Bee sting induced Allergic Acute Coronary Syndrome - Kounis syndrome

ABSTRACT

Bee sting cause local allergic reactions to life threatening conditions. It is well known that during mast cell activation, the release of inflammatory mediators which can cause coronary arteries spasm and atheromatous plaque rupture 2. Kounis syndrome is the concurrence of acute coronary syndrome caused by allergic or hypersensitivity reaction due to a drug or substance associated with mast cell activation 1. Herein, we report a 31-year-old man without known risk factors for coronary artery disease (CAD) who developed MI following bee sting.

Keywords: Bee sting; Hymenoptera toxin; Allergic Myocardial Infarction; Kounis syndrome.

INTRODUCTION:

The Kounis syndrome is described as an acute coronary syndrome after bee stings or exposure to environmental toxins or drugs 1. Kounis syndrome was first described in 1991 by Kounis and Zavras. It is also known as "allergic angina syndrome" or "allergic myocardial infarction. Bee sting may cause hypersensitivity reaction ranging from simple allergic reaction to life-threatening anaphylactic reaction, sometimes leading to death. Although rare, cardiac involvement is a possible complication, varying from vasospasm to acute ST-elevation myocardial infarction (MI) in the presence of underlying coronary artery disease and without underlying coronary artery disease.

CASE REPORT 1

A 31-year-old male presented with complaints of severe retrosternal pain radiating to both arms and profuse sweating associated with nausea and vomiting. He had more severe generalized erythematous rash over the face, neck, and thorax regions accompanied by itching. He had a history of multiple honey bees sting on the head, neck and bilateral upper arms while travelling in a bike along with his father one day before. His father has more severe generalized rashes associated with itching and wheezing. He died due to anaphylaxis at a hospital elsewhere. Patient himself reported a short period of dizziness and respiratory discomfort after stung. The patient was not a smoker or alcoholic or substance abuse and with no history of dyslipidemia, hypertension, diabetes mellitus, coronary artery disease or other significant illness.



Physical examination and investigations

He was afebrile with blood pressure of 110/70 mmHg and the pulse revealed 82 beats/min with oxygen saturation 98% at room. The ECG revealed elevation of ST segment in leads I, II, III, AVF, tall R wave in V1-V4, compatible with acute inferior and posterior wall myocardial infarction (Figure 1). Echocardiography revealed mild mitral regurgitation, mild diastolic dysfunction, and left ventricular ejection fraction 45%. His cardiac enzymes were elevated.

