

Case Report

Undertaking Unexpected Catastrophe: Dual Antiplatelet Allergy in a Patient With Acute ST-Elevation Myocardial Infarction

Zakka Zayd Zhullatullah Jayadisastra¹, MD; Putrika Prastuti Ratna Gharini^{1*}, MD; Hendry Purnasidha Bagaswoto¹, MD; Budi Yuli Setianto¹, MD; Deshinta Putri Mulya², MD

ABSTRACT

Acute coronary syndrome (ACS) is caused by a thrombotic condition in the coronary arteries. It may present as acute ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation acute coronary syndrome (NSTEMI). Dual antiplatelet therapy (DAPT) is the primary strategy to reduce mortality and prevent future thrombosis in patients with acute STEMI. Nonetheless, allergy to these agents remains a clinical challenge during treatment. We describe a 68-year-old man with inferolateral STEMI who developed an allergic reaction to acetylsalicylic acid and clopidogrel after administration of a loading dose of DAPT. The patient was treated with fibrinolysis, which was considered successful. Angiography was not performed because of the patient's antiplatelet allergy. The DAPT allergy was successfully managed by reintroducing and rapidly desensitizing DAPT through the ADAPTED registry protocol. Alternative strategies are available when desensitization is not feasible. (*Iranian Heart Journal 2026; 27(1): 88-92*)

KEYWORDS: DAPT; allergy; ACS; STEMI

¹ Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada – Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

² Department of Internal Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada – Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

* **Corresponding Author:** Putrika Prastuti Ratna Gharini, MD; Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada – Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

Email: pgharini@ugm.ac.id

Tel: +62 (274) 588 688

Received: June 9, 2025

Accepted: August 11, 2025

Acute coronary syndrome (ACS) is caused by a thrombotic condition in the coronary artery. It may present as acute ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation ACS (NSTEMI). Both require antiplatelets to treat thrombosis and prevent further thrombosis after revascularization.^{1,2} Rare cases of allergy to antiplatelets have been reported.³ Measures to desensitize antiplatelets allow reuse; nevertheless, in de novo cases in ACS settings, management is more challenging.⁴

Case Report

A 68-year-old man presented with acute chest pain of 5 hours' duration. Shortness of breath, palpitations, and fever were denied. He had a history of hypertension and was an active smoker; drug allergy was denied. Vital signs and physical examination were unremarkable. Electrocardiography (ECG) showed sinus rhythm with ST elevation at II, III, aVF, V₇, V₈, and V₉, and he was diagnosed with inferoposterior STEMI (Figure 1). He was given a loading dose of acetylsalicylic acid ([ASA], 320 mg) and

clopidogrel (300 mg) for initial therapy. Minutes after drug administration, he developed facial pruritus with rash, consistent with a drug allergy reaction. He was then treated with alteplase (100 mg) for fibrinolysis, which was considered successful, and was transported to the intensive cardiovascular care unit (ICCU). The next day, after resolution of the rash, the patient was reintroduced to ASA in the morning and clopidogrel in the evening. Both reintroductions exacerbated the rash,

confirming suspicion of allergy to both ASA and clopidogrel. Reintroduction was repeated the following day and showed no reaction to clopidogrel. Accordingly, the Aspirin Desensitization in Patients With Acute Coronary Syndrome and History of Hypersensitivity (ADAPTED) protocol was initiated.⁴ Evaluation during and after desensitization showed resolution of the allergic reaction. The patient was discharged on dual antiplatelet therapy (DAPT) with ASA and clopidogrel.

