

From Allergies to ATAK: A Complex Case Report Following Ciprofloxacin Administration

Soorampally Vijay^{1,3}; Bharath Raj Kidambi^{2*}; Sriram Veeraraghavan²

¹Department of Cardiology, Trinity Hospital, Bangalore, India.

²Department of Cardiology, SRM Medical College and Research Centre, Potheri, Chengalpattu, Tamil Nadu - 603203, India.

³Specialist Cardiologist, Department of Cardiology, Al Dhannah Hospital, Ruwais, Abu Dhabi, UAE.

Corresponding Author: Bharath Raj Kidambi

Department of Cardiology, SRM Medical College and Research Centre, Potheri, Chengalpattu, Tamil Nadu - 603203, India.

Tel: +971-551384611; Email: drbkid@gmail.com

Article Information

Received: Jul 08, 2024

Accepted: Aug 22, 2024

Published: Aug 29, 2024

SciBase Clinical & Medical Case Reports - scibasejournals.org
Kidambi BR et al. © All rights are reserved

Citation: Vijay S, Kidambi BR, Veeraraghavan S. From Allergies to ATAK: A Complex Case Report Following Ciprofloxacin Administration. SciBase Clin Med Case Rep. 2024; 2(3): 1028.

Abstract

This case report describes a complex clinical scenario involving a previously healthy middle-aged woman who received ciprofloxacin for acute otitis media and subsequently developed symptoms of allergic hypersensitivity and anaphylaxis. Following an intramuscular adrenaline injection for anaphylaxis, she experienced chest pain consistent with Inferior Wall Myocardial Infarction (IWMI), with discordant echocardiography findings and normal epicardial coronary arteries on coronary angiography. The case is the intricate interplay of the ATAK (Adrenaline, Takotsubo, Anaphylaxis, Kounis) complex, with implications for diagnosis and management.

Keywords: ATAK; Kounis syndrome; Allergic Myocardial infarction; Anaphylaxis.

Case presentation

Introduction: Acute otitis media is commonly treated with antibiotics such as ciprofloxacin. However, adverse reactions, including allergic hypersensitivity leading to anaphylaxis, can occur. The ATAK complex, encompassing adrenaline-induced Takotsubo syndrome, anaphylaxis, and Kounis syndrome, represents a diagnostic challenge and is difficult to manage in clinical practice.

Patient presentation: A 35-year-old woman, without any prior co-morbidities, presented to the emergency department with symptoms of generalized itching and swelling of both hands and feet, which started 2 hours after the intake of ciprofloxacin for acute otitis media. There was no known history of allergy to any drugs or atopy in the past. On initial examination, her blood pressure was 132/84 mm of Hg; pulse rate was 96 per minute, and a new onset of swelling on the hands and feet (Figure 1).

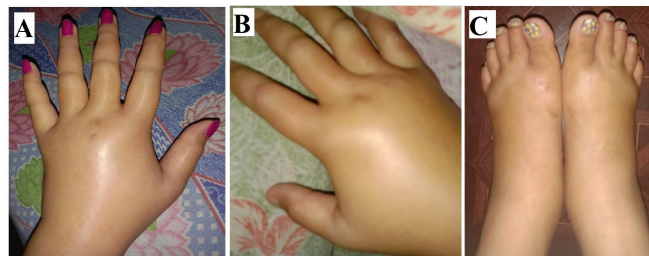


Figure 1: Depicts swelling over the dorsum of the left hand (A), right hand (B), and both feet (C).

Systemic examination revealed a bilateral wheeze, with progressive worsening breathlessness. Considering impending anaphylaxis, 0.5 mg of adrenaline 1:1000 dilution was given. A few minutes after administration of adrenaline, she complained of severe retrosternal chest pain [12] lead ECG was obtained (Figure 2). She developed hypotension with the blood pressure of 90/60 mmHg.

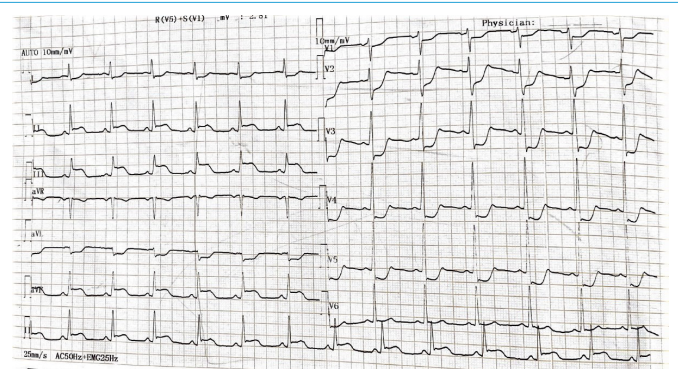


Figure 2: ECG showed ST elevation in inferior leads with reciprocal ST depressions in I, aVL, and V1-V5.