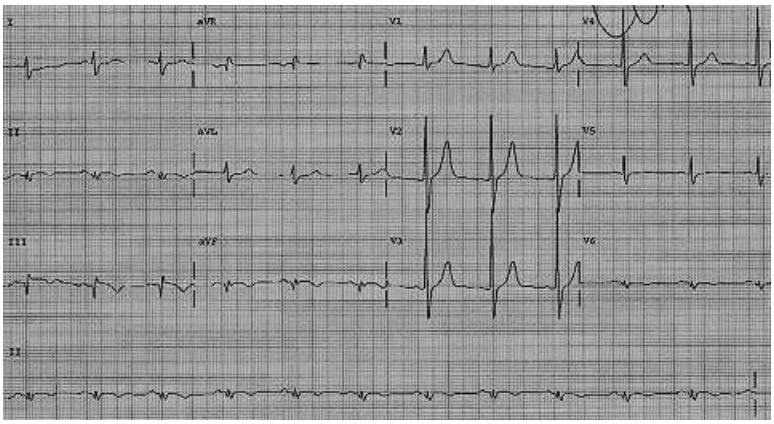


Figure 1

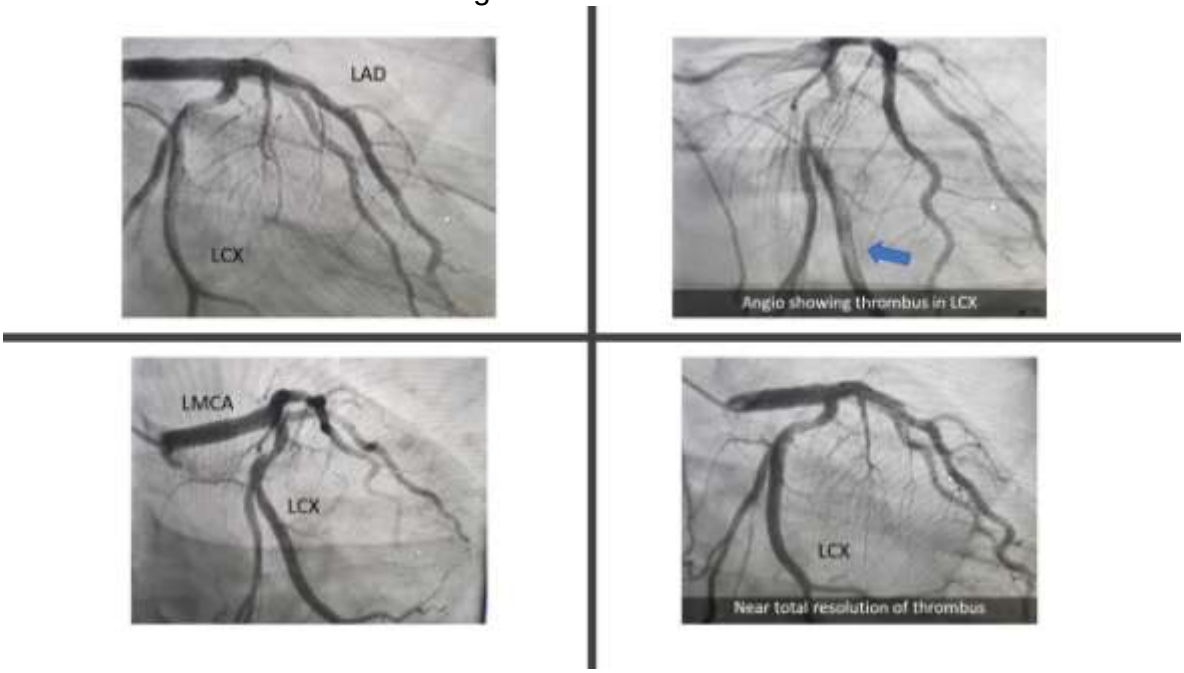


Figure 2

Treatment

He was immediately administered Aspirin 325 mg, Morphine 10 mg, Chlorpheniramine 10 mg and Infusion Nitroglycerin of 1.2 µg/kg/min. Following primary management, the patient was shifted to the coronary angiogram which revealed near total occlusion of Proximal LCX with TIMI 3 flow. As he had heavy thrombus burden, plaque erosion and thrombosis (type 2 Kounis syndrome) were considered and decided to treat conservatively (Figure 2). He was started on intracoronary Tirobifan (Glycoprotein 2b3a Inhibitors) and IV infusion was continued for 24 hrs. He was also treated with antiplatelets, heparin, statins and vasodilators.

His symptoms improved gradually over 48 hrs. He underwent check angiogram which showed near complete revascularization with minimal residual thrombus.
The medication prescribed for patient was as followings: Aspirin, clopidogrel, beta-blocker, angiotensin converting enzyme inhibitor and nitrocantin 2.6 mg and statin

creatine. The patient had uncomplicated hospital follow-up and was discharged uneventfully on 5 th day after admission.

CASE REPORT 2



A 43-year-old male presented with complaints of itching, generalized tiredness and chest discomfort. He had more severe erythematous rash over face and upper limb. He had a history of multiple honey bees sting on the head, neck and upper limb 5 hours before. Patient initially went to outside hospital immediately after the stung. ECG shows ST elevation V1-V4,I,AVL, ST depression II,III,AVF. Patient was treated conservatively and referred to us for further management. The patient was not a smoker or alcoholic or substance abuse and with no history of dyslipidemia, hypertension, diabetes mellitus, coronary artery disease or other significant illness.