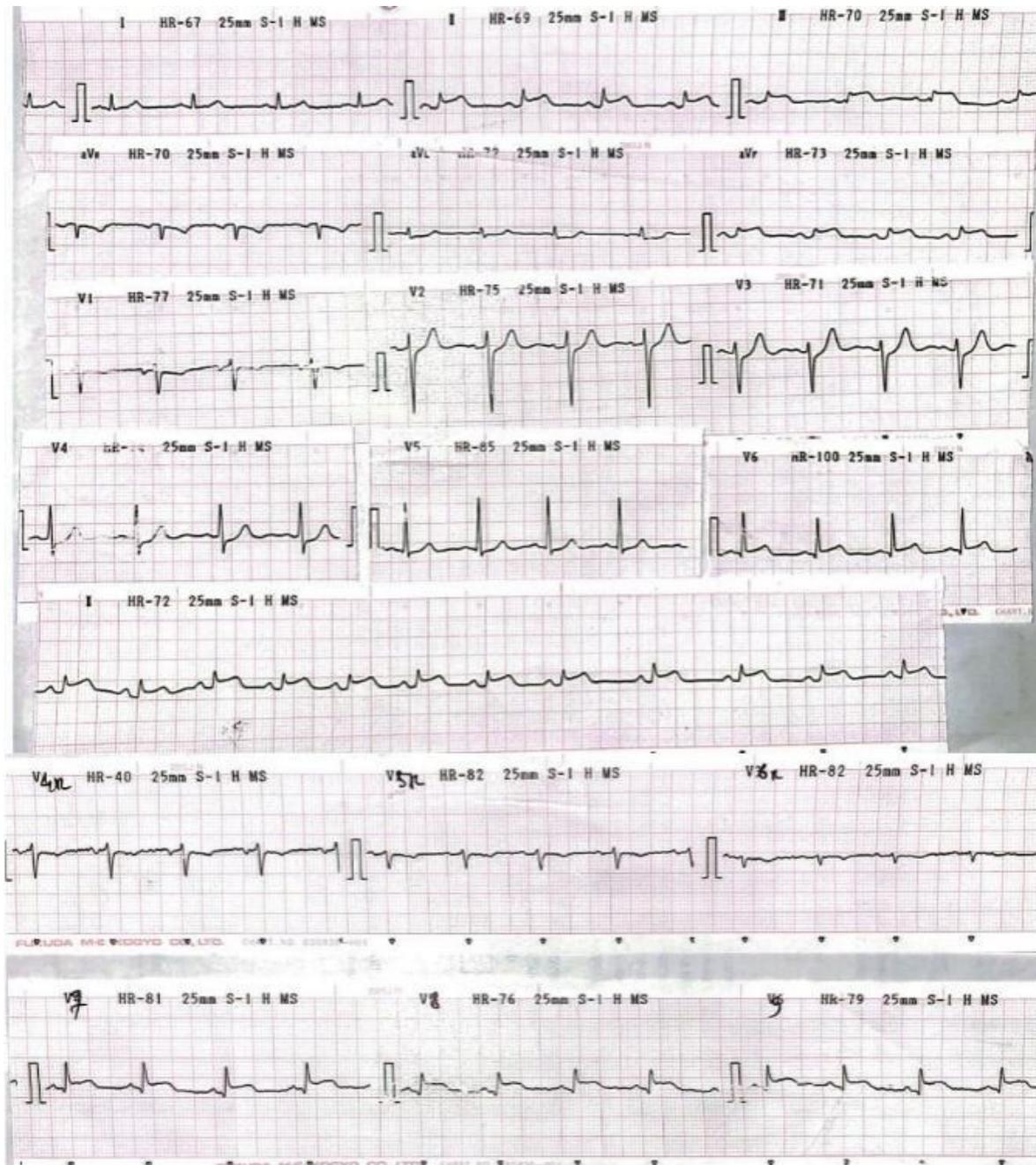


Figure 1. Electrocardiograms showing sinus rhythm with ST elevation at II, III, AVF, V₇, V₈, and V₉. The patient was diagnosed with inferoposterior ST-segment elevation myocardial infarction.

DISCUSSION

Antiplatelet therapy is the principal treatment for STEMI. The primary DAPT strategy uses a combination of ASA and a P2Y₁₂ receptor adenosine 5'-diphosphate (ADP) antagonist, such as clopidogrel.⁵ Hypersensitivity reactions to antiplatelets, including ASA and

clopidogrel, have long been reported in the CAPRIE trial.³ ASA hypersensitivity is caused by cyclooxygenase-1 (COX-1) inhibition, which reduces prostaglandin, arachidonic acid, and other prostanoids such as prostaglandin E₂ (PGE₂). Inhibition of PGE₂ leads to mast cell and proinflammatory

activation, resulting in hypersensitivity reactions in the skin and respiratory system.⁶ This was consistent with the patient's presentation of skin rash. Clopidogrel hypersensitivity, on the other hand, is mediated by immunoglobulin E (IgE), which causes skin rash. Another proposed pathophysiology is delayed hypersensitivity mediated by T cells.⁷ In this patient, the drug allergy was more likely rapid; consequently, IgE appears to be the most likely pathway for clopidogrel hypersensitivity.

The primary goal for this patient was to administer antiplatelet therapy as rapidly and safely as possible. Desensitization decreases calcium ion influx and prevents remodeling of actin filaments and mast cell degranulation. It leads to the creation of immunological memory and prevents further allergic reactions.⁸ Several desensitization protocols exist for both inpatient and outpatient settings. We used the ASA desensitization protocol from the ADAPTED registry⁴ because it was the fastest available. This protocol consists of a rapid, stepwise escalation using ASA diluted in water to achieve a low drug concentration until the solid preparation can be tolerated. Steps were advanced only if no allergic reactions occurred; otherwise, the step was repeated until no reaction was observed.

