CASE REPORT

A Case of Acute St-elevation Myocardial Infarction (STEMI) Secondary to Anaphylactic Reaction: Type 2 Kounis Syndrome

Toh Chong Rui[1], Huzairi Sani[2], Nada Syazana Zulkufli[3]

[1] Medical department, Selayang Hospital, B21, Lebuhraya Selayang - Kepong, 68100 Batu Caves, Selangor, Malaysia
[2] Cardiology unit, Medical Department, Faculty of Medicine, Universiti Teknologi MARA, Jalan Hospital, 47000 Sungai Buloh, Selangor
[3] Pakar Klinikal Patologi Kimia, Jabatan Patologi, Hospital Pulau Pinang, Jalan Residensi, 10990 George Town, Pulau Pinang

ABSTRACT

Kounis syndrome (KS) is defined as acute coronary syndrome (ACS) induced by coronary vasospasm associated with an anaphylactic reaction. This condition was described in 1991 by Kounis, detailing potential pathophysiological pathways for coronary spasm. We report a case of Type 2 KS – a patient with stented coronary artery disease who presented with ST-elevation myocardial infarction (STEMI) following intramuscular Diclofenac Sodium.

Keywords: Kounis syndrome, Anaphylaxis, Acute coronary syndrome

Corresponding Author:
Toh Chong Rui, MBBS
Email: toh_chongrui92@hotmail.com
Tel: +6013-2567961

CASE REPORT

A 55-year-old gentleman with no known allergies or history of atopy presented to the Emergency Department (ED) with a brief pre-syncopal episode followed by a generalized pruritic body rash shortly after receiving 75 mg of intramuscular Diclofenac Sodium from the General Practitioner for lower back pain. He has a background history of coronary artery disease (CAD) for which stents were inserted into the left anterior descending artery and right coronary artery. Apart from being an active smoker, he is otherwise compliant to his ACS treatment.

In the ED, he was found to be hypotensive at 88/56 mmHg, tachycardic at 120 bpm and saturating well at 100% on ambient air. There was widespread urticarial rash, however, lung fields were clear on auscultation. He was diagnosed with anaphylactic shock secondary to Diclofenac Sodium hence was given intramuscular Adrenaline 0.5 mg, intravenous Hydrocortisone 200 mg and intravenous Chlorphenamine Maleate 10 mg. He responded well alongside adequate fluid therapy, where his blood pressure picked up to 115/70 mmHg and his pulse rate reduced to 92 bpm.

Two hours later, he complained of severe central chest pain typical of angina. Electrocardiogram showed significant ST-elevations over V2 to V4 with reciprocal ST-depressions over leads II, III and aVF (Figure 1a). Transthoracic echocardiogram showed anterior wall hypokinesia. His serum creatinine kinase was elevated at 4582 IU/L and Troponin T was raised to >2 ng/mL. Given the impression of anteroseptal STEMI, he was given tablet Aspirin 300 mg, tablet Clopidogrel 300 mg and intravenous Streptokinase 1.5 Mu and referred to the Internal Medicine team. An hour later, the chest pain resolved and ECG showed >50% resolution of ST-elevation (Figure 1b).

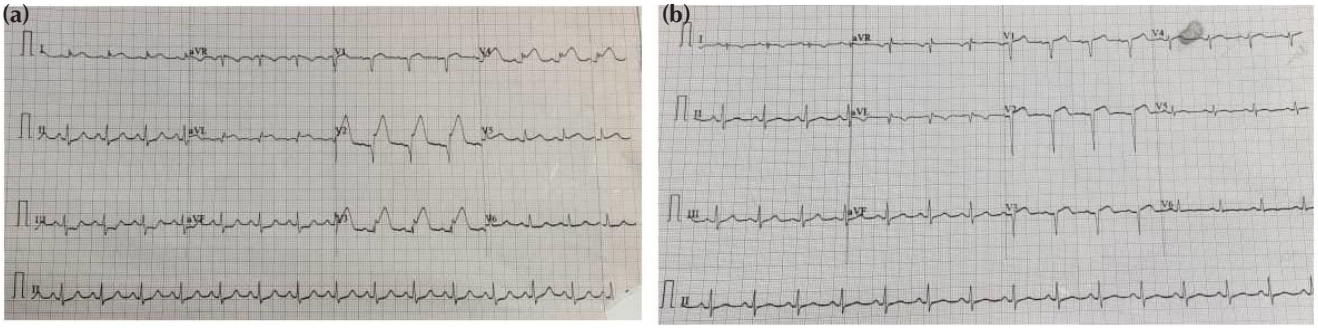

Figure 1: (a) 1 Electrocardiogram showed anteroseptal ST-elevation with reciprocal changes. (b) Electrocardiogram 1 hour post thrombolysis (I.V Streptokinase)

He was then referred to a central cardiac centre for an urgent coronary angiography which revealed no acute culprit lesions in the left anterior descending artery. No remnants to suggest a recent thrombus or plaque rupture were also found (Figure 2a and 2b). He consequently had his regular medical therapy continued and was discharged well a few days later.

DISCUSSION

Kounis syndrome (KS) is an acute coronary syndrome resulting from the release of inflammatory mediators during an allergic or anaphylactic insult. It was first described by a Greek physician, Dr Nicholas Kounis in 1991, in a case report of coronary spasm progressing to allergic acute myocardial infarction. Mast cell degranulation following an allergic reaction, causing the release of vasoactive mediators, proteases such as tryptase and chymase, platelet-activating factors and cytokines have been described as its aetiology. Reported triggers of KS include antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), chemotherapy agents, food and insect bites (1).

KS does not affect a specific ethnicity, geographical location or age group. It is believed that KS is not rare, however, as it is not well-recognized, it is underdiagnosed and not well treated. To date, resources on KS is limited and the majority of information come from clinical case reports. Diagnosing KS is therefore a challenge as neither diagnostic criteria nor confirmatory tests are available. Signs and symptoms of anaphylaxis alongside acute changes on electrocardiogram and echocardiogram should raise the suspicion of KS. An urgent coronary angiography should entail to confirm the presence or absence of a culprit lesion. Other helpful albeit non-specific diagnostics include serum tryptase, histamine and cardiac enzymes (1).

There are three variants of KS. Type 1 involves patients with normal coronary arteries who develop coronary vasospasms following exposure to inflammatory mediators during an acute anaphylactic reaction. Type 2 comprises of patients with pre-existing atheromatous disease who develop coronary vasospasms or atheromatous plaque rupture during an allergic reaction. Type 3 variant includes patients with coronary artery stent thrombosis due to mast cell and eosinophilic infiltration.

The differential diagnoses considered in this case included STEMI secondary to [1] stent thrombosis/plaque rupture; [2] adrenaline injection; [3] hypotension i.e. Type 2 myocardial infarction; and [4] Kounis syndrome. As angiography showed no evidence of recent thrombosis or rupture, the first differential diagnosis was minimised. Adrenaline-induced STEMI was also deemed unlikely as symptoms did not occur until two hours post-adrenaline. Typically, ACS precipitated by adrenaline occurs within minutes of administration and is more common with the intravenous route (2). Allergic ACS, on the other hand, may take hours from the time of allergic reaction to manifest (3). Given the delayed onset of 2 hours from a brief hypotensive episode in addition to the severity of ST-elevation and marked Troponin T elevation that are usually seen in Type 1 MI, Type 2 MI was also ruled out. As our patient had pre-existing CAD, an acute anaphylactic reaction that occurred a few hours prior to developing STEMI and a coronary angiography revealing no acute culprit lesions, he was classified as Type 2 KS. Of note, this patient's early elevation of creatine kinase is most likely due to the Diclofenac Sodium injection as intramuscular needling and the direct cytotoxic effect of Diclofenac Sodium may independently increase creatine kinase levels within an hour (4).

There is no current consensus on the management of KS. Treating the allergic reaction in Type 1 KS is reportedly sufficient to resolve the ACS whilst treating

