Myocardial Depression in Anaphylaxis: Report of a Case and Review of the Literature

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Cardiac involvement in anaphylaxis has been recognized for a long time. There have been several clinical articles reporting cardiac changes in human anaphylaxis, mostly manifested as arrhythmia or ischemic changes on electrocardiograms. However, many of these previous reports had problems in attributing a direct anaphylactic effect to the heart, and rarely was a direct myocardial depression reported. We report the case of a patient with rapidly reversible myocardial dysfunction and acute pulmonary edema during an episode of anaphylaxis caused by an insect bite. The medical literature that pertains to this phenomenon is discussed.

Key words: anaphylaxis, acute pulmonary edema, myocardial depression

Introduction

It has been known that the heart can be the target organ of an allergic response. This concept is supported by clinical experience, as well as in vivo and in vitro models of anaphylaxis, and by the analysis of the effects of anaphylactic mediators and inhibitory drugs on cardiac function. Although the clinical literature regarding anaphylaxis is replete with references to these cardiac effects[1-16], in most of the reported cases, the contribution of cardiac anaphylaxis cannot be clearly separated from the effects of hypoxia, hypotension, or drugs such as epinephrine. In the literature, there have been very few reported cases in which direct myocardial depression caused by anaphylactic mediators was suspected[1,12,13]. We herein report a patient with nearly fatal anaphylaxis after an insect sting, in whom profound primary myocardial depression was observed.

Case Report

A 15 year-old girl was brought to the emergency room because of sudden collapse. She had been well and had had no history of allergy before. She denied the abuse of drugs. On that evening, she had experienced being bitten on the neck by an unidentified insect which "looked like an ant with wings." Some itching urticaria had soon developed on her neck. About 15 minutes later, while taking a shower, she had collapsed on the floor. She was then rushed to our emergency room. On arrival, her vital signs included: blood pressure (BP), 80/40 mmHg; temperature, 36.5℃; heart rate, 116 beats per minute; and respirations, 36 per minute. She had a clear state of consciousness. Urticaria over her neck and trunk were observed, and her lips and nail beds were cyanotic. Crackles, but no wheezing or stridor, were

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heard diffusely over the chest. A grade 2 systolic murmur was heard over the apex of the heart. The abdomen was unremarkable. Under the impression of anaphylactic shock, epinephrine, diphenhydramine, and hydrocortisone were given intravenously by bolus, followed by a continuous dopamine infusion. Soon, she was admitted to the intensive care unit.

An electrocardiogram (ECG) demonstrated sinus tachycardia and otherwise a normal tracing. A chest x-ray (CXR) disclosed frank pulmonary edema without cardiomegaly (Fig. 1). The echocardiograms obtained about 30 minutes after her collapse showed profound global hypokinesia of the left ventricle (LV), moderate mitral regurgitation, and mild tricuspid regurgitation (Fig. 2A). The left atrium (LA) diameter measured 3.8 cm, the LV diameter at end diastole 5.7 cm, and the left ventricular ejection fraction (LVEF) was 20%. The initial arterial blood gas measurements included pH 7.346, PCO_2 42.3 mmHg, PO_2 44.2 mmHg, and HCO_3^- 22.0 mEq/L. A complete blood count was within normal limits except for a white cell count of 22800/mm^3. The absolute eosinophil count was 17.8/mm^3. The serum level of IgE was increased (682 I.U./ml), and those of IgG and IgA were normal. The BUN and creatinine levels were normal. CK, CK-MB, GOT, and LDH values obtained on admission were 304 (normal, 35 to 235), 6 (normal, < 10), 48 (normal, 5 to 40), and 172 u/L (normal, 100 to 200), respectively. CK and CK-MB increased to peak values of 852 u/L and 20 u/L, respectively, 40 hours after admission.

