Case Report

Bee Sting Induced Acute Myocardial Infarction?

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ABSTRACT
Apart from anaphylaxis, myocarditis and transient conduction disturbances, allergic angina and acute myocardial infarction can follow a bee (*Hymenoptera*) sting. Kounis syndrome encompasses symptoms and signs of myocardial ischaemia accompanying allergic reactions. Coronary vasospasm due to release of vasoconstrictor cytokines, and vulnerability to plaque rupture due to release of matrix metalloproteinases from cardiac mast cells are thought to be the principal mechanisms.

Key Words: Allergic angina; Bee sting; *Hymenoptera* sting; Kounis syndrome

Introduction
A 57 year-old female presented with a history of having sustained multiple honey bee (*Apis sp.*) stings 2 days ago, following which she developed puffiness of face and generalized weakness. She denied having chest pain or abdominal discomfort. On elicitation, she had a past history of a cerebrovascular accident with left-sided weakness 6 months ago, from which she had completely recovered. No further medical details were available. She was not on any medications. She denied having heart disease, hypertension or diabetes mellitus.

At presentation, the patient had a regular pulse of 88 beats per minute, respiratory rate of 17 breaths per minute, and a supine blood pressure of 106/70 mmHg with no postural drop, was afebrile and was pale. There was obvious facial puffiness. There was no icterus or lymphadenopathy. Cardiac examination revealed a pansystolic murmur of grade III in mitral area conducted to the base of the heart. There were no clicks, rubs, or gallops. Abdominal and respiratory system examination were unremarkable. Nervous system examination revealed a left-sided mild residual weakness. Optic fundi were normal.

Electrocardiogram performed at admission showed 'J' point elevation in lead V3 and ST segment depression in lateral precordial leads. A repeat ECG done 3 hrs later showed new onset ST segment elevation in V2 and V3, and normalization of ST depression in lead V4. Follow up ECGs done daily did not show evolution of these changes.

Laboratory data revealed the following: haemoglobin 7.7 g/dl, haematocrit 22.2 %, total leukocyte count of 13,000/ mm^3 (76% granulocytes, 16% lymphocytes, 8% eosinophils), platelets 1.85 L/mm^3; peripheral blood smear - microcytic hypochromic anaemia, absolute eosinophil count 750; ESR of 130 mm; routine serum biochemistry - sodium 136 mmol/l, potassium 4.9 mmol/l, blood urea 63 mg/dl, creatinine 1.0 mg/dl, total bilirubin 0.9 mg/dl with 0.6 mg/dl of direct bilirubin, total proteins 7.0 gm/dl, albumin 4.0 gm/dl, A/G ratio 1.3, AST 350 IU and ALT 110 IU, and alkaline phosphatase 110 IU. Serological tests for viral hepatitis markers and HIV were negative. Chest radiograph did not demonstrate any radiological abnormality. Abdominal sonography revealed a normal picture.

Cardiac biomarkers were studied in view of the ECG changes, which showed an elevated cardiac specific troponin I of 8.234 ng/ml (17-fold elevation), CK-MB 170 U/l (8-fold elevation), and LDH 2080 U/l (4-fold

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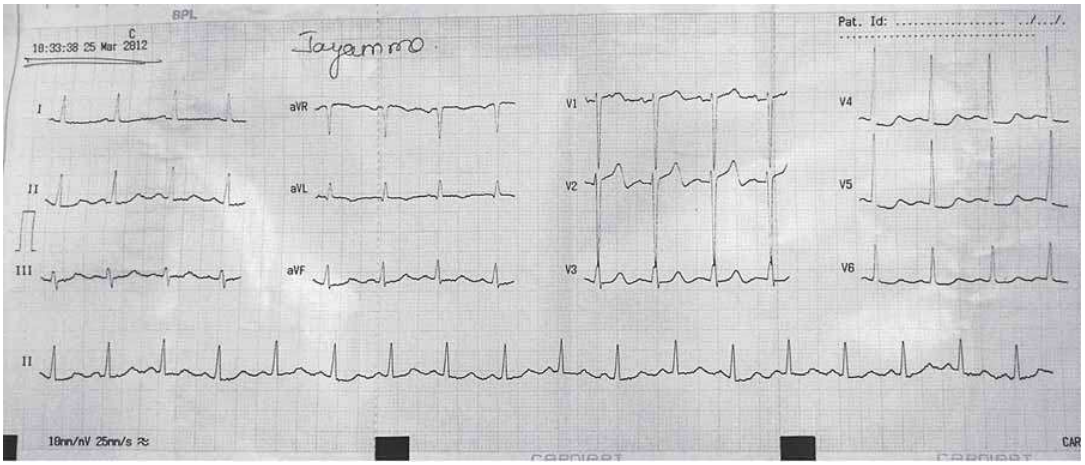

