Angioedema and Epinephrine Causing a Stress-Induced Cardiomyopathy

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ABSTRACT

Presentations of angioedema range from mild edema to immediate life-threatening airway involvement. Management is typically straightforward and dependent on the degree of presentation. In our case, a 61-year-old female presented with angioedema requiring immediate intubation. Before admission to the intensive care unit, a screening ECG was obtained that revealed ST segment elevations which redirected our patient to the cardiac catherization lab. Our patient was ultimately diagnosed with a stress-induced cardiomyopathy after initially presenting with ACE-inhibitor induced angioedema.

KEYWORDS: angioedema, stress-induced cardiomyopathy, epinephrine, STEMI, Takotsubo cardiomyopathy

CASE REPORT

A 61-year-old woman presented to our urban academic emergency department with facial edema, diffuse urticarial rash and dyspnea with wheeze that began acutely ten minutes prior while driving to work. She denied chest pain. There was no clear precipitant. Her medical history included non-insulin dependent diabetes and hypertension for which she was prescribed lisinopril. She reported taking lisinopril for the past 2 years. She denied a history of angioedema or anaphylaxis, and had previously been well.

Initial vital signs revealed a pulse of 110 BPM, respiratory rate of 25, blood pressure 140/70 mm Hg, and a room air oxygen saturation of 98%. She was afebrile. On initial physical examination, the patient was in moderate distress with mild uvular, peri-orbital, facial, and lip edema, along with scattered wheezes. An urticarial rash was noted on her chest and upper back. Intramuscular epinephrine, along with intravenous methyl-prednisolone, diphehydramine, and famotidine, were administered.

Within minutes our patient reported increasing dyspnea. Her oropharyngeal edema worsened and she developed notable voice muffling. Given impending airway compromise, she was successfully orotracheally intubated with a video laryngoscope using etomidate and succinylcholine to facilitate rapid-sequence intubation.

A screening ECG was obtained after appropriate sedation (**Figure 1**). ST segment elevations, meeting STEMI criteria were noted in the anterior-lateral distribution. No prior ECGs were available for comparison. Given clear ST elevations on ECG, lack of ability to obtain further history and recent epinephrine administration, interventional cardiology was consulted.

Our patient was transferred to the cardiac catheterization lab for suspected STEMI secondary to epinephrine. Kounis syndrome, known as allergic acute coronary syndrome, was also considered and has been reported in similar clinical scenarios.[4] On catheterization her cardiac vessels were unremarkable. There was no evidence of vasospasm or coronary vessel dissection. Despite normal vessels, the ejection fraction was globally reduced, and estimated at 30% with apical ballooning (**Figures 2, 3).** She was admitted to the medical intensive care unit with a diagnosis of Takotsubo cardiomyopathy.

During the subsequent 24 hours her angioedema resolved, and the patient was extubated on hospital day two. Complement pathways were within normal range, suggesting that hereditary angioedema was not the cause of her symptoms. Angioedema was concluded to be ACE-inhibitor mediated, and lisinopril was discontinued. She was initiated on an alternative anti-hypertensive, and successfully discharged

Figure 1. Initial ECG with ST segment elevation in leads V2-6. ST elevation also present in I & aVL.

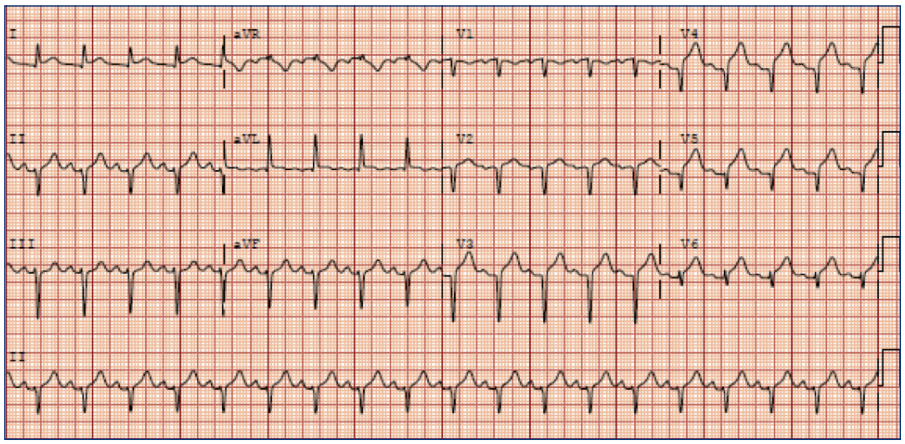


Figure 2. Catheterization revealing normal coronary vessels.

