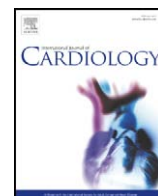




Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Acute stent thrombosis and atopy: Implications for Kounis syndrome

George Almpanis^{a,*}, Andreas Mazarakis^a, Grigorios Tsigkas^a, Constantinos Koutsojannis^b, George N. Kounis^b, Nicholas G. Kounis^b^a Department of Cardiology Patras State General Hospital, Patras, Greece^b Patras Highest Institute of Education and Technology, Patras, Greece

ARTICLE INFO

Article history:

Received 24 February 2010

Accepted 8 April 2010

Available online xxxx

Keywords:

Allergy

Anaphylaxis

Atopy

Hypersensitivity

Kounis syndrome

Stent thrombosis

1. Introduction

Atopy is a genetic predisposition to produce significant amounts of IgE or IgM antibodies. Mast cells, from atopic patients, are prone to degranulate easily when specific antigens bridge their corresponding receptor-bound IgE antibodies on their surface [1]. Patients undergoing stent implantation receive several substances, which have antigenic properties. These substances include the metal stent, which is made from 316 L stainless steel containing nickel, chromium, manganese, titanium and molybdenum, and drug eluting devices include the polymer coating and the impregnated drugs which for today are the antimicrotubule, antineoplastic agent paclitaxel, the anti-inflammatory, immunosuppressive and antiproliferative agent rapamycin [2]. The much feared intrastent thrombosis is regarded as multifactorial process but so far there is much clinical, experimental and laboratory evidence that hypersensitivity involving eosinophils, mast cells, T-lymphocytes and macrophages play an important role [3].

The following report is of a patient with history of atopic diathesis who developed severe, nearly fatal, acute myocardial infarction in the stented area soon after stent implantation.

2. Case report

A 59 year old male developed chest discomfort and within an hour was transferred to the local hospital. The admitting physician diagnosed acute inferior wall and right ventricular acute myocardial infarction (Fig. 1). Thrombolysis was administered immediately and the patient's symptoms abated. The patient was subsequently transferred to our hospital for further assessment and angiography. From his past history we noticed that he has been suffering from bronchial asthma, nasal polyposis, hay fever and he was allergic to some non steroidal anti-inflammatory drugs. On admission he was stable and cardiac troponin I levels were elevated to 8.18 ng/ml. Coronary arteriography, the following day, showed a total proximal occlusion of the right coronary artery for which coronary angioplasty with Cypher stenting was performed successfully. After the procedure, the patient was transferred to the cardiology ward in stable condition without any symptoms.

However, 2 h later the patient developed again acute chest pain and the electrocardiogram showed again elevation of the ST segment in the inferior leads. His condition was deteriorated quickly into cardiogenic shock with electrocardiographic evidence of ventricular flutter (Fig. 2). Cardiac defibrillation with 300 J applied and restored the flutter to sinus rhythm but the patient required the use of inotropic agents dopamine and dobutamine for hemodynamic support. Intravenous fluid repletion was also initiated with use of normal saline. The patient was then transferred immediately to catheterization laboratory for emergent repeat coronary angiography.

Coronary angiography demonstrated acute reocclusion at the site of the stent implantation (acute stent thrombosis). The patient underwent successful coronary angioplasty and was moved to the coronary care unit for close monitoring. However, he remained hemodynamically unstable with signs of pulmonary congestion. Supplemental oxygen via mask was used to improve arterial oxygenation and the patient promptly received IV diuretics. Patient's symptoms were related to dyspnea without chest discomfort. Due to the prolonged period of hypotension, liver enzymes were elevated. An episode of atrial flutter occurred which was initially reverted to sinus rhythm with the intravenous use of amiodarone but half an hour later atrial flutter recurred. An echocardiographic examination revealed dilation of the right ventricle with reduced systolic function and moderate to severe tricuspid regurgitation. Over the next four days the patient's condition improved and there was gradual reduction in the dose of dopamine and dobutamine. Right heart catheterization revealed pulmonary artery saturation 61% and arterial saturation 96%. The patient was subsequently improved clinically and hemodynamically and finally discharged home on the 14th day of hospitalization with mild symptoms. One year later the patient remains asymptomatic.

3. Discussion

In stent thrombosis, biopsy studies [4] and thrombus aspiration reports [5] have shown that the intima, media and adventitia as well as thrombus itself are infiltrated by eosinophils, mast cells, lymphocytes, macrophages and other inflammatory cells. These cells, particularly mast cells and eosinophils constitute the allergic effector unit [6], and represent an allergic hypersensitivity reaction to stent components. Additionally, there are many important interactions, through bidirectional stimuli, among these inflammatory cells [7].

* Corresponding author. Department of Cardiology, "Agios Andreas" State General Hospital, Patras, Greece.

E-mail address: galmpan@gmail.com (G. Almpanis).



Fig. 1. Electrocardiogram on admission showing inferior wall and right ventricular acute myocardial infarction.

Platelets play a central role in the pathophysiology of stent thrombosis. Platelet-rich thrombus in between the stent struts is the result of platelet adhesion, aggregation and activation [4]. Platelet surface membrane contains receptors, including receptors for thromboxane, adenosine diphosphate, glucoprotein IIb/IIIa, histamine, high affinity Fc ϵ RI and low affinity Fc ϵ RII. Additionally, multiple exogenous agonists contribute to platelet activation. These include thrombin, serotonin, epinephrine and histamine. Following their activation, platelets secrete pro-inflammatory (platelet factor 4, platelet derived growth factor, CD40L), pro thrombotic (factor V, factor XI, and PAI-1), adhesive (thrombospondin, fibrinogen, p-selectin, and von Willbrand factor) and chemotactic (ADP, ATP, serotonin, histamine, calcium, magnesium) mediators that propagate, amplify and sustain the thrombotic process.

There are reports of patients developing intrastent thrombosis contemporarily with generalized allergic reaction from other causes showing that stents, like magnet, constituted the area of possible intracoronary mast cell activation and development of stent thrombosis. In one of such patient [8], stent thrombosis and acute myocardial infarction coincided with allergic symptoms such as glottis edema, cold sweat, and tongue enlargement followed a flavonate-propyphenasone administration a week after stent implantation. In another patient [3] acute myocardial infarction in the stented area coincided with allergic reaction following intravenous administration of the non-anionic contrast material iopromide during a routine excretory urography.

In the described patient an intracoronary mast cell activation, by stent components, with release of inflammatory mediators inducing stent thrombosis and sudden spam and collapse of the collateral coronary circulation is possible. This can explain the discrepancy between the stable condition after thrombolysis and the dramatic worsening after stent insertion.

We believe that patients undergoing stent implantation should be interrogated for any atopic diathesis and measures should be taken in order to avoid Kounis syndrome [9] and any other serious consequences.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [10].

References

- [1] Mytas DZ, Stougiannos PN, Zairis MN, et al. Acute anterior myocardial infarction after multiple bee stings. A case of Kounis syndrome. *Int J Cardiol* 2009 May 29;134:e129–31.
- [2] Kounis GN, Hahalis G, Soufras GD, Mazarakis A, Niarchos C, Kounis NG. Kounis syndