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Case Report: Hypersensitivity Mediated ST-Elevation Myocardial Infarction—"Kounis Syndrome with Cronovich Phenomenon"

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"Kounis Syndrome with Cronovich Phenomenon"

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Abstract

Introduction: ST elevation myocardial infarction in concurrence with angioedema, anaphylaxis, hypersensitivity, or platelet activation is an event well published in literature known as Kounis-Syndrome. Classically, these events are linked by the administration of epinephrine either intravenously or intramuscularly for the treatment of the acute immunologic response.
Case Report: This particular case is a 78 year old male with history of c1 esterase inhibitor deficiency, angioedema, and hypertension presenting with angioedema. His symptoms started the previous night and were managed in the ED with methylprednisolone, diphenhydramine, and famotidine. The patient was intubated for airway protection and extubated about 24 hours later. About 48 hours after symptom onset, the patient developed acute chest pain and STEMI. He underwent PCI and stent placement after a 99.9% occlusion of the proximal LAD was identified.
Discussion: This case is unique because the patient did not receive epinephrine for the treatment of his immune response, and the 48 hour latency of STEMI symptoms. This particular case is unlike classic Kounis syndrome and suggests that ACS in the setting of acute immune response is independent of epinephrine administration. It also postulates that latent mediators of immune response and/or their degradation may play an important role in the development of ACS.
Conclusions: Kounis syndrome and this case in particular provide a novel area of study for the pathophysiology, prevention, and treatment of ACS. In patients with a history of CAD presenting with acute immune response, emergency providers should keep a high suspicion for the potential of ACS and use epinephrine judiciously.

Introduction

- Kounis Syndrome is described as an acute hypersensitivity induced STEMI or other ACS.
- Type I Kounis Syndrome variant refers to coronary artery vasospasm in normal coronary arteries as a result of the acute release of inflammatory mediators. (1)
- Type II Kounis Syndrome variant refers to either coronary artery vasospasm or acute plaque rupture in known coronary atheromatous disease. (2)
- Type III Kounis Syndrome variant refers to coronary stent restenosis or repeat thrombosis as a result of inflammatory infiltration or induced by inflammatory mediators. (3)
- Each variant may present along the spectrum of acute coronary syndrome with or without troponin elevation.

Case Report

This case is a 78 year old male with history of c1 esterase inhibitor deficiency, angioedema, and hypertension presenting with angioedema. His symptoms started the previous night and were managed the following morning in the ED with methylprednisolone, diphenhydramine, and famotidine. The patient was intubated for airway protection and extubated about 24 hours later. As an inpatient, the patient received a dose of c1 esterase inhibitor. About 48 hours after symptom onset, the patient developed acute chest pain and STEMI. He underwent PCI and stent placement after a 99.9% occlusion of the proximal LAD was identified. A 75% RCA stenosis was also identified during the procedure. Following the procedure, an echocardiogram revealed an EF of 21%. The patient underwent catheterization and stenting of the RCA a month later after presenting with an episode of SVT. One day following the procedure, repeat echocardiogram revealed an EF of 62%.

Pathophysiology

- Coronary thrombosis results from activated mast cells and their mediators (histamine and bradykinin) acting on platelets expressing similar IgE. The activated platelets undergo conformational change and express glycoprotein 1b to bind VWf to the endothelial wall. Platelets release proinflammatory and prothrombotic mediators (thromboxane A2), and the coagulation cascade ensues. (4)
- Further, mast cells infiltrate preexisting coronary artery plaques and reside in the lesions along with macrophages and T-cells. Once activated, the release of pro-inflammatory mediators (histamine, leukotrienes, prostaglandins, cytokines, proteases, tryptase) contribute to plaque instability and rupture. (5)
- Plaque rupture and thrombosis of the coronary artery goes on to cause ischemia and subsequent necrosis of the myocardium if perfusion is not restored.