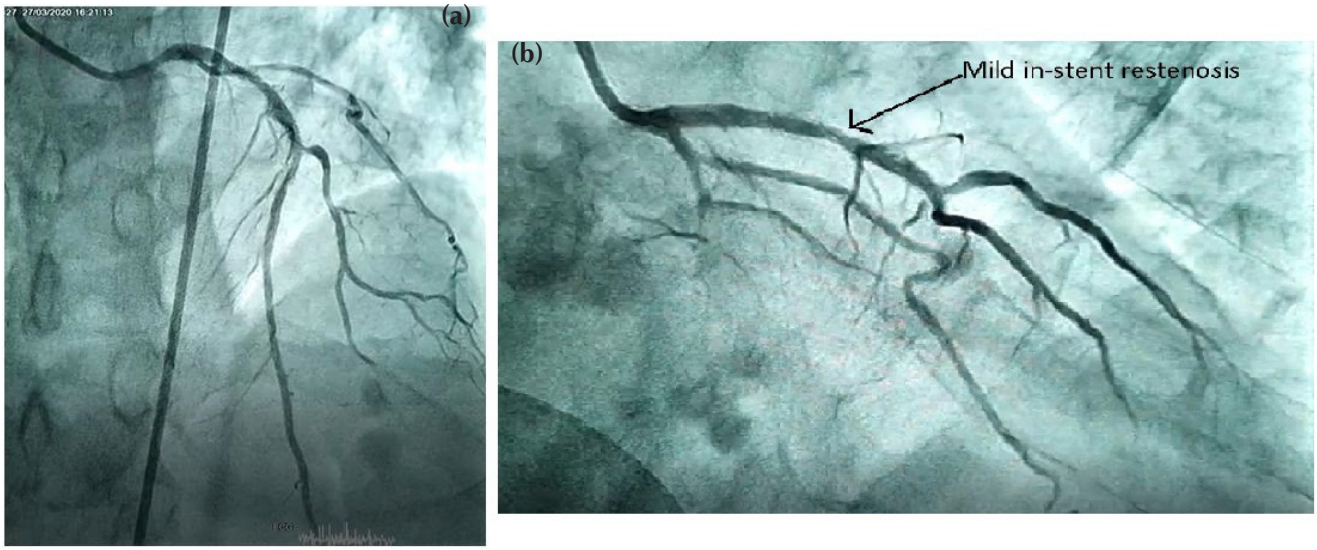

Figure 2: (a) Left anterior descending artery on coronary angiogram showed no acute culprit lesion. (b) Mild In-Stent Restenosis (ISR) in left anterior descending artery

both allergic reaction and ACS is required in Type 2 and Type 3 KS, given the pre-existing CAD. Nitrates and calcium channel blockers may be given to relieve vasospasm if necessary (1). In patients with pre-existing CAD, Adrenaline should only be reserved for severe anaphylaxis as its adrenergic effects causing coronary vasoconstriction and tachycardia may be detrimental (2). Morphine is also cautioned as its histamine-releasing property may complicate KS (1). Steroids have been implicated in inducing ACS and delaying myocardial healing, however, a meta-analysis has shown mortality benefit and proven no harm of corticosteroids in ACS (5).

For the long term, patients with pre-existing CAD should be maintained on ACS treatment, with close attention being given to Aspirin hypersensitivity especially in patients with NSAID allergies. Should an Aspirin allergy develop, patients may be switched to an alternative anti-platelet or offered Aspirin desensitization. Patients should also be advised on avoiding allergic triggers (including all drugs with cross-sensitivity to the primary drug) and educated on first-aid management should an allergic reaction occur. An allergy card or medical alert bracelet detailing the diagnosis is also beneficial.

CONCLUSION

At present, no diagnostic test or validated diagnostic algorithms are available to diagnose Kounis syndrome. A high index of suspicion is therefore required in cases of ACS in the context of an allergic reaction. Given its postulated mechanism of action, treatment is directed at both allergic reaction and myocardial damage. Early suspicion is crucial in the management of KS as immediate anaphylactic treatment is life-saving and prevents unnecessary thrombolytic therapy and invasive interventions – both of which are not without complications. More case reports and studies are needed to produce congruent guidelines in diagnosing and managing this disease.

ACKNOWLEDGEMENTS

Our utmost gratitude goes to our colleagues, supervisors and family members for their active guidance and encouragement.

REFERENCES

1. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. Clin Chem Lab Med. 2016;54(10):1545-59.
2. Zakka K, Gadi S, Koshlelashvili N, Maleque NM. Acute myocardial injury after administration of intravenous epinephrine for allergic reaction. SAGE Open Med Case Rep. 2020;8:2050313X20933104.
3. Kasim S, Abu Bakar R, McFadden E. Anaphylaxis from Wasp Stings Inducing Coronary Thrombus. Case Reports in Cardiology. 2012;2012:1-3.
4. Probst M, Kuhn JP, Modess C, Scheuch E, Seidlitz A, Hosten N, et al. Muscle Injury After Intramuscular Administration of Diclofenac: A Case Report Supported by Magnetic Resonance Imaging. Drug Saf Case Rep. 2017;4(1):7.
5. Giugliano GR, Giugliano RP, Gibson CM, Kuntz RE. Meta-analysis of corticosteroid treatment in acute myocardial infarction. The American Journal of Cardiology. 2003;91(9):1055-9.