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Hypersensitivity, Allergic Reactions and Coronary Disease - A Literature Review on the Pathophysiology and Management of Inflammatory Cascade Leading to Myocardial Ischemia

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Abstract:

An interesting case of a 54-year-old Caucasian gentleman who presented with a ST elevated electrocardiogram changes and a significant troponin leak secondary to anaphylactic reaction post ampicillin administration. Epinephrine infusion was started which has resulted in the improvement of Blood pressure. ST changes were resolved over 15 minutes. Initial Troponin was 148 (< 20) with a repeat of 1100 in 2 hours. Transthoracic echocardiogram was normal with no regional wall motion abnormality. Coronary angiogram has revealed a normal coronary artery with no atheromatous plaque. Allergic testing in the outpatient setting has confirmed the strong reaction with Ampicillin which was the likely culprit.

Keywords: Hypersensitivity, Allergic reaction, Coronary Vasospasm, Kounis Syndrome

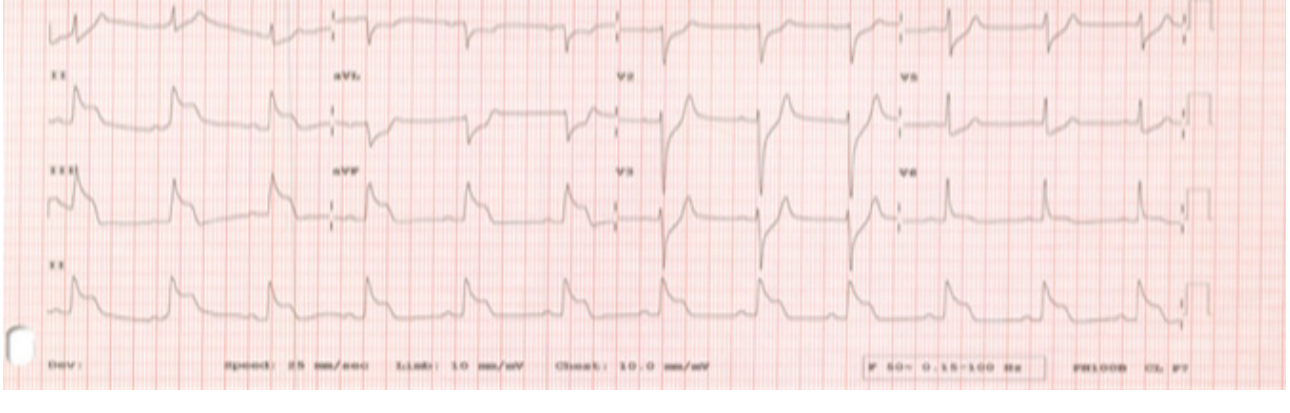
Introduction

An interesting case of Kounis syndrome in the setting of Ampicillin allergy mimicking ST elevation myocardial infarction.

Presentation

A 64-year-old Caucasian gentleman presented for scheduled dental extraction in day unit setting. As per the protocol of extraction IV Ampicillin 1gram was administered 15 minutes before the procedure. Within minutes of this he started to feel unwell with obvious sweating, light headedness and chest discomfort. Blood pressure was dropped to systolic 70mm Hg with a heart rate of 65/min. Urgent Electrocardiogram (ECG) was done and a cardiac monitor was attached. There was impressive ST elevation of 4-5 mm (Figure 1.1) in inferior leads (II, III, avF) with a ST depression in V5 chest lead.

Figure 1.1 showing ST elevation in lead II, III and avF with a ST depression in V5



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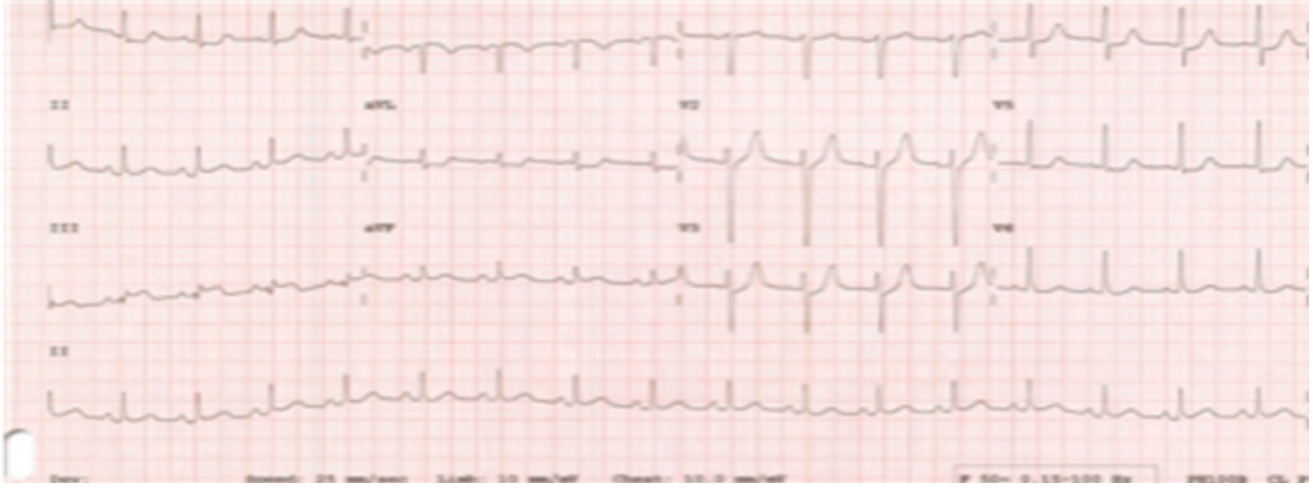
The clinical presentation with the given ECG changes were alarming though in the setting of post Antibiotic administration an anaphylactic episode was considered and IM adrenaline was administered on urgent basis. Cath lab and emergency department were notified in a nearest public hospital which was at the distance of 5 minutes of drive. Over the next 15 minutes IV fluids -Normal saline bolus was given to improve the Blood pressure. In the post Epinephrine administration phase, there was a quick response in BP improvement and gradual resolution of ST elevation was noted (Figure 1.2)

Figure 1.2 Resolution of ST elevation within 15 minutes post Adrenaline administration



On arrival in ED formal blood work up and Chest x ray was arranged. The X ray was not showing any signs of Pulmonary edema and heart size was within the normal range. Initial Troponin was 148 (< 20) with a repeat of 1100 in 2 hours.

Given the clinical presentation, acute coronary syndrome treatment was started enroute to ED and Aspirin loading dose of 300 mg has ben administered by paramedic services. Bedside Transthoracic echocardiogram was done on arrival in ED which was showing a normal Left ventricular function and no regional wall motion abnormality (Figure 2). There was no evidence of apical ballooning in echo ruling out the suspicion of TakatsuboCardiomyopathy

Figure 2.1-2.3 - Apical 4, 3 and 2 chamber view showing normal size of Chambers and no apical ballooning