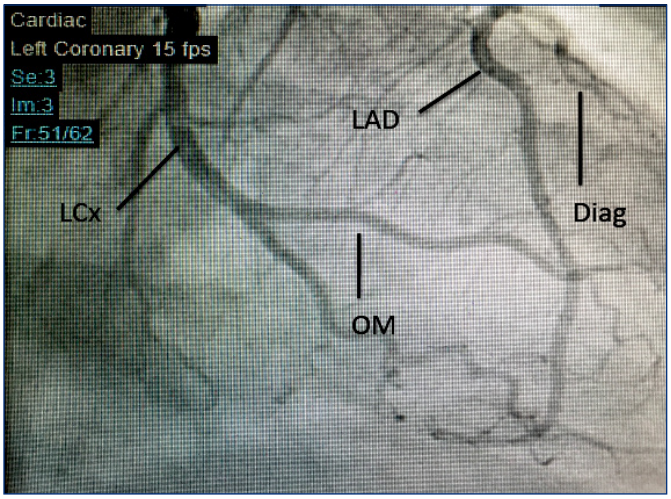
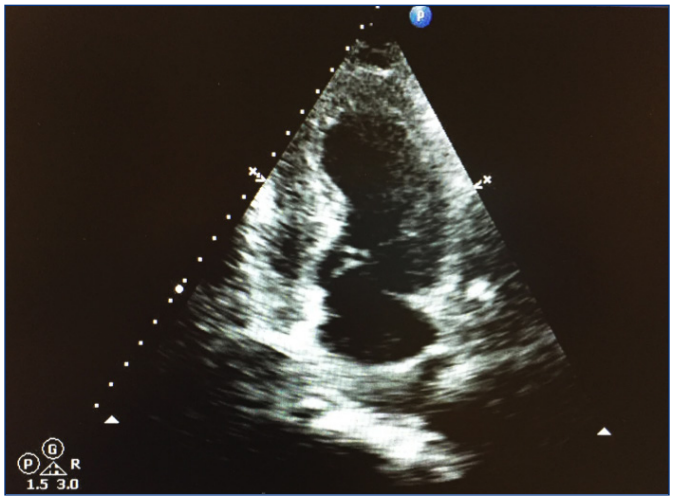


Figure 3. Apical ballooning on cardiac echocardiography.



home. A follow- up echocardiogram was normal a few months after her hospitalization, at which time the patient was well.

DISCUSSION

In patients who present acutely to the emergency department with angioedema, the cause is often uncertain. Our patient met criteria for anaphylaxis, and thus warranted epinephrine [**Table 1**].[1,12] Epinephrine is the cornerstone of treatment for anaphylaxis, although its use in patients with ACE-I angioedema has limited evidence.[1,6] However, it is generally considered safe when given at standard doses and route.[2,3,5] Adverse cardiovascular effects can occur following epinephrine administration, ranging from inconsequential transient tachycardia to myocardial infarction. Stress-induced cardiomyopathy is also a potential iatrogenic complication of epinephrine administration. A recent systematic review found 41 cases of epinephrine-triggered stress-induced cardiomyopathy.[7] A recent case report describes the development of Takotsubo cardiomyopathy in an acute angioedema presentation of a patient who also received epinephrine.[8] Our patient had normal coronary arteries on cardiac catheterization (**Figure 2**) and displayed characteristic apical ballooning and left ventricular dysfunction on echocardiography found in stress-induced cardiomyopathy (**Figure 3**). She returned to baseline physiologic function several weeks after her admission, a finding frequently noted in Takotsubo cardiomyopathy.[9]

Table 1. NIAID/FAAN clinical criteria for diagnosing anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:
1. Sudden onset of an illness (minutes to several hours) with skin, mucosal, or both involved and at least one of the following: a. Dyspnea, bronchospasm, stridor, decrease in PEF, and hypoxia b. Drop in blood pressure or symptoms of end-organ dysfunction (eg, decreased tone, syncope, loss of bladder/bowel control)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): a. Skin or mucosal tissue involvement (eg, widely distributed urticarial, pruritus, flush, swelling of the lips-tongue-uvula) b. Dyspnea, bronchospasm, stridor, decrease in PEF, and hypoxia c. Drop in blood pressure or symptoms of end-organ dysfunction (eg, decreased tone, syncope, loss of bladder/bowel control) d. Gastrointestinal symptoms (abdominal pain, emesis)
3. Drop in blood pressure after exposure to known allergen for that patient (minutes to several hours): a. Infants and children: low age-specific systolic blood pressure or more than a 30% decrement in systolic blood pressure b. Adults: systolic blood pressure lower than 90 mm Hg or more than a 30% decrement from that person's baseline

FAAN, Food Allergy and Anaphylaxis Network; NIAID

We are presenting this case of Takotsubo cardiomyopathy in the setting of acute angioedema and epinephrine administration. A similar case has been reported.[10] Although the exact mechanism of this disease pathology remains unclear, exogenous epinephrine is a theoretical culprit. Alternatively, it is possible that the cardiomyopathy was induced by endogenous catecholamine response incited by her angioedema. Despite lack of clarity regarding the pathogenesis of Takotsubo cardiomyopathy, this case provides additional evidence that a stress-induced cardiomyopathy is a possible adverse consequence of epinephrine use.

Angioedema is not an uncommon presentation in the emergency department, and accounts for 80,000 to 112,000 Emergency Department visits per year.[11] While initially thought to be straightforward, our case followed an atypical and unusual course. This case illustrates the nuanced complexity of the practice of medicine, especially within the bounds of the emergency department, and illustrates a rare adverse reaction to epinephrine. It is important for physicians treating angioedema in an emergency setting to recognize that administration of epinephrine can lead to significant cardiac complications.

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