Fig 1 ECG at Admission Showing ST Elevation in Precordial Leads V2 with ST Depression in V4 –V6

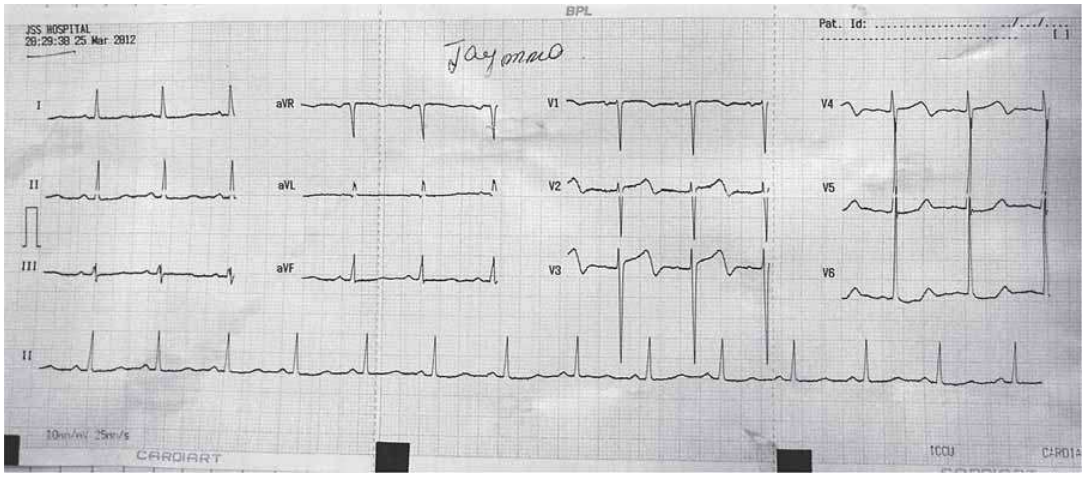

Fig 2 ECG After 3 Hrs Showing Evolution of ST Elevations in Precordial Leads V2 Through V4 and ST Depression in V5–V6

elevation). As the cardiac biomarkers were elevated, the patient was initiated on treatment for acute coronary syndrome with low molecular weight heparin, oral anti-platelet agents and statins. Thrombolysis was not offered in view of contraindications for the same, and also because the diagnosis of ST elevation myocardial infarction was not confirmatory. Systemic glucocorticoids were started initially since there was a possibility of toxin-induced myocarditis, but sine signs of heart failure.

Echocardiography showed dilated LA and LV, normal LV systolic function , EF 58%, RHD- mild MS, severe MR, moderate AR, moderate TR , mild pulmonary hypertension, and no regional wall motion abnormality. Once echocardiography report was available, steroids and heparin were withdrawn. Carotid Doppler study revealed diffuse atherosclerotic changes with less than 50% luminal narrowing, with no significant haemodynamic compromise. Statins which were initially started, had to be discontinued as the patient developed deranged hepatic function. Symptomatic and supportive care was continued. The patient made a satisfactory recovery and was discharged and referred for coronary angiography to a cardiology institute.

Discussion

This case demonstrates the little known clinical entity named Kounis syndrome or allergic angina/myocardial infarction which encompasses symptoms and signs of myocardial ischaemia accompanying allergic reactions.[1] Two types of Kounis syndrome are described. Type I occurs in patients with angiographically normal coronary