Figure 2.1 apical 4 chamber view

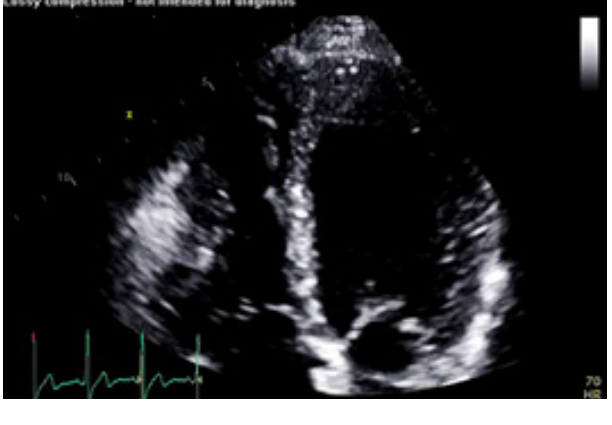


Figure 2.2 3 chamber view

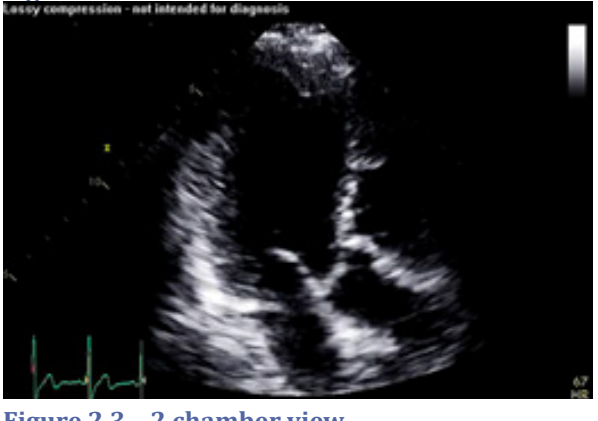


Figure 2.3 – 2 chamber view

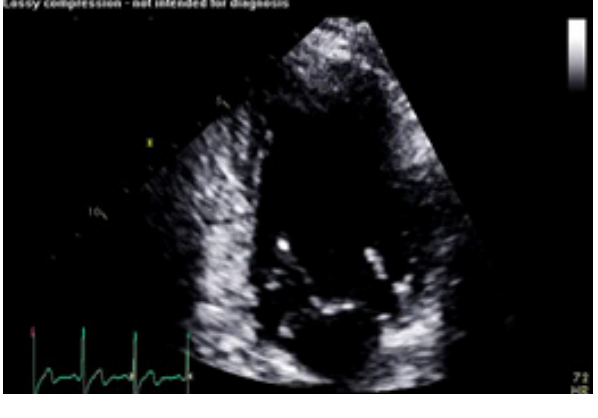


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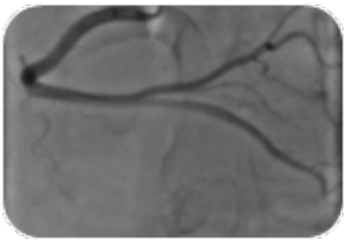
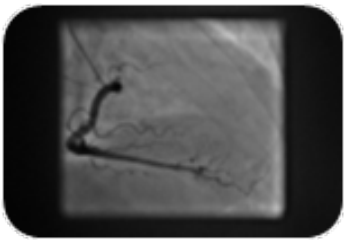
Figure 3.1-3.4 showing normal patent coronary arteries and normal left ventriculogram

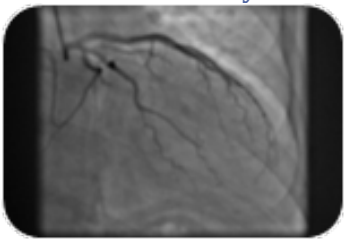
3.1 Normal flow to LAD and CCX



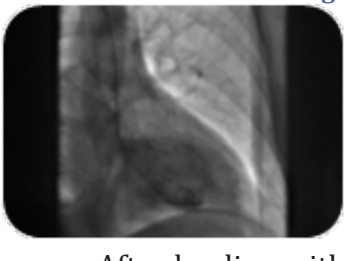
3.2 Normal RCA flow



3.3 Normal Coronary flow



3.4 Normal Left ventriculogram



After loading with the dual antiplatelets an urgent coronary angiogram was performed revealing a completely normal coronaries with no evidence of any plaque or obstruction (Figure 3.1,3.2,3.3).

A raised level of Tryptase was noted which was further indicative of underlying inflammatory aetiology leading to this clinical presentation. A referral to outpatient immunology clinic was arranged for the follow up where several allergic testings has been performed. Aconfirmed strong reaction with Ampicillin was found in testing making it the likely culprit.

Discussion

Coronary artery disease in the setting of allergic and anaphylactic reactions are long known and has been frequently reported in last few years. The first report in this lineage was done in 1938 by Eugene Clark for reactive arteritis and carditis in a young patient after receiving anti-pneumococcal serum. (1) The first case of acute MI associated with Urticaria secondary to Penicillin was reported in 1950 by Pfister and Plice (2) however it was not until 1991 when Kounis and Zavras described the allergic angina syndrome as Allergic acute MI (3).

Allergic reaction leads to mast cell activation with the release of histamines, leukotrienes, prostaglandins, and platelet activation factor. These factors can induce coronary artery vasoconstriction or atheromatous plaque rupture with coronary artery thrombosis (4,5). Kounis Syndrome can affect any age group but mostly its incidences have been found in 6th to 7th decade of life with the risk factors of Hypersensitivity, Hypertension, Smoking, DM2 and dyslipidaemia. Various causes have been found to trigger KS with the common ones as Antibiotics and insect bites (4).

The pathophysiology of Kounis Syndrome is largely driven by coronary vasospasm, plaque erosion or rupture in the setting of allergic cascade. This is profoundly a mast cell activity which is abundant in Cardiac cells with the preferential location to plaque site leading to its interaction to macrophages and T lymphocytes (6). Most of the clinical onset is within an hour of the anaphylactic trigger. This can be explained by the concept of Mast cell degranulation, Antigen-Antibody reaction on the surface of mast cell, release of inflammatory mediators and activation of complement system (7-9). Cases with delayed onset of clinical manifestation up-to 48 hours has been reported as well which implicates the role of slow mediators of inflammation in the setting of Kounis syndrome (10).