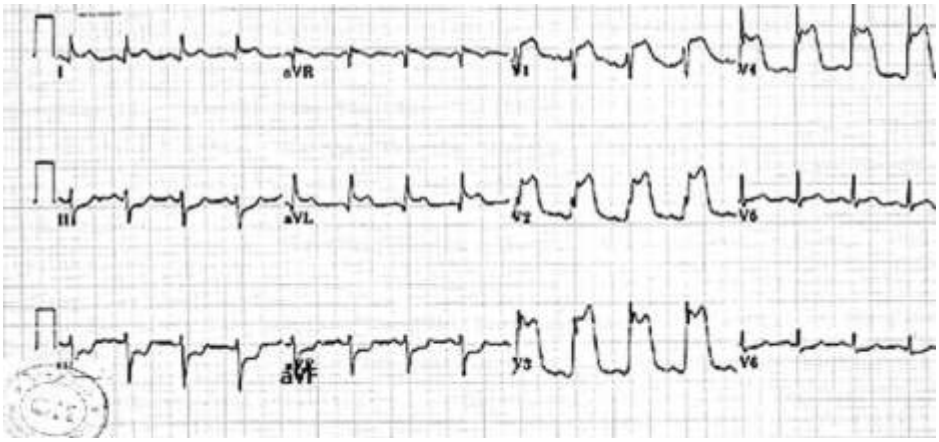


Figure 3

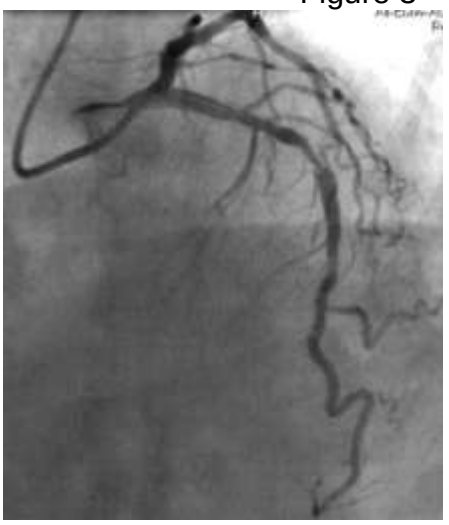


Figure 4



Figure 5

Physical examination and investigations

He was tachypneic with blood pressure of 160/100 mmHg and the pulse revealed 106 beats/min regular with oxygen saturation 98% at room. The ECG revealed elevation of ST segment in leads I, II, III, AVF, tall R wave in V1-V4, compatible with extensive

anterior wall myocardial infarction (Figure 3). Echocardiography revealed Hypokinesia of anterior and septum with Ejection fraction 40%. His cardiac enzymes were elevated.

Treatment

He was immediately administered Aspirin 325 mg, Clopidogrel 300mg, Atorvastatin 80 mg, Morphine 10 mg, Chlorpheniramine 10 mg and Infusion Nitroglycerin of 1.2 µg/kg/min. Following primary management, the patient was immediately shifted to the coronary angiogram which revealed recanalized thrombus with narrowing of 80-90% of mid to proximal part of left anterior descending (LAD) artery (Figure 4). A decision was taken to revascularize LAD artery for this patient and Percutaneous coronary intervention PCI with one drug eluting stent was done for him (Figure 5). He had no other complication after PCI and discharged on Atorvastatin 80 mg daily and clopidogrel 75 mg daily.

The patient had uncomplicated hospital follow-up and was discharged uneventfully on 8 th day after admission.

DISCUSSION

Bee stings exposure is commonly encountered worldwide public health concern. The Hymenoptera – Greek word (hymen-membrane; pteron-wing) includes Apidae - honeybees and bumble bees; Vespidae - Wasp, yellow jackets and hornets; Formicidae - Fire ants. Honey bees are widely distributed in India, especially in the rural area. Allergic reactions of any grading to honeybee or wasp stings are seen in up to 5% of the total population 2.