Clinical course: The patient was being stabilized with an Intravenous fluid bolus of normal saline, and was being prepared for catheterization lab. The ECG was suggestive of inferior Wall Myocardial infarction due to probable RCA occlusion (ST elevation in lead III, II, and avF, ST depression in I, aVL, and V1-V5). However, a quick echocardiogram revealed apical ballooning Due to moderate hypokinesia of the mid to distal septum, apical septum, apex, and apicolateral segments with a reduced ejection fraction of 35% (Supplementary video 1).

As this did not correlate with the infarct-related territory on ECG, she was shifted urgently to the catheterization lab which revealed normal epicardial coronaries (Figure 3).

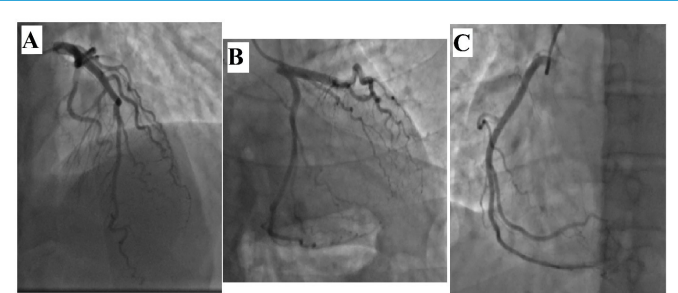


Figure 3: Depicts the normal left anterior descending artery (A), left circumflex artery (B), and right coronary artery (C).

Anaphylaxis: IM adrenaline 0.5 mg (1:1000 dilution) was given initially, later started on IV diphenhydramine 50 mg twice daily, and IV ranitidine Twice daily. She was started on oral prednisolone at 40 mg once daily with a plan to taper on follow-up.

Inferior wall MI (Type I Kounis): She received loading doses of aspirin 150 mg, ticagrelor 90 mg, and atorvastatin 80 mg before angiography. After the angiography atorvastatin 80 mg was continued and DAPT was discontinued. Oral diltiazem was started to treat coronary vasospasm.

Takotsubo cardiomyopathy: There was a dilemma in starting an ACE inhibitor or beta blocker for the low EF, due to fear of exacerbation of angioedema and coronary vasospasm.

Avoidance of allergen triggers: Extensive medication reconciliation was done and patient education was provided for avoidance of known allergens, especially antibiotics. She was referred to an Allergen specialist for further evaluation and management.

Follow-up: The patient was stabilized in the ICU, and discharged 3 days later with atorvastatin 80 mg, diltiazem 60 mg, prednisolone 40 mg (with a plan to taper every week), levoce-tirizine 5 mg. 1 week later she was started on medications for

Labs

Test	Result	Normal range
Complete Blood Count (CBC)		
White Blood Cell Count (WBC)	14,000 cells/ μ L	4,000-11,000 cells/ μ L
Eosinophil Count	754 cells/ μ L	0-450 cells/ μ L
Serum cardiac biomarkers		
Troponin	Initial: 0.14 ng/mL	0-0.04 ng/mL
	After angiography: 2.5 ng/mL	
Creatine Kinase-MB (CK-MB)	36 U/L	0-25 U/L
Electrolyte panel		
Potassium (K ⁺)	4.8 mmol/L	3.5-5.0 mmol/L
Calcium (Ca ²⁺)	9.3 mg/dL	8.5-10.5 mg/dL
Magnesium (Mg ²⁺)	2.2 mg/dL	1.7-2.2 mg/dL
Liver Function Tests (LFTs)		
Alanine Aminotransferase (ALT)	21 U/L	0-40 U/L
Aspartate Aminotransferase (AST)	25 U/L	0-35 U/L
Alkaline Phosphatase (ALP)	78 U/L	40-130 U/L
Total Bilirubin	0.8 mg/dL	0.3-1.0 mg/dL
Renal Function Tests (RFTs)		
Blood Urea Nitrogen (BUN)	15 mg/dL	7-20 mg/dL
Creatinine	0.9 mg/dL	0.6-1.1 mg/dL
Coagulation Profile		
Prothrombin Time (PT)	12 seconds	10-13 seconds
International Normalized Ratio (INR)	1.0	0.8-1.2
Activated Partial Thromboplastin Time (aPTT)	30 seconds	25-35 seconds
Other Tests		
Serum Tryptase	25 ng/mL	2-15 ng/mL
Serum Chymase	30 ng/mL	5-15 ng/mL