She was intubated and ventilated with positive end-expiratory pressure. Hydrocortisone, diphenhydramine, and dopamine were continued. With the mean arterial blood pressure kept higher than 60 mmHg, intravenous furosemide was cautiously given on two occasions (20 mg/20 mg). Fluid therapy, with either colloid or crystalloid, was not undertaken. Her condition improved progressively. Dopamine was discontinued within 2 days. The ventilator was removed on the following day. Serial CXRs showed that the patient's lungs had become clear on the fourth hospital day. Follow-up echocardiograms obtained on the same day were normal with an LVEF of 76% (Fig. 2B). The LA diameter measured 3.5 cm and the LV diameter at end diastole 4.0 cm. Mitral and tricuspid regurgitation were no longer present. On day 6, she was discharged with complete recovery. Throughout the course, she did not experience chest pain nor were there ischemic changes on serial ECGs.

Discussion

As early as 1910, it was known that anaphylaxis is associated with disturbances in cardiac rate and rhythm[17]. In vivo studies using guinea pigs, rabbits, dogs and monkeys have shown that in ana-

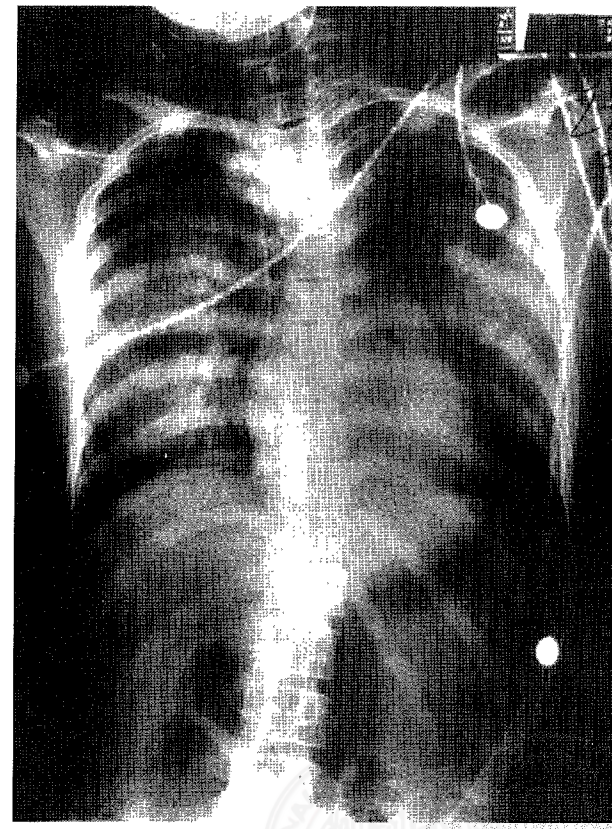
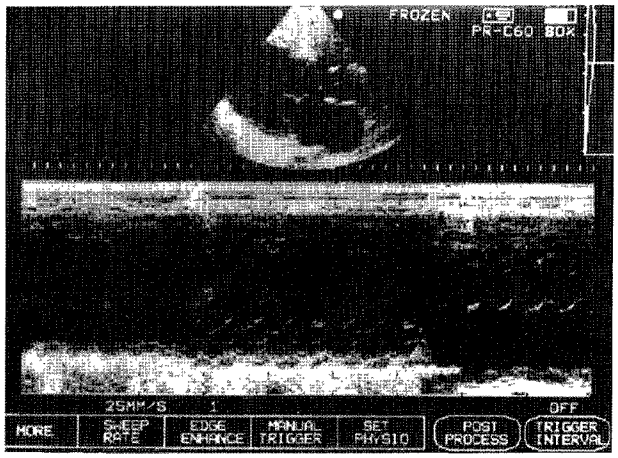
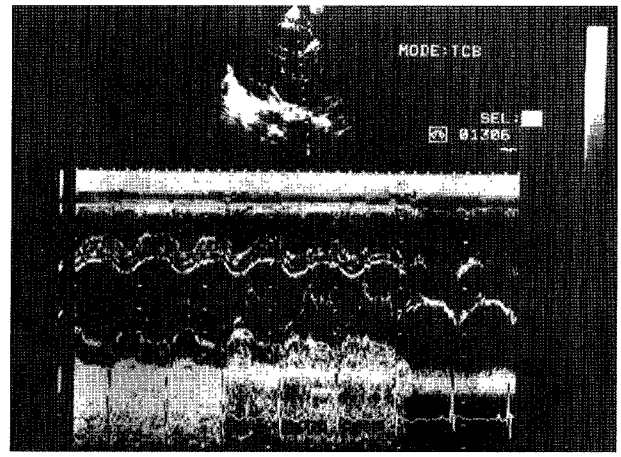


Fig. 1 The initial chest x-ray disclosed pulmonary edema.



