Epinephrine induced cardiomyopathy in a child with anaphylaxis

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Abstract

Transient cardiomyopathy is an uncommon occurrence in patients with anaphylaxis. Catecholamine induced direct toxicity is one of the proposed mechanisms. We report a case of cardiomyopathy in a child with anaphylaxis who was treated with multiple doses of epinephrine as well as a continuous infusion of epinephrine. A twenty one month old girl with egg allergy presented to our hospital with anaphylaxis, after multiple doses of epinephrine injections, developed cardiorespiratory dysfunction and required endotracheal intubation and mechanical ventilation. Work up showed depressed cardiac function, which improved with milrinone and furosemide infusions. Conclusion: Epinephrine is the treatment of choice for anaphylaxis however caution should be exercised when administering multiple doses of epinephrine. Myocardial function needs to be assessed in children with persistent hypotension after anaphylaxis and catecholamine-induced cardiomyopathy should be considered in children with anaphylaxis when severe myocardial dysfunction is present.

Key words: anaphylaxis, epinephrine, cardiomyopathy, children

Introduction

Transient cardiomyopathy is an uncommon occurrence in patients with anaphylaxis and catecholamine induced direct toxicity is one of the proposed mechanisms. Epinephrine is the treatment of choice for anaphylaxis. Catecholamine-induced cardiomyopathy should be considered in children with persistent hypotension following multiple doses of epinephrine and needs myocardial function assessment.

Case presentation

A twenty-one-month old female presented to our hospital emergency room with an acute onset of a perioral rash, vomiting, cough, and generalized itching. She had a past medical history of egg allergy; one hour prior to admission she had eaten meat loaf, which had been prepared with milk and eggs. Her parents administered an oral antihistamine and brought her to the emergency room because of continued respiratory distress.

In the emergency room, during a period of twenty minutes, the patient received three injections of epinephrine at a dose of 0.01mg/kg (one dose intramuscular (IM) and two doses intravenous (IV)) and a racemic epinephrine nebulization. Despite these treatments, her work of breathing continued to increase and she became hypotensive. Three boluses of 20 ml/kg of normal saline were infused and a continuous infusion of epinephrine was initiated at a dose of 1 mcg/kg/min for treatment of the hypotension.

Upon admission to the Pediatric Intensive Care Unit (PICU), the child was noted to have increased work of breathing, tachycardia (180-200 bpm) and poor peripheral perfusion. The patient was intubated and mechanically ventilated. The patient developed pink frothy secretions at the time of intubation. Her chest X-ray was interpreted as consistent with pulmonary edema. Sinus tachycardia and nonspecific ST segment and T wave changes were noted on the electrocardiogram and an echocardiogram revealed depressed left ventricular systolic function with an ejection fraction of 44%. Initial cardiac enzyme levels were elevated: troponin (3.2 ng./ml, upper normal level 0.08ng./ml), Creatine phosphokinase (CPK-MB) (11.5 ng./ml, upper normal level 3.5 ng./ml) and beta type natriuretic peptide (BNP- B)(5,000 pg. /ml, upper normal level 99 pg. /ml). Continuous infusions of milrinone at 0.25mcg/kg/min and furosemide at 0.02mg/kg/hr were started and the epinephrine infusion was weaned off. Over the next ten days, serial echocardiograms showed improvement in cardiac function with a final ejection fraction of 69% and normalization of cardiac enzymes. The child was discharged home fourteen days after admission. Serial laboratory and ejection fraction values are presented in table 1.

Discussion

Anaphylaxis is an acute life-threatening event which may manifest with severe systemic symptoms. Patients with the most severe symptoms develop these symptoms more rapidly. (1) In patients with anaphylaxis onset outside of the hospital setting, food is the most common etiology; food induced anaphylaxis is the cause of 30% of all fatal anaphylactic reactions. (1) Peanuts, tree nuts, and biphasic reactions are more commonly associated with fatal outcomes and require more than one dose of epinephrine. (2)

Patients with severe anaphylaxis may also present with cardiac complications. (3) As mast cells are abundant in the heart, activated cardiac mast cells may act both as source and target for chemical mediators during anaphylaxis. (3) Thus, our patient's hemodynamic status worsened after escalation of epinephrine therapy and her cardiac enzyme levels increased suggesting possible myocardial injury. Because the child improved after epinephrine was discontinued, we suspect the patient may have developed a catecholamine-induced cardiomyopathy.

Epinephrine is the cornerstone of anaphylaxis treatment. (1) It has a narrow therapeutic index and produces transient adverse effects; rarely it can cause serious side effects. (1) High dose of epinephrine administration can cause myocardial stunning and severe global myocardial hypokinesis. (4) Very high plasma catecholamine levels and sustained sympathetic stimulation have been associated with progression of heart failure and a decreased left ventricular ejection fraction. (4) Diffuse myocardial destruction with myocyte loss, necrosis, and extensive fibrosis were observed in experimental studies following administration of high doses of epinephrine. (5) Such pathological changes have also been noted in patients with catecholamine excess states, such as those with pheochromocytoma, who developed catecholamine-induced cardiomyopathy. (6)

Studies have shown that in patients with stress induced cardiomyopathy (also known as Tako-tsubo cardiomyopathy) and with catecholamine excess states, endomyocardial biopsies demonstrate a unique form of myocyte injury with contraction band necrosis. (7) Myocardial stunning from neurogenic causes has a similar mechanism, resulting from enhanced sympathoneural activity causing elevated catecholamines and neuropeptides levels. (8) One of the proposed mechanisms of myocardial dysfunction after high dose epinephrine therapy is the unfavorable effect of high dose epinephrine on the balance between myocardial oxygen supply and demand. (9) Furthermore, there is experimental evidence that high dose epinephrine may have a negative inotropic influence through activation of GI pathways. (10)

Patients with catecholamine induced cardiomyopathy can present with congestive heart failure and pulmonary edema. (6) Treatment includes diuretics, ACE inhibitors, and inotropic support. Milrinone is indicated in progressive heart failure as it decreases systemic vascular resistance, improves lusitropy and increases cardiac output; furthermore, milrinone, does not increase myocardial oxygen consumption. (11) In refractory cases,Extra Corporeal Membrane Oxygenation (ECMO) is a valuable treatment option. (12) Once the epinephrine levels return to normal, cardiomyopathy changes reverse within days to weeks of the acute insult. (13)

Conclusion

In summary, our patient with allergy to eggs developed severe anaphylaxis after exposure to eggs. Subsequently, she developed myocardial dysfunction and injury associated with epinephrine administration. She improved after discontinuation of epinephrine and with supportive therapy. However, we cannot rule out direct cardiac effects of the anaphylactic response itself. (4) Vasodilatory shock is still the most common type of shock in children with anaphylaxis, however catecholamine-induced cardiomyopathy should be considered in children with anaphylaxis when myocardial dysfunction is present. Myocardial function needs to be assessed in children with persistent hypotension after anaphylaxis. Caution should be exercised when administering multiple doses of epinephrine for management of anaphylaxis.

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Table 1. Showing serial myocardial injury markers and ejection fraction on echocardiogram.

Day of Admission	**1**	**2**	**3**	**5**	**7**	**10**
BNP (pg/ml)	5000	4940	2720	1391	607	454
Troponin (ng/ml)	3.2	2.8	1.28	0.34	0.15	0.01
CPKMB (ng/ml)	11.5	29.9	43	32.8	12.9	5
Ejection Fraction (%)	44	48	—	55	62	69

BNP, beta type natriuretic peptide; CPK MB, Creatine phosphokinase.

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