her LV dysfunction - carvedilol 3.125 mg, and valsartan 80 mg due to their low chances of coronary vasospasm and angioedema. She tolerated these tablets well and at 3 months follow-up, there was complete resolution of LV dysfunction.

Diagnosis

Timeline of events:

0 Hours: Received ciprofloxacin for acute otitis media.

2 hours: Onset of allergic hypersensitivity symptoms.

2 hours 30 minutes: Intramuscular adrenaline injection for suspected anaphylaxis.

2 hours 40 minutes: (Shortly after adrenaline injection): Development of chest pain and ECG changes suggestive of IWMI.

2 hours 45 minutes: Takotsubo cardiomyopathy noted in Echocardiography.

3 hours: Coronary angiography - normal epicardial coronaries.

Based on the clinical presentation, ECG findings, laboratory investigations, and echocardiography demonstrating apical ballooning, the patient was diagnosed with ciprofloxacin-induced anaphylaxis, Kounis syndrome type I (Coronary vasospasm),

Adrenaline associated Takotsubo consistent with the ATAK complex [1].

Discussion

Drug-induced anaphylaxis is commonly seen with penicillin, NSAIDs, sulphonamides, and antibiotics. Anaphylaxis has been reported with the first-ever dose of fluoroquinolones without the need for sensitization [2,3]. Adrenaline is the drug of choice for anaphylaxis, but it has been shown in some reports to precipitate cardiac events due to its metabisulphite component in certain preparations [4,5]. The catecholamine surge along with inflammatory mediators of anaphylaxis play a central role in orchestrating Kounis syndrome and stress-induced cardiomyopathy. Antibiotics, notably ciprofloxacin in our case, are one of the most common triggers of Kounis syndrome, with approximately 70% of cases occurring within 30 minutes post-administration. Type I Kounis syndrome, accounting for 72.6% of cases, is primarily characterized by coronary artery spasms triggered by the release of inflammatory mediators, which may or may not be accompanied by an elevation in cardiac enzymes. Type II occurs in individuals with underlying atheromatous disease; here, the inflammatory mediators can induce a coronary vasospasm and potentially lead to the rupture of atheromatous plaques, culminating in an acute myocardial infarction. Type III is associated with patients who have a coronary artery stent in place, where

inflammatory mediators can cause stent thrombosis. It's important to note that coronary artery spasm is typically a hyperacute condition [6,7].

Additionally in our patient, symptoms encompassing chest pain, following adrenaline administration with features suggestive of Takotsubo cardiomyopathy on Echocardiography are consistent with previous literature on ATAK complex [8,9]. During extreme stress, elevated catecholamines, along with exogenously administered epinephrine, can trigger a negative inotropic effect on the heart via β -adrenoceptors, potentially due to biased agonism leading to phosphorylation and signaling disruption. This surge can cause reversible myocardial stunning, notably in the apical and midventricular regions, a hallmark of Takotsubo Syndrome (TTS). Our case aligns closely with the documented clinical manifestations of the ATAK complex [10].

Management challenges: There are no specified guidelines for managing ATAK complex, and treatment has been individualized based on a few case reports. Managing patients with the ATAK complex requires a multidisciplinary approach, encompassing allergists, cardiologists, and emergency physicians. Treatment strategies may include addressing allergic reactions, managing Takotsubo syndrome, and mitigating coronary vasospasm. It differs from conventional management of STEMI in the following way [11,12].