EKG

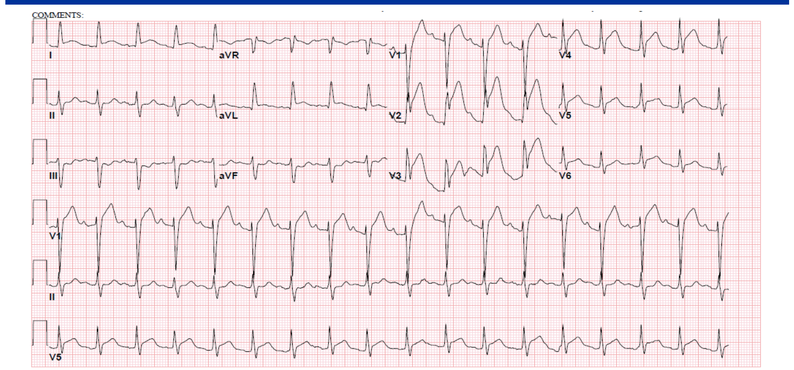

Figure 1 – 12 Lead EKG taken at the time of symptom onset. Sinus tachycardia with significant ST-elevation visualized in anterior and lateral leads.

Therapeutic Intervention

Percutaneous Coronary Intervention

1. Hemodynamics: Moderately elevated systemic pressure.[SEP]2. LV angiography: LVEF: 50-55%. Global left ventricular systolic function was normal.[SEP]3. Coronary angiography: Two vessel (involving proximal LAD) obstructive coronary artery disease.[SEP]4. LAD: 99% left anterior descending artery stenosis.[SEP]5. RCA: 75% right coronary artery stenosis.[SEP]6. Interventional Results (Lesion 1): Successful Primary PCI of proximal left anterior descending using Xience Sierra 3.5 x 28mm.

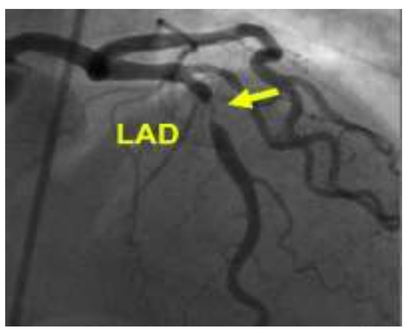

Figure 2 – Coronary angiography indicating 99% occlusion of proximal LAD pre-stenting.

Discussion

- This patient's presentation mostly closely aligns with type II Kounis syndrome variant as evidenced by existing coronary artery disease in the RCA during catheterization.
- This patient had a history of c1 esterase inhibitor deficiency and received c1 esterase inhibitor prior to the STEMI. Patients receiving c1 esterase inhibitor less than 6 hours between symptom onset and reperfusion had significantly lower TnI serum levels postoperatively compared to patients who did not receive c1 esterase inhibitor therapy or therapy after greater than 6 hours ($p < .05$). This RCT demonstrated the complement system as a significant contributor to cardiac ischemic-reperfusion injury. (6)
- Kounis syndrome has also been linked to the administration of epinephrine during the acute immune response. Classically, the pathophysiology and literature suggest concurrent immune response and STEMI symptoms. The patent did not receive epinephrine and his STEMI symptoms started about 48 hours following the acute immune response. This presentation suggests latent mediators of immune response activation and/or their degradation as cause for STEMI, and provides novel areas of study in pathophysiology, treatment, and prevention of ACS. Lastly, the investigators of the case suggest the name Cronovich phenomenon for latent STEMI in the setting of acute immune response.

Conclusions

- In the setting of acute immune response, atheromatous mast cell activation, vessel permeability leading to hypoperfusion, complement activation, and systemic vasodilation reducing cardiac output all must be considered in playing a role in ACS.
- In patients with a history of CAD presenting with acute immune response, all providers should keep a high suspicion for the potential of ACS presenting acutely as Kounis Syndrome or latent as Kounis Syndrome with Cronovich phenomenon.

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