(A)



(B)

Fig. 2 (A)An M-mode echocardiogram obtained on admission showed poor contractility of the myocardium and increased mitral E point-septal separation.
(B)A follow-up echocardiogram obtained 2 days later was normal.

phylaxis, the heart may respond with sinus tachycardia, increased ventricular automaticity, atrioventricular (AV) conduction delay, ventricular tachycardia, rightward QRS axis shifts, ST segment depression, and decreased cardiac output[17, 18]. Zavecz and Levi demonstrated that intracardiac challenge with antigen resulted in arrhythmia and increases in left ventricular pressure, which occurred 60 seconds before a rise in bronchial resistance[19]. Correa and colleagues demonstrated decreased left ventricular contractility not related to a reduction of venous return, systemic hypotension, hypoxia, or myocardial ischemia in IgE-mediated anaphylactic shock in dogs and suggested that the myocardium can be primarily involved in anaphylaxis[18].

The effects of anaphylactic mediators on the heart have been studied[26-29]. Compliment-derived anaphylatoxins may cause slowing of AV nodal conduction, a short-lasting increase followed by a prolonged decrease in LV contractility, and coronary vasoconstriction. The positive inotropic effect during the early stage of anaphylaxis is mediated by stimulation of H_2 receptors. Activation of H_1 and platelet activating factor (PAF) receptors may directly decrease myocardial contractility. PAF may also impair the diastolic function of the LV. Coronary vasoconstriction is mediated by H_1, thromboxane A_2, and, perhaps, leukotriene receptors, and the inhibition of AV nodal conduction by adenosine receptors.

There have been several clinical articles reporting cardiac changes in human anaphylaxis[1-16]. In some of them, arrhythmia or a conduction disturbance, including sinus tachycardia, premature ventricular beats, ventricular tachycardia, atrial fibrillation, supraventricular tachycardia, and left bundle branch block, was implied to be caused by cardiac anaphylaxis. Others reported ischemic changes on ECG or myocardial infarction, in some cases of which anaphylaxis-induced coronary artery spasm was suspected [8,10,15,16]. However, there are problems in attributing a direct anaphylactic involvement of the heart to these manifestations[17]. First, in most previous case reports, the preceding hypotension due to decreased peripheral resistance and intravascular volume, and the hypoxia due to bronchospasm or laryngeal edema may have resulted in the cardiac damage. Second, many of the reported cardiac manifestations in anaphylaxis are very nonspecific. For example: sinus tachycardia is frequently seen in patients with

stress; premature ventricular contraction is a common arrhythmia; and ST segment depression can be secondary to tachycardia. Third, medications, particularly large doses of epinephrine, may lead to myocardial ischemia and a variety of arrhythmias[4]. Fourth, several patients described in the literature were elderly and/or had evidence of preexisting coronary artery disease, such as a history of angina pectoris, a history of myocardial infarction, or abnormal coronary arteriograms. In these patients myocardial ischemia or even infarction could have occurred coincidentally during anaphylaxis or have been precipitated by it[6].

