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A rare case report of catecholamine-induced takotsubo in a patient with anaphylaxis shock due to amoxicillin–clavulanate

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Abstract:

Takotsubo syndrome (TTS), also known as stress cardiomyopathy, is a life-threatening condition characterized by transient left ventricular dysfunction with nonischemic abnormalities. This syndrome in scenarios of anaphylactic shock is quite rare, with only a few cases reported. Early diagnosis and treatment are crucial. We presented a rare case of 58-year-old woman presented to our hospital due to an anaphylactic shock. The patient was stable and in the de-escalation dose of adrenaline (0.05 μg/kg/h). Twenty-two hours from exposure, the patient experienced pulmonary edema that required intubation, both adrenaline and dobutamine to maintain blood pressure. Echocardiography revealed a reduced ejection fraction of 35%. Subsequent coronary angiography showed no signs of coronary obstruction and left ventriculography provided typical apical ballooning and hyperkinesia in the basal region, highly suggesting TTS. The patient was successfully treated with inotrope and vasopressor and was discharged in stable condition after 7 days and improved normal heart function after 4 weeks. This case demonstrates the delayed onset of adrenaline-induced takotsubo complicated with pulmonary edema in a patient with anaphylactic shock due to antibiotics despite a de-escalation dose of adrenaline. Regardless of the duration of the event or the optimal epinephrine dosage in patients with anaphylactic shock, physicians should be aware of the risk of TTS.

Keywords:

Anaphylaxis, antibiotics, catecholamine, takotsubo

Introduction

Takotsubo syndrome (TTS) is characterized by transient left ventricular dysfunction, often triggered by emotional or physical stressors, and mimics the symptoms of acute coronary syndrome (ACS).[1] TTS could be triggered by either the sudden release of endogenous catecholamines or the administration of high doses of exogenous catecholamines. TTS occurring in scenarios of anaphylactic shock is quite rare; only a few cases have been reported.[2] Almost all cases of these conditions happened in the early stage within a few minutes to hours after injection of adrenaline.[3] Moreover, there are currently no guidelines for the management of adrenaline-induced takotsubo.

In this case, we presented a rare case of delayed onset of TTS after adrenaline administration complicated by pulmonary edema in a patient with anaphylaxis shock due to the antibiotic amoxicillin–clavulanate.

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Case Report

A 58-year-old healthy postmenopause female presented to our hospital with anaphylactic shock. Thirty minutes after taking Curam (amoxicillin plus clavulanate) 1000 mg for pharyngitis, the patient developed urticaria and dyspnea. At the nearby local hospital, she had hypotension and received an anaphylaxis protocol, including 2 shots (0.5 mg) of intramuscular adrenaline, followed by intravenous adrenaline, then transferred to our hospital for further management.

Thirty minutes later, at our emergency department, the patient remained with dyspnea, whereas all rashes had resolved. Physical examination showed a blood pressure of 85/52 mmHg (on continuous adrenaline infusion at 0.2 μg/kg/h). No other abnormalities were found on her examination. An echocardiogram, the electrocardiogram (ECG), and a chest X-ray performed upon admission showed normal results. The patient was diagnosed with anaphylactic shock due to the antibiotic and then transferred to the intensive care unit.

After 22 h from onset, the patient was stable without shortness of breath. The adrenaline infusion was de-escalated to 0.05 μg/kg/h, intended to stop, with a blood pressure of 100/60 mmHg. Suddenly, the patient experienced dyspnea again without any signs of rashes. Physical examination revealed a heart rate of 130 beats/min, blood pressure of 160/70 mmHg, respiratory rate of 30 breaths/min, and SpO_2 of 90% room air. Lung examination showed bilateral coarse crackles. A quick point-of-care ultrasound revealed hyperkinesia in the basal region and hypokinesia in the apical region of the heart, a reduced ejection fraction of 35% [Figure 1]. Arterial blood gas revealed an increased lactate level of 5.64 mmol/L. Her ECG showed ST elevation in V4 and V5 [Figure 2]. The chest X-ray revealed bilateral opacities arising from the hilar regions.

She was subsequently diagnosed with pulmonary edema, suspected to be due to TTS, with differential diagnoses including myocardial infarction and Kounis syndrome. She received oxygen through a mask and diuretics. Adrenaline was stopped due to hypertension and suspected adrenaline-induced TTS. However, her condition deteriorated after the 5 min of discontinuation of adrenaline. The blood pressure decreased to 60/40 mmHg, which did not respond with dobutamine alone. Therefore, the patient was intubated, and adrenaline was used to maintain mean blood pressure >65 mmHg due to not excluding the presence of remaining anaphylaxis. Her high-sensitivity troponin T increased from 546 to 950 ng/L, and NT-proBNP was 8136 ng/L.