Aspect	Standard acute MI management	Kounis syndrome management
Trigger	Atherosclerotic plaque rupture or thrombosis	Allergic reaction or hypersensitivity trigger
Initial treatment	Immediate reperfusion therapy (e.g., PCI, thrombolysis)	Treatment of anaphylaxis (e.g., adrenaline, antihistamines, corticosteroids)
Antiplatelet therapy	Aspirin, P2Y12 inhibitors (e.g., clopidogrel, ticagrelor)	May be used cautiously due to the increased risk of bleeding in anaphylaxis
Anticoagulation therapy	Heparin, low molecular weight heparin	May be used cautiously due to the increased risk of bleeding in anaphylaxis
Beta-blockers	Recommended for secondary prevention	May be used cautiously due to potential exacerbation of bronchospasm, coronary vasospasm
Coronary angiography	Essential for diagnosis and management	May be deferred in certain cases to avoid exacerbating anaphylaxis
Allergen avoidance	N/A	Essential to prevent future allergic reactions
Long-term management	Secondary prevention strategies (e.g., statins, ACE inhibitors, beta-blockers)	Focus on allergen avoidance and management of allergic reactions along with OMT for HF.

Conclusion

This case highlights the diagnostic and therapeutic issues associated with the ATAK complex, stressing the significance of appropriate diagnoses and managing the complex interplay between adrenaline, Takotsubo syndrome, anaphylaxis, and Kounis syndrome. A full understanding of these illnesses and their possible interactions is required for the best patient care and outcomes.

Disclosure statement: The authors report no financial relationships or conflicts of interest regarding the content herein.

References

- Margonato D, Abete R, Di Giovine G, Delfino P, Grillo M, et al. Takotsubo cardiomyopathy associated with Kounis syndrome: A clinical case of the ATAK complex. *J Cardiol Cases*. 2019; 2(2): 52-6. <https://doi.org/10.1016/J.JCCASE.2019.03.007>.
- Dhopeswarkar N, Sheikh A, Doan R, Topaz M, Bates DW, et al. Drug-Induced Anaphylaxis Documented in Electronic Health Records. *J Allergy Clin Immunol Pract*. 2019; 1(1): 103-11. <https://doi.org/10.1016/j.jaip.2018.06.010>.
- Navarro-Navajas A, Casallas I, Isaza D, Ortiz P, Baracaldo-Santamaría D, et al. Type III Kounis Syndrome Secondary to Ciprofloxacin-Induced Hypersensitivity. *Medicina (B Aires)*. 2022; 58(7). <https://doi.org/10.3390/medicina58070855>
- Borchert T, Hübscher D, Guessoum CI, Lam TDD, Ghadri JR, et al. Catecholamine-Dependent β -Adrenergic Signaling in a Pluripotent Stem Cell Model of Takotsubo Cardiomyopathy. *J Am Coll Cardiol*. 2017; 70(8): 975-91.
- Ballesteros RV, Carlos Gómez J, Olmos C, Vilacosta I. Case Report Kounis and Takotsubo, Two Syndromes Bound by Adrenaline: The ATAK Complex. 2023. <https://doi.org/10.1155/2023/7706104>.
- Renda F, Landoni G, Trotta F, Piras D, Finco G, et al. Kounis Syndrome: An analysis of spontaneous reports from international pharmacovigilance database. *Int J Cardiol*. 2016; 203: 217-20.
- Kounis NG, Koniari I, Velissaris D, Tzani G, Hahalis G. Kounis syndrome-not a single-organ arterial disorder but a multisystem and multidisciplinary disease. *Balkan Med J*. 2019; 36(4): 212-21.
- Margonato D, Abete R, Di Giovine G, Delfino P, Grillo M, et al. Takotsubo cardiomyopathy associated with Kounis syndrome: A clinical case of the ATAK complex. *J Cardiol Cases*. 2019; 20 2(2): 52-6. <https://doi.org/10.1016/J.JCCASE.2019.03.007>.
- Minciullo PL, Amato G, Vita F, Pioggia G, Gangemi S. ATAK Complex (Adrenaline, Takotsubo, Anaphylaxis, and Kounis Hypersen-

- sitivity-Associated Coronary Syndrome) after COVID-19 Vaccination and Review of the Literature. *Vaccines* (Basel). 2023; 11(2). <https://doi.org/10.3390/vaccines11020322>.
10. Lyon A. Stress in a Dish: Exploring the Mechanisms of Takotsubo Syndrome. *J Am Coll Cardiol*. 2017; 70(8): 992-5.
 11. Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, et al. Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2016; 18(1): 8-27. Available from: <https://doi.org/10.1002/ejhf.424>.
 12. Badami KG. Transfusion double whammy? Adrenaline-takotsubo-anaphylaxis-Kounis complex post transfusion? *Vox Sang*. 2022; 117(6): 862-5. <https://doi.org/10.1111/vox.13257>.