In the literature, there have been very few reported cases in which direct myocardial depression caused by anaphylactic mediators was suspected[1, 12-13]. Langsjoen and Stinson reported the case of a 22-year-old man who developed cyanosis and dyspnea with blood-tinged saliva soon after receiving intramuscular penicillin and tetanus toxoid. On postmortem examination, the major changes observed were in the heart, including edema and interstitial infiltration and the perivascular cuffing of eosinophils. The death was believed to be the result of an allergic myocarditis with acute and fatal cardiac decompensation[1]. Our patient, a young girl who had been in good health previously, exhibited acute myocardial depression with pulmonary edema, an unusual presentation of anaphylaxis, following localized urticaria a short while after an insect sting. There was no wheezing noted on auscultation. Hence, hypoxemia seems to have been more related to pulmonary edema than to bronchospasm in this case. Because the period of hypotension was short before an echocardiogram was obtained, the patient seemed not to be of poor reserve to respond to stress, and there were no signs or symptoms of myocardial ischemia (she had no chest pain and the serial ECGs were free of ST-T changes), myocardial dysfunction could hardly be explained by the foregoing hypotension and hypoxemia. Therefore, in this case the heart, more specifically, the myocardium but not the coronary arteries or the elctrophysiology, was very likely to have been directly involved by the mediators of anaphylaxis, although myocardial depression secondary to hypotension and/or hypoxemia could not be ruled out. In addition, pulmonary edema can also occur in anaphylaxis with a mechanism of increased permeability of the pulmonary vasculature [20-24]. We admit that that mechanism cannot be excluded in this patient. However, with the echocardiographic finding of profound myocardial depression, cardiogenic pulmonary edema seems to be a more attractive hypothesis.

There is no way to estimate the incidence of direct myocardial depression in anaphylaxis. It is quite possible that with reduction of the effective intravascular volume or with less severe myocardial dysfunction, pulmonary edema may not appear, so that the myocardial involvement is overlooked. Therefore, it may be worthwhile to perform echocardiography or Swan-Ganz catheterization to study the heart function and to monitor fluid replacement therapy in selected patients with anaphylactic shock. In addition to vasopressors, inotropic agents should be administered if the heart shows pumping failure. However, the use of catecholamine should be prudent because it has been shown that high levels of circulating catecholamine may produce myocardial necrosis, possibly by causing spasticity in the microvasculature, increasing cellular permeability to calcium, and increasing phospholipase activity[25]. Since not all patients with an anaphylactic response will have life-threatening cardiac decompensation, an initial intravenous injection of adrenaline may be life-saving. However, in those in whom cardiovascular function subsequently deteriorates, it may be prudent to use non-catecholamine inotropic agents [25]. Amrinone was reported as being effective in one case in which catecholamine failed[13]. Intra-aortic balloon counterpulsation has been reported to be effective in two patients[12]. In addition, the use of H_2

antagonists should be avoided because it has been shown in animal studies that H_2 receptors mediate both coronary vasodilation and an increase in myocardial contractility. An H_2 receptor blockade during cardiac anaphylaxis may unmask the effects of other mediators and is disadvantageous[26, 27].

In conclusion, direct myocardial depression caused by allergic myocarditis or unknown pathologic changes may occur in anaphylaxis. There is a two-stage effect of anaphylactic mediators on the myocardium: a transient positive inotropism stage mediated by H_2 receptors and a prolonged negative inotropism stage mediated by H_1 and PAF receptors. Of note, the use of epinephrine in such a case should be prudent because high levels of circulating catecholamine may produce myocardial necrosis, and amrinone and balloon counterpulsation should be considered as therapeutic alternatives. H_2 blockers may inhibit the positive inotropic effect mediated by H_2 receptors, and hence should be avoided.

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過敏反應導致心肌抑制：一病例報告

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過去曾有過敏反應導致心臟損傷的臨床報告，這些病例多數呈現爲心律不整或心肌缺血性變化，過敏反應直接造成心肌抑制的情況則絕少爲人提出。我們報告一位原本健康狀況良好的十五歲女孩，在蟲咬後短時間內出現急性肺水腫及低血壓，血清IgE升高，心臟超音波顯示左心室射血分率極度降低(僅20%)。經投予抗組織胺、類固醇、利尿劑及多巴胺治療，短期內即完全復原，追蹤心臟超音波也顯示心臟功能恢復正常。我們整理相關文獻，對此類病例的治療提出幾點建議：(1)高濃度兒茶酚胺(catecholamine)可能造成心肌壞死，應愼重使用；(2) 避免使用H_2阻斷劑； (3)可考慮使用主動脈氣球幫浦或amrinone。

關鍵詞：過敏反應，急性肺水腫，心肌抑制

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