK-MB and troponin I), and complete reversal of myocardial dysfunction within weeks of cessation or inhibition of adrenergic activation of the heart.[10,13,14]

Our case illustrates the serious consequences of medical errors that can be avoided through improved medication labeling and staff supervision. ■

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Main Points

- This case is the first to document not only LV systolic but also profound LV diastolic dysfunction during reversible myocardial stunning.
- LV dysfunction demonstrates the most significant features of acute catecholamine-induced myocardial stunning: rapid development of profound LV systolic dysfunction, significant hemodynamic compromise, a large discrepancy between of LV contractile impairment and rise in serum markers of myocardial necrosis, and complete reversal of myocardial dysfunction.
- Serious consequences of medical errors can be avoided through improved medication labeling and staff supervision.