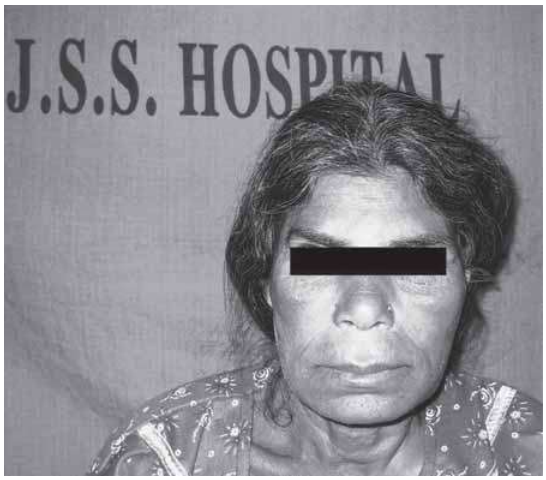

Fig 3 Facial Angioneurotic Oedema

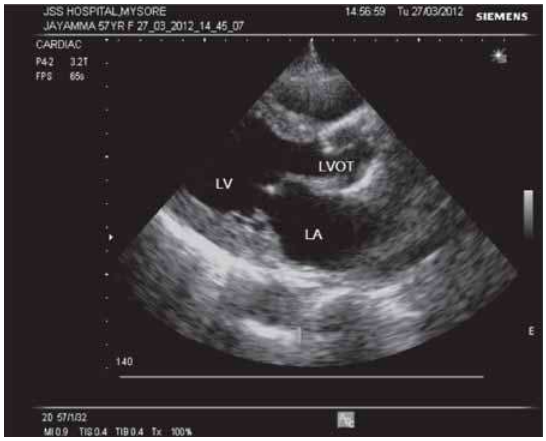

Fig 4 Echo - Parasternal Long Axis View Suggesting Rheumatic Mitral Valve Disease

vessels, and the probable cause of vasospasm is endothelial dysfunction. In Type II, concomitant atheromatous lesions are found. Vasospasm develops in both types.[2]

Mechanisms of Kounis syndrome:

Acute coronary events in the course of allergic reactions have been described after exposure to intravenous drugs,[3] *Hymenoptera bee* venom,[3] food allergens,[2,4] and even oral drugs.[5] Acute vascular neurological events have also been reported after insect stings.[6] The cause of the majority of acute deaths caused by insect stings remain undiagnosed.[7]

Exact pathogenesis of this syndrome is not known. Mast cells located in the heart, between cardiomyocytes[8,9] are the key elements of Kounis syndrome. They are thought to occur in considerably higher amounts in the intima and adventitia of vessels in those with pre-existing atheromatous lesions, particularly in marginal regions of atherosclerotic plaques. Probably the activation of these cells is one of the key steps leading to plaque destabilization.[2,9]

In the course of anaphylactic reaction, anaphylotoxin generation from complement activation, and interaction with specific receptors on the surface of cardiac mast cells leads to mast cell degranulation. This results in histamine, tryptase and chymase release, as well as prostaglandin and leukotriene synthesis.[11] Peptidases released from stimulated mast cells activate matrix metalloproteinases (MMP-1, MMP-3 and MMP-9) which degrade connective tissue covering the atheromatous plaque, making it more prone to rupture.[12]

The tumour necrosis factor-α (TNF-α), a strong pro-inflammatory cytokine, which, on release from mast cells, activates inflammation and transforms stable plaque into vulnerable plaque.[13]

Rupture of the atheromatous plaque and thrombosis with subsequent vessel occlusion would be the final step. Allergic reactions relating to cardiac muscle are not only limited to the development of ischaemia, but also includes disturbances of rhythm and contractility which occur after exposure to allergens.

In-vitro and in-vivo experiments using insect venoms have demonstrated histamine release and coronary vasospasm.[14,15]

ECG may show ST segment deviation (depression or elevation) and flattening or inversion of T waves.[16] In some studies, it has been demonstrated that ectopic and sinoatrial node automatism stimulation is H2 receptor dependent, whereas conduction disturbances are H1 receptor mediated.[15]

Though the patient in this case did not have symptoms of chest pain, the generalized weakness was considered an anginal equivalent, and ECG findings and elevated cardiac biomarkers were strongly suggestive of an acute coronary syndrome. But even if it could account for the elevated biomarkers, due to a good left ventricular systolic function and no other findings consistent with myocarditis, this possibility is remote. Also of interest in this case was an associated asymptomatic rheumatic heart disease picked up incidentally. We conclude that this was a case of type II Kounis syndrome as she had a history of prior cerebrovascular disease and diffuse carotid atherosclerosis reflecting possible coronary artery disease.

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