Clopidogrel desensitization could also have been used for this patient via a different protocol⁹ (Table 1). Still, because a provocation test with the therapeutic dose did not provoke an allergic reaction, we did not proceed with desensitization and continued the therapeutic dose.

An alternative strategy for acute situations in which desensitization is not feasible is to delay ASA administration before percutaneous coronary intervention and to begin desensitization afterward.¹⁰ Clopidogrel could be replaced with ticagrelor¹¹ or a "treating-through" strategy could be employed, which involves continuing clopidogrel with the addition of prednisone (30 mg every 12 hours

for 5 days) and tapering the dose (by 5 mg/d over 15 days).¹² Single-agent ticagrelor therapy for 12 months, followed by switching to clopidogrel, has also been proposed as an alternative strategy.

Table 1. Clopidogrel desensitization protocol (Adapted from⁹)

Minute	Dose (mg)	Concentration (mg/mL)
0	0.005	0.5
30	0.01	0.5
60	0.02	0.5
90	0.04	0.5
120	0.08	0.5
150	0.16	0.5
180	0.3	0.5
210	0.6	0.5
240	1.2	5
270	2.5	5
300	5	5
330	10	5
360	20	5
390	40	5
420	75	Tablet 75 mg

CONCLUSIONS

The desensitization protocol is the primary strategy for treating antiplatelet allergy to ensure the administration of DAPT in patients with ACS. Alternative strategies are also available for situations in which desensitization is not feasible.

Ethics Statement

The present study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient.

Conflict of Interest

The authors have no conflicts of interest to disclose.

Acknowledgements

None

REFERENCES

- Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur. Heart J.* 2018; 39:119–177. doi:10.1093/eurheartj/ehx393
- Collet JP, Thiele H, Barbato E, Bauersachs J, Dendale P, Edvardsen T, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur. Heart J.* 2021; 42:1289–1367. doi:10.1093/eurheartj/ehaa575
- CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996; 348:1329–1339. doi:10.1016/s0140-6736(96)09457-3
- Rossini R, Iorio A, Pozzi R, Bianco M, Musumeci G, Leonardi S, et al. Aspirin Desensitization in Patients with Coronary Artery Disease. *Circ. Cardiovasc. Interv.* 2017;10:10–15. doi:10.1161/CIRCINTERVENTIONS.116.004368
- Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. *Eur. J. Cardiothoracic Surg.* 2017; 53:34–78. doi:10.1093/ejcts/ezx334
- Minaldi E, Cahill K. Recent Updates in Understanding NSAID Hypersensitivity. *Curr. Allergy Asthma Rep.* 2023; 23:181–188. doi:10.1007/s11882-023-01064-3
- Ford MK, Cohn JR. Clopidogrel Hypersensitivity: Pathogenesis, Presentation and Diagnosis. *Curr. Vasc. Pharmacol.* 2018;17:110–112. doi:10.2174/1570161116666181031143628
- Kang SY, Seo J, Kang HR. Desensitization for the prevention of drug hypersensitivity reactions. *Korean J. Intern. Med.* 2022; 37:261–270. doi:10.3904/kjim.2021.438
- Lee-Wong, M., Gadhvi, D., Resnick, D. Clopidogrel desensitization. *Ann. Allergy, Asthma Immunol.* 2006; 96:756–757. doi:10.1016/S1081-1206(10)61080-0
- Bianco M, Gravinese C, Cerrato E, Nuñez-Gil I, Destefanis P, Luciano A, et al. Management of aspirin intolerance in patients undergoing percutaneous coronary intervention. The role of mono-antiplatelet therapy: A retrospective, multicenter, study. *Minerva Cardioangiol.* 2019; 67:94–101. doi:10.23736/S0026-4725.19.04787-X
- Chang GSW, Imran SS, Leow KL, Tan D. Ticagrelor Monotherapy in Aspirin-Allergic Patients Post-Coronary Stenting After Acute Coronary Syndrome: a Case Series. *J. Am. Coll. Cardiol.* 2018; 71:A1212. doi:10.1016/s0735-1097(18)31753-4
- Ramotowski B, Budaj A. Clopidogrel allergy successfully treated with corticosteroids without clopidogrel withdrawal. *Kardiol. Pol.* 2016; 74:489. doi:10.5603/KP.2016.0066