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Cardiovascular

KOUNIS SYNDROME (ALLERGIC ANGINA):AN ELUSIVE DIAGNOSIS

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ABSTRACT We studied case series of 6 patients admitted with hypersensitivity and acute coronary syndrome. Kounis syndrome is local manifestation of generalised hypersensitivity reaction. Kounis syndrome (allergic angina) is not rare but rarely recognized and under-diagnosed. Serum tryptase is diagnostic biomarker of diagnose KS. Patients were treated with antihistaminic, adrenaline, steroid. In all patient having hypersensitivity reaction due to various triggers kounis syndrome should be suspected with high index of suspicion .

KEYWORDS : acute coronary syndrome, allergic angina, kounis syndrome, serum tryptase, hypersensitivity

INTRODUCTION

Kounis Syndrome was firstly described in 1991 as "the allergic angina syndrome" which could progress to acute myocardial infarction, which was named "allergic myocardial infarction" .KS was first described in 1991 by Kounis and Zavras as the simultaneous appearance of acute coronary events and anaphylactic or anaphylactoid allergic reactions.[1] In an editorial published in 1998, Braunwald described that vasospastic angina could be induced by allergic reactions, with mediators such as histamine and leukotrienes acting upon the smooth muscle of the coronary arteries[2] Kounis syndrome is local manifestation of generalised hypersensitivity reaction associated with allergic reactions and acute coronary syndromes has gained acceptance as a new cause of coronary artery syndrome.

KS has been divided into three types:-

Type I (without coronary disease): chest pain during an acute allergic reaction in patients without risk factors or coronary lesions, in which the allergic event induces coronary spasm that causes chest pain and electrocardiographic changes secondary to ischemia.

Type II (with coronary disease): chest pain during an acute allergic reaction in patients with pre-existing atheroma disease (whether known or otherwise).

Type III: It Includes patient coronary artery stent thrombosis in whom aspirated thrombus specimen stained with hematoxylin eosin and giemsa demonstrated the presence of eosinophil and mast cell respectively.

pathophysiology of kounis syndrome

Allergens such as foods, insect venom, iodine contrast media or drugs induce mast cell degranulation, resulting in release locally and into the systemic bloodstream of a number of vasoactive mediators (histamine, leukotrienes, serotonin) and proteases (tryptase, chymase).[2]Histamine and the leukotrienes are potent coronary vasoconstrictors, while tryptase and chymase activate the metalloproteinases, inducing collagen degradation and erosion of the atheroma plaque which in turn initiates the coronary event. Cardiac histamine acts upon four types of receptors each of which can contribute to the severity of allergic myocardial damage. The H1 receptors mediate coronary vasoconstriction, while the H2 receptors to a lesser degree intervene in coronary relaxation. The interaction between both receptor activities induces a drop in diastolic blood pressure and an increase in pulse pressure. The H3 receptors in turn inhibit noradrenaline release, while the H4 receptors regulate mast cell, eosinophil and lymphocyte chemotaxis---producing a change in eosinophil shape and favouring molecular adhesion.[4]Likewise, histamine can activate platelets, enhance the aggregation response of other agonists such as adrenalin or thrombin[4 5] and reduce tissue factor expression and activity---this enzyme being a key element in the coagulation cascade, favouring the final formation thrombin.

MATERIALAND METHOD

We studied 6 patients who were admitted to our hospital in the last two and half years .These patients had allergic triggers associated with acute onset chest pain, electrocardiographic changes and elevated cardiac enzymes. The characteristics of the patients who developed KS are given in Table 1. Etiological Agent of KS were drugs in two patients, snake bite in two patients and radiocontrast agent in the other patient. They did not have previous history of allergy, bronchial asthma, dermatitis, eczema, coronary artery disease. echocardiographic examination

PATIENT	1	2	3	4	5	6
O	22	24	62	52	48	56
Sex	M	M	F	F	M	M
Allergic insult	Snake bite	Insect bite	Ceftriaxone allergy	Radiocontrast (iohexol) allergy	Radiocontrast (iohexol) allergy	Amoxycillin-CLAVULENIC ACID allergy
ST SEGMENT ELEVATION	V1 -v4	V1-V4	II III v1 -Avf	V3- V4	V5V6	II III AVF
SYMPTOM	Chest pain	Pruritic skin rash	Erythematous rash dyspnea	Chest pain Pruritic rash	Erythematous rash Chest pain	Erythematous rash chest pain hypotension
TRPONIN T	Positive	Positive	Positive	Positive	positive	positive
WALL MOTION abnormality	Anterior and septal	Anterior	Inferior	Anterior	Anterior	Inferior
TOTAL eosinophil LEVEL(30-350)	950	920	900	1000	800	870
Sr tryptase level (5-15ng/ml)	60	40	40	32	36	38
CORNARY ANGIOGRAPHY	LAD (30%)Stenosis	LAD(40%) stenosis	Right coronary artery 40% Stenosis	Left anterior descending 30% stenosis	30% left anterior descending	Right coronary artery 40% stenosis

and coronary angiography was performed in all patients. While echocardiography showed segmental wall motion abnormality, coronary angiography revealed non-critical plaques in the all patient

RESULT

In this study we described 6 patient who diagnosed as kounis syndrome. out of 6 patient two are female and four are male patient are in age group of 22- 62 year median age group is 44 year.the etiological agent identified for producing allergic reaction are radiocontrast agent(iohexol) in two patient ,snake bite in one patient , insect bite in one patient, amoxycillin-clavulanic acid in one patient and ceftriaxone in one patient .In all patient presenting complaint was allergic rash with chest pain and hypotension in one patient . In two patient ST elevation in inferior lead in three patient in anterior lead while in one patient in lateral lead. Echocardiographic finding matches with ecg changes. Qualitative troponin T was positive in all patient. Eosinophil level was raised in all patient denoting toward allergic etiology of myocardial infraction. serum tryptase(normal 5-15 ng/ml) which was raised in all patient support our diagnosis .Coronary angiography done in all patient right coronary involved in 2 patient while left anterior descending artery involved in two patient in all of them non critical stenosis was present . all patient are treated with antihistaminic and steroid.

DISCUSSION

Kounis syndrome was first described in 1991 by Kounis and Zafras as "the coincidental occurrence of chest pain and allergic reactions accompanied by clinical and laboratory findings of classical angina pectoris caused by inflammatory mediators released during an allergic insult [1].
there are three types of KS have been described.

Type 1 occurs in patients with normal coronary arteries
Type 2 occurs in patients with preexisting atheromatous coronary artery disease.
Type 3 will lead to stent thrombosis.

All three conditions can lead to angina and myocardial infarction.
In our study etiological agent enlisted are snake bite, sting bite , radiocontrast agent(iohexol) , amoxicillin and ceftriaxone .In our study 2 cases are related to amoxycillin-clavulanic acid and ceftriaxone induce kounis syndrome are reported in literature case related to allergy of certain drug are like antibiotic, are reported by kulratne et al. fagley et al described rocuronium induced allergic vasospasm.(6) most commonly involved NMB are rocuronium and succinylcholine .(shibuya et al. describe 11 case associated with contrast induce among which three case are related to iopomide ,three are iohexol associated while two are iopomidol remaining contrast agent are unknown (7) In literature various causes enlisted These include viper venom ,priyankara et al. reviewed a case related cobra bite induced anaphylaxis .(9) manjur et al .describe a case of vasospastic angina related to scrombide fish consumption. (8) frangid et.al. describe shellfish consumption induced vasospastic angina,(8)
Few cases are reported in literature which produce type III KS. There are also a few cases of KS associated with different types of contrast materials. Low-osmolar non-anionic contrast materials are less toxic than anionic and monomeric contrast materials, however, most of the KS cases described in literature were caused by low-osmolar non-ionic contrast materials(.7) In our study 2 cases reported with kounis in both case contrast material was iohexol.

In our study two patient coronary artery are normal and remaining have non critical plaque so in first two cases type I kounis syndrome is suspected while remaining have type II kounis syndrome. In literature k. Shibuya e. al . reviewed 11 case of radio contrast induced kounis syndrome where 6 case of type II KS while 4 cases are type II KS(7). In our study both are type II . Also evaluated insect bite related kounis syndrome rao et. case series of 6 patient out of which 4 patient having type II KS .

One case is related to snake bite induce anaphylactic reaction. Ruth and colleagues reported hypersensitivity to spitting airborne cobra venom among cobra handlers.(10) Snake venom can induce allergic or anaphylactic reactions due to various substances like toxic peptides, phospholipase A2, and various other proteins present in their venom [11].Hypovolemia, direct cardiotoxicity, hypercoagulability, and vasospasm are reported as possible mechanisms. Myocardial infarction is more reported mainly in viper bites than in cobra bites [11].

Patients with Kounis syndrome usually involved inferior w all myocardial infarction 14 In present study out of six patient three are developed anterior wall infraction while two patient developed inferior wall myocardial infraction and one patient had anteroseptal wall infraction. though right coronary most commonly involved in most of study (12). we have found that left anterior descending artery involved in four patient and RCA involved in two patient.

In literature one case of scromboid fish ingestion was associated with vasospastic angina which was reviewed where histamine level was elevated (1347) (8). In this study this was not done in any of our patient but this is one of the marker for diagnosis of kounis syndrome.
In present study patients were treated with antihistaminic, steroid and anti ischemic agent like aspirin and calcium channel blocker and nitrate.

Conclusion

Kounis syndrome is local manifestation of generalised hypersensitivity reaction. Kounis syndrome (allergic angina)is not rare but rarely recognized and under-diagnosed. Serum tryptase is diagnostic biomarker of diagnose KS. Patients were treated with antihistaminic, adrenaline, steroid . In all patient having hypersensitivity reaction due to various triggers kounis syndrome should be suspected with high index of suspicion

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