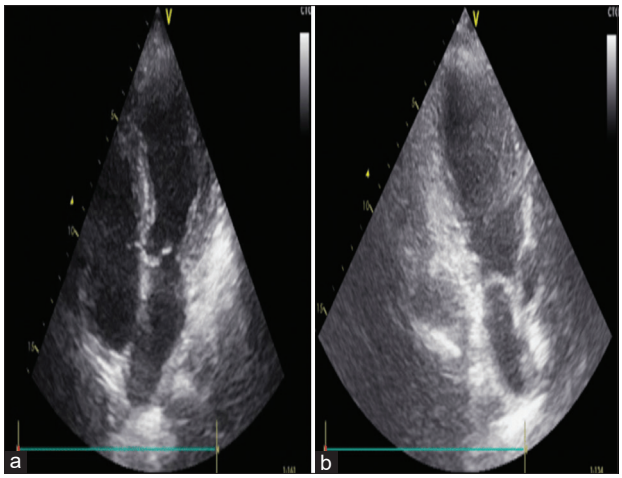

Figure 1: Echocardiogram (ECG) after 22 h from onset. The ECG showed a reduced ejection fraction of 35%, hyperkinesia in the basal, and hypokinesia at the apical regions. (a) Apical 4-chamber view, (b) Apical 2-chamber view

The patient was transferred to the catheterization room, where coronary angiography revealed no signs of obstruction, vasoconstriction, or thrombus. The left ventriculography showed typical features of TTS, with hyperkinesia in the basal region and hypokinesia in the apical region [Figure 3]. The final diagnosis was anaphylactic shock complicated by TTS and pulmonary edema. Kounis Type 1 may also not be excluded from the study. The patient gradually improved after extubating and stopping adrenaline with reduced ST elevation on V4-V5 [Supplementary Figure S1] on day 2 and dobutamine on day 4 of admission. She was discharged in stable condition after 7 days, and a 4-week follow-up showed improved normal heart function.

Written informed consent was obtained from the patient following the journal's patient consent policy.

Discussion

To the best of our knowledge, this is the first case of delayed onset of adrenaline-induced takotsubo complicated with pulmonary edema in a patient with anaphylactic shock due to amoxicillin–clavulanate.

TTS constitutes 1%–2% of patients admitted to hospitals with ACS.[4] TTS predominantly affects postmenopausal women, with women accounting for up to 90% of cases in some studies.[5] TTS can occur at any age, but the average age of onset is around 60–75 years.[6] The mechanism of TTS includes various factors. The adrenergic crisis is one of the most recognized hypotheses for TTS stimulated by stress or emotional events. This stimulation leads to the secretion of large amounts of catecholamines into the bloodstream. Furthermore, TTS may also result from the exogenous administration of a high dose of catecholamines. The prevalence of cardiac injury,

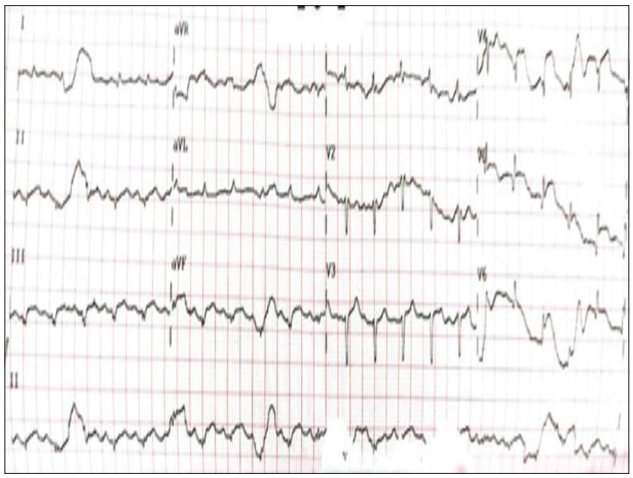

Figure 2: Echocardiogram (ECG) after 22 h from onset. The ECG showed ST elevation in V4 and V5

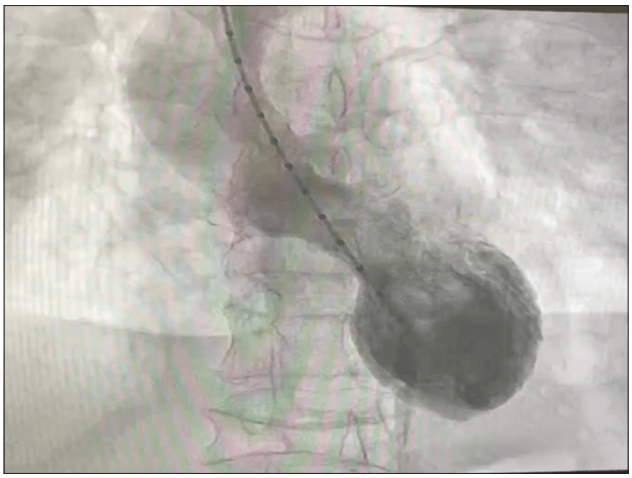

Figure 3: The left ventriculography. It showed the typical apical ballooning

including TTS and Kounis syndrome in anaphylaxis patients, is about 7.3%.[7] Regardless of the causes, the fundamental pathophysiology remains consistent: microvascular dysfunction and catecholamine-induced myocardial stunning.

According to InterTAK Diagnostic Criteria for TTS, coronary angiography with left ventriculography is considered the gold standard diagnostic tool to exclude or confirm TTS.[8] In our case, the patient fulfilled this criterion [Supplementary Table 1]. The major differential diagnosis in the context of anaphylactic shock is Kounis syndrome. However, these two clinical entities can coexist, and some authors have termed this combination the ATAK complex (adrenaline-induced TTS and Kounis syndrome).[9-12] Kounis syndrome, also known as allergic myocardial infarction, can lead to coronary artery spasm, atherosclerotic plaque erosion, or rupture, resulting in myocardial ischemia or infarction. Typically, patients with Kounis syndrome exhibited allergic symptoms during an ACS episode, often within 30–60 min of allergen exposure, especially an antibiotic.[13,14] In our case, the patient was stable on the de-escalated adrenaline 22-h postexposure to antibiotics, had typical apical ballooning, and maintained ECG abnormalities after 2 days, which highly suggested TTS. However, Kounis syndrome type 1 cannot be ruled out, and there was potential for A.T.A.K. given that no lesions were observed in the angiography since the spasm of coronary arteries may regress.

Our case is unique due to several reasons. First, this patient developed TTS after 22 h from the onset of anaphylaxis when the patient was quite stable. According to Hassan, with 33 cases of anaphylactic shock, almost all cases (85%) with TTS occurred rapidly within minutes after adrenaline injection, and only one case reported onset after a day.[4] Second, the adrenergic hypothesis was also considered the potential for adrenaline-induced TTS. Our case had TTS at a low dose of adrenaline (0.05 μg/kg/min), which was different from other cases with short-time high doses of adrenaline injection.[15] Our case suggests that TTS may be associated with an accumulation of adrenaline rather than a rapid injection of catecholamine excess. This patient received a total of 4.2 mg of adrenaline before the onset of TTS. Furthermore, it has been stated that the adrenaline used contains sodium metabisulfite as a preservative, resulting in anaphylactic shock. This raises concerns about the adrenalin and its doses in these patients.[10] Third, this is the first case of adrenaline-induced takotsubo due to the amoxicillin–clavulanate antibiotic. In one study, the majority of cases with TTS occurred during the perioperative procedure, and none of the cases were caused by antibiotics.[4] It is unclear whether the pathology was caused by the antibiotics. In brief, anaphylaxis associated with adrenaline injection may play a key role in the pathophysiology of our cases.

Currently, there is no consensus for managing TTS, which is predominantly supportive. In the early stable stage of anaphylactic shock, it is unclear whether doctors can stop adrenaline in patients with adrenaline-induced takotsubo, like in our case. Since our patient had recurrent hypotension and did not exclude the remaining anaphylaxis, we continued adrenaline infusion until a stable condition was reached. There have also been no studies showing any harmful effects of continuing adrenaline infusion in patients with adrenaline-induced takotsubo; it should be individualized treatment.

Conclusion

Catecholamine-induced TTS is a rare and fatal disease that requires early recognition and prompt treatment. In the context of anaphylaxis shock, regardless of the duration of anaphylaxis or the optimal dose of

epinephrine therapy, physicians should be well aware of the risk of TTS, especially in postmenopause women with sudden cardiogenic shock. Further large studies are needed to make a consensus on managing this syndrome.

Author contributions statement

LQT: Conceptualization (Equal); writing – Original draft (lead); formal analysis (Equal); writing – Review and editing (equal). NHT: Conceptualization (Lead); writing – Original draft (Equal); formal analysis (lead); writing – Review and editing (equal). VAD: Methodology (Equal); writing – Review, and editing (equal). PDH: Conceptualization (supporting); Writing – Review, and editing (Lead).

Conflicts of interest

None Declared.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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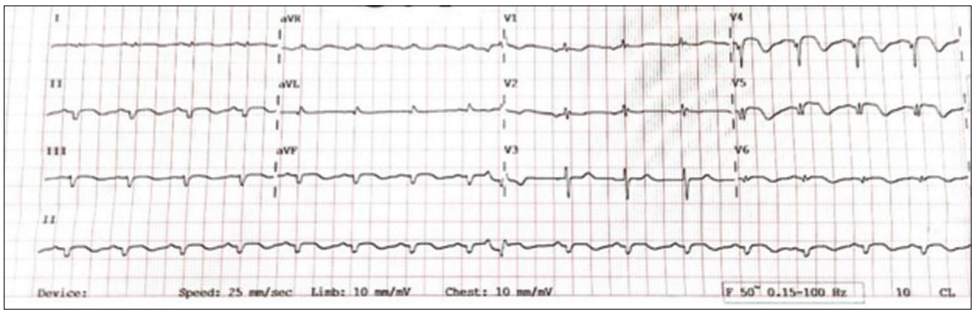
References

1. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, *et al.* International expert consensus document on takotsubo syndrome (Part II): Diagnostic workup, outcome, and management. Eur Heart J 2018;39:2047-62.
2. Pelliccia F, Kaski JC, Crea F, Camici PG. Pathophysiology of takotsubo syndrome. Circulation 2017;135:2426-41.
3. Surineni K, Afzal MR, Barua R, Parashara D. Epinephrine-induced takotsubo cardiomyopathy. Fed Pract 2016;33:28-30.
4. Hassan SY. Clinical features and outcome of epinephrine-induced takotsubo syndrome: Analysis of 33 published cases. Cardiovasc Revasc Med 2016;17:450-5.
5. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, *et al.* Clinical features and outcomes of takotsubo (Stress) cardiomyopathy. N Engl J Med 2015;373:929-38.
6. Singh T, Khan H, Gamble DT, Scally C, Newby DE, Dawson D. Takotsubo syndrome: Pathophysiology, emerging concepts, and clinical implications. Circulation 2022;145:1002-19.
7. Cha YS, Kim H, Bang MH, Kim OH, Kim HI, Cha K, *et al.* Evaluation of myocardial injury through serum troponin I and echocardiography in anaphylaxis. Am J Emerg Med 2016;34:140-4.
8. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, *et al.* International expert consensus document on takotsubo syndrome (Part I): Clinical characteristics, diagnostic criteria, and pathophysiology. Eur Heart J 2018;39:2032-46.
9. Puri P, Kachhadia MP, Sardana P, Bhagat R, Dekowski SS, Fohle E. Adrenaline, takotsubo, anaphylaxis, and kounis syndrome (ATAK) complex unveiled: Integrating takotsubo and kounis syndromes in the context of chemotherapy-related anaphylaxis. Cureus 2024;16:e53145.
10. Kounis NG, Grapsas N, Soufras GD, Lianas D, Patsouras N, Hahalis G. The ATAK complex (Adrenaline, Takotsubo, Anaphylaxis, and Kounis hypersensitivity-associated coronary syndrome) in neurological conditions. Indian J Crit Care Med 2016;20:255-6.
11. Margonato D, Abete R, Di Giovine G, Delfino P, Grillo M, Mazzetti S, *et al.* Takotsubo cardiomyopathy associated with Kounis syndrome: A clinical case of the "ATAK complex". J Cardiol Cases 2019;20:52-6.
12. Minciullo PL, Amato G, Vita F, Pioggia G, Gangemi S. ATAK complex (Adrenaline, Takotsubo, Anaphylaxis, and Kounis Hypersensitivity-Associated Coronary Syndrome) after COVID-19 vaccination and review of the literature. Vaccines (Basel) 2023;11:322.
13. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): A natural paradigm? Int J Cardiol 2006;110:7-14.
14. Abdelghany M, Subedi R, Shah S, Kozman H. Kounis syndrome: A review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. Int J Cardiol 2017;232:1-4.
15. Wei J, Zhang L, Ruan X, He K, Yu C, Shen L. Case report: Takotsubo syndrome induced by severe anaphylactic reaction during anesthesia induction and subsequent high-dose epinephrine resuscitation. Front Cardiovasc Med 2022;9:842440.

Supplementary Table 1: International Takotsubo diagnostic criteria

Patients show transient left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery. (X)
An emotional, physical, or combined trigger can precede the TTS event, but is not obligatory. (X)
Neurologic disorders (such as subarachnoid hemorrhage, stroke/transient ischemic attack, or seizures) as well as pheochromocytoma may serve as triggers for TTS. NO
Although ECG abnormalities typically are present (ST- segment elevation or depression, T-wave inversion, and QTc prolongation), in rare cases, patients may have no ECG changes. (X)
Levels of cardiac biomarkers (troponin T or I and CK-MB) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common. (X)
Significant coronary artery disease does not exclude TTS. (X)
Patients have no evidence of infectious myocarditis. (X)
Predominantly affects postmenopausal women. (X)

ECG: Electrocardiogram, TTS: Takotsubo syndrome, CK-MB: Creatine kinase myocardial band



Supplementary Figure S1: Echocardiogram after 48 h from exposure with reduced ST elevation