There are three different variants proposed for Kounis Syndrome. In 1st one there are no cardiovascular risk factors and coronary arteries are normal. The vasospasm is produced due to allergic cascade. In second type there is pre-existing coronary disease where the plaque rupture happens with the onset of allergic reaction (9). Type three is associated with stent thrombosis in the setting of allergic reactions (11). The onset is generally marked with chest pain with or without rise in cardiac enzyme, dizziness, syncope, nausea, vomiting , urticaria, diaphoresis, hypotension and bradycardia (12).

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ECG, cardiac enzymes and troponins are relatively insensitive to Kounis syndrome cases. Case reports have been published with Kounis syndromes where all these parameters have been normal (13). In these clinical situation biopsies has been considered for the diagnosis of underlying dilemma presenting with heart failure. Cardiac imaging has been used to provide the supportive information. Echocardiography and Single Photon emission Computed Tomography has low spatial resolution and has missed the small myocardial involvement if its particularly subendocardial (14). Use of CTCA is limited with its ability to characterize the myocardial lesion along with exposure to radiation and contrast (15). Recently use of Cardiac MRI has been rising in diagnosis of various cardiovascular disease. It can distinguish between viable and non-viable myocardium using dynamic contrast enhanced MRI images.MRI features suggestive of subendocardial involvement, contrast defect on first-pass MR images, normal washout of contrast agent on delayed images, and sensitivity to the left ventricle are specific findings for patients with Kounis syndrome type 1 (16).

Management of Kounis syndrome has largely been postulated with several case reports published. As per the current AHA/ACC guidelines use of Aspirin, Nitrates, Antihistamines, epinephrine, Steroid, B blockers and CCB has been considered in the given clinical context. Imaging techniques as mentioned above along with invasive catheterization is a part of treatment strategy. Overall Aspirin use in the anaphylactic setting is controversial given its direct effect on COX pathway which can lead to shunting of arachidonic acid and increased production of leukotrienes which are important mediators of anaphylaxis (17). Use of Oral or intravenous nitro-glycerine has been found safe with occasional caution of hypotension and tachycardia. Its mechanism of action is largely based on increased myocardial oxygen delivery, vasodilation of both peripheral and coronary circulation and decreased myocardial preload. Allergic reactions with nitrate is largely manifested as contact dermatitis and urticaria and these patients have tolerated the Oral and Intravenous nitrates well (18). B blockers are of proven benefit in the treatment of acute coronary syndrome though its use in Kounis Syndrome is more complex. Given Epinephrine has major role in Kounis syndrome treatment, use of B blocker can offset its beneficial effect and can complicate the treatment. Due to this consideration of B blocker, use of Non dihydropyridine CCB which has direct effect on reduction of vasospasm has proven benefit in the management of Kounis syndrome. On contrary to ACS management, In KS management Oxygen therapy has been given the 1st line preference by AHA guidelines.

Use of Epinephrine has been cautioned in several case reports due to possibility of an overlap between isolated Kounis syndrome with underlying acute coronary syndrome. In concurrent cases of Anaphylaxis and ACS its use can aggravate coronary ischemia, prolongation of QT interval, coronary vasospasm and arrhythmia. Worsening of vasospasm is possible due to unopposed Alpha-adrenergic actionspecially if a B blocker has been used as a part of treatment. Glucagon infusion has been recommended to overcome these pronounced B blockade effects. The current consensus is for use of IM 1:1000 IM Epinephrine in the setting of Kounis syndrome. Use of successful intracoronary adrenaline in the setting of vasospasm has been reported by Rankin et al in 2015 (19). This is on the basis of role of Coronary B2 epinephrine receptors producing vasodilation even with the small doses of epinephrine while alpha receptors needing higher doses to produce vasoconstriction.

The use of H1 and H2 blockers in the management of KS is considered second line. Mas cell stabilizers has been discussed however lacks any clear evidence in the management of Kounis syndrome setting.

Conclusion

The association of anaphylaxis with acute coronary syndrome is well documented. Here we report another case of Kounis syndrome secondary to Ampicillin reaction. Our article review highlights the pathophysiology of inflammatory cascade explaining the coronary vasospasm, reports the successful use of adrenaline in the setting of Kounis syndrome which was cautioned in past, refers to the novel use of Intracoronary adrenaline in the setting of low blood pressure and possible use of cardiac

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MRI in the setting of Type 1 Kounis if there is no troponin leak (20).

Consent

The Author/s confirms the written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Abbreviations:

ED: Emergency Department; MI: Myocardial Infarction; KS: Kounis Syndrome; CTCA: CT Coronary Angiogram; MRI: Magnetic Resonance Imaging; CCB: Calcium Channel Blocker; ACS: Acute Coronary Syndrome; IM: Intramuscular; AHA: American Heart Association;

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