The reactions followed by sting vary from local reactions to systemic conditions such as rash and itching to respiratory, gastrointestinal or cardiovascular or neurological reactions, as in presented case. The clinical manifestations of bee sting can be divided into three groups: local inflammatory reactions, immunological reactions usually leading to anaphylaxis and systemic toxic reactions caused by large doses of venom. A single sting can inject an amount of 0.3mg of venom. Local reactions are more common, generally self-limiting and subside within a few hours. Fatal reactions can occur within few hours to days. However, mortality rates for multiple bee stings were approximately 15-25% in many published studies. It has been estimated that about 1500 stings would be required to deliver a lethal dose of venom for an allergic adult with 70 kg weight 3.

Hymenoptera venoms are mainly aqueous solutions that contain Protein enzymes (phospholipase, hyaluronidase), peptides (melittin, apamin) and biological amines (histamine, serotonin, dopamine, norepinephrine and acetylcholine). The Phospholipase A2 is the key enzyme causing endogenous amine release from mast cells during allergic reaction, which leads to vasoconstriction and platelets aggregation. Still the mechanism of this syndrome is unclear.

A rare clinical manifestation of such reactions is allergic acute coronary syndrome referred as Kounis syndrome which is characterized by symptoms that range from vasospastic angina to ST elevation myocardial infarction (MI) that occurs as hypersensitivity reaction after allergen exposure. Several drugs (nonsteroidal anti-inflammatory drugs, antibiotics, and antineoplastic agents); bees, wasp stings and viper venom (hymenoptera venom); Foods (mushroom); Latex contact have been implicated as causes for Kounis syndrome 4.

- Type I: Patient with no underlying coronary artery disease.
- Type II: Patient with underlying asymptomatic coronary artery disease.
- Type III: Patient with stent thrombus.

Type I variant includes patients with normal coronaries without predisposing factors for coronary artery disease, in which acute allergic insult induces either coronary artery spasm with normal cardiac enzymes or coronary artery spasm progressing to AMI with raised cardiac enzymes. This variant might represent a manifestation of endothelial dysfunction 1.

Type II variant has quiescent preexisting atheromatous disease in whom acute allergic episode induces plaque erosion or rupture manifesting as AMI 1.

Type III variant is described as a coincidence of hypersensitivity reactions following implantation of drug-eluting stents, causing stent thrombosis 1.

Type I variant has a better prognosis than Type II and type III variant. However, prognosis depends on the initial allergic response, patient's sensitivity, comorbidity, allergen concentration and route of allergen entrance.

Concerning our case, anaphylaxis is the most severeand prevalent insect sting reaction, which could be the possible cause of death of the patient father. Although our patients had no significant risk factors and was asymptomatic with ordinary activities. He could have had occult atheromatous coronary artery disease. As it is characteristic of the Type II variant of Kounis syndrome, the acute allergic reaction due to bee sting must have probably induced plaque erosion or rupture manifesting as acute allergic myocardial infarction.

Therapeutic approach of the patient victim after multiple bee stings should be considered a medical emergency. Removal of the causative agent: the removal of previously inoculated stings should, be carried out as soon as possible. The longer the sting-to-skin contact time, higher the venom inoculation rate in the patients. Type I syndrome can be managed with steroids, antihistamine, mast cell stabilizers and vasodilators whereas type II and type III need additional ACS protocol treatment.

CONCLUSION

Although allergic reactions to bee stings are common, recognition of Kounis syndrome in bee sting is important to provide appropriate treatments. Despite increasing number of cases, exact pathophysiology and treatment guidelines of Kounis syndrome remain unanswered. Kounis syndrome should be considered in differential

diagnosis while diagnosing patients with no cardiovascular risk factors who experience acute coronary syndrome and bee sting exposure accompanied by symptoms of anaphylaxis. In future, further studies are needed to understand the mechanisms of allergy causing acute coronary syndromes as this will pave the way to effective therapeutic interventions.

Reference

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