ATAK Complex due to Amoxicillin: A Case Report

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Takotsubo cardiomyopathy (TTC), also known as broken heart syndrome, transient left ventricular dysfunction syndrome, and stress cardiomyopathy, is a temporary and reversible systolic abnormality of the apex of the left ventricle (LV) approaching myocardial infarction in the absence of coronary artery disease [1]. It was named after a round-bottomed and narrow-necked fishing pot (takotsubo in Japanese) for trapping octopi owing to its resemblance to left ventricle ballooning on echocardiogram. TTC mainly affects postmenopausal women and is preceded by an emotional or physical trigger.

Kounis syndrome (KS) has been defined as the coincidental occurrence of acute coronary syndrome in the setting of hypersensitivity reactions following an allergic event [2]. It was first described by Kounis and Zavras [3] in 1991, and more than 300 cases have been published since, with frequency increasing in recent years, even among children [4]. Nevertheless, it is easily overlooked and underdiagnosed. KS is caused by various triggers, including drugs, insect stings, foods, and medical conditions [2].

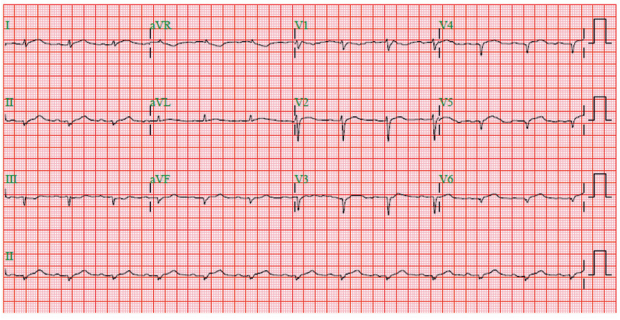
The term ATAK complex (association of adrenaline, takotsubo, anaphylaxis, and Kounis syndrome) was recently coined, and few cases have been reported [5-7]. We report an additional case of this challenging, new complex. The study was approved by the local ethics committee, and the patient gave her informed consent for her data to be published.

A 77-year-old woman whose history was remarkable for obesity (body mass index, 31) and diabetes attended the emergency department with pruritus, generalized erythema, lingual edema, and discomfort after visiting the dentist. She lost consciousness a few minutes after arrival. On recovering, she reported chest and back pain. Intravenous adrenaline 0.5 mg, hydrocortisone 150 mg, and dexchlorpheniramine 5 mg were administered. An electrocardiogram revealed diffuse ST segment elevation of 3 mm in D-I, D-II, D-III, aVF, and V3 to V6 (Figure). Laboratory tests showed positive cardiac enzymes with elevated troponin T (Figure). Serum tryptase was not determined. The patient was transferred to the referral hospital with a suspected diagnosis of anaphylactic

A

Laboratory test: Biochemical markers of myocardial damage					
		Troponin T (0-14)	**CK (24-170)**	**Myoglobin (<70)**	**proBNP (0-300)**
Day 1	(1st determination) 12:38 pm.	142 ng/L	35 U/L	-	-
	(2nd determination) 4:17 pm.	660.6 ng/L	CK 73 U/L	-	-
Day 2	(3rd determination) 01:47 am.	519.3 ng/L	73 U/L	44 ng/mL	1724 pg/mL
	(4th determination) 07:45 am.	365.4 ng/L	64 U/L	40 ng/mL	2353 pg/mL

B



C

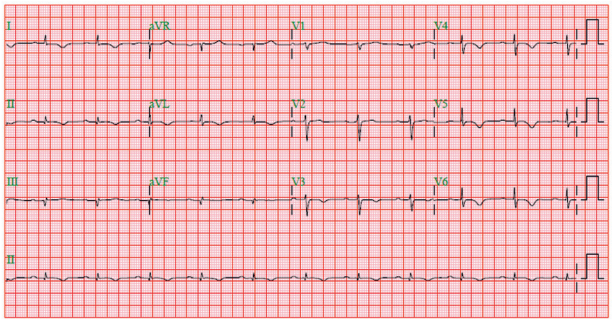


Figure. A, Laboratory test; B, Electrocardiogram on admission; C, Discharge electrocardiogram.

shock and secondary acute coronary syndrome. Upon arrival, she received clopidogrel 300 mg and acetylsalicylic acid 300 mg and was admitted to the cardiology unit. Coronary angiography performed the following day revealed angiographically normal epicardial coronary arteries. The first echocardiogram performed revealed a moderately hypertrophic LV with depressed ejection fraction (EF, 0.45), akinesis of the apical segments, hypokinesis of the middle segments, and hypercontractility of the basal segments. LV systolic function was mildly to moderately reduced, and moderate LV hypertrophy was observed (Online repository). The echocardiogram performed prior to discharge, however, showed normal LVEF and regional abnormalities, suggesting that the stress cardiomyopathy had resolved. We consulted with the Allergy Unit while the patient was admitted. The patient reported having taken a 1-g amoxicillin tablet 30 minutes before the dental procedure. Therefore, ß-lactam antibiotics were preventively prohibited. She was discharged a few days later with a diagnosis of KS and stress cardiomyopathy.

Six weeks later, the patient was seen at the Allergy Unit. She reported a previous history of allergy to penicillin with a pruritic erythematous generalized reaction approximately 45 years earlier and has avoided penicillin since.

Skin testing was performed with penicilloyl-poly-L-lysine, minor determinant mixture, benzylpenicillin, amoxicillin, cefazolin, cefuroxime, ceftriaxone, cefepime, imipenem, and meropenem according to the European Network and European Academy of Allergy and Clinical Immunology Drug Allergy (ENDA/EAACI) Interest Group protocol [8]. The results were positive for amoxicillin (2 mg/mL intradermal test [ID]), benzylpenicillin (10000 IU/mL [ID]), and imipenem (0.05 mg/mL [ID]). Laboratory tests revealed basal tryptase of 9.3 µg/L and 12.2 µg/L on 2 separate occasions, IgE 123 IU/mL, and negative results for specific IgE to cefaclor and penicillin (<0.1 kU/L). Unfortunately, specific IgE to ampicillin and amoxicillin were not available at the time. The patient tolerated oral challenge with cefuroxime well.

KS is caused by activation of mast cells and platelets and involves interrelated and interacting inflammatory cells and mediators capable of inducing coronary events. Predisposing factors include a previous history of allergy, hypertension, diabetes, and hyperlipidemia [9]. Antibiotics are the most common cause, and 70% of cases occur within 30 minutes after administration [9]. A recent review regarding KS due to amoxicillin showed the main clinical manifestations to be chest pain, rash, pruritus, erythema, and, less frequently, altered state of consciousness [9]. The authors reported that echocardiography at onset showed hypokinesis in 45% of patients, reduced EF in only 15%, and normal coronary angiography findings in 50% [9]. All the symptoms and cardiological abnormalities named above were recorded in the present case.

KS must be treated quickly not only to revascularize the myocardium, but also to treat the concomitant allergic reaction. Epinephrine is the main life-saving drug for treating anaphylaxis [10], although its adverse effects include prolongation of the QTc interval, myocardial damage, and/or coronary vasospasm and arrhythmias, especially when administered intravenously, as happened in the present case.

TTC is usually associated with overstimulation of the sympathetic nervous system, microvascular and myocardial tissue metabolism abnormality, and coronary artery vasospasm [1]. Therefore, both KS and administration of epinephrine favor onset of the condition. Bearing in mind the severe cardiac adverse effects, intramuscular administration of adrenaline should be preferred.

In addition, suspicion of anaphylaxis requires measurement of serum tryptase [10], although troponin should probably also be assessed in order to detect and treat potential myocardial damage immediately.

We report a new case of ATAK complex in which acute coronary syndrome followed an anaphylactic reaction requiring epinephrine that in turn triggered TTC. We also highlight transient changes in ventricular dysfunction. The slightly increased tryptase levels suggest underlying hereditary α-tryptasemia or another mast cell disorder.

ATAK complex may not be such a rare entity and may merely go underdiagnosed. Considering that both KS and TTC are themselves frequently misdiagnosed, as mentioned above, suspecting ATAK complex seems challenging. Physicians should be aware of ATAK complex to ensure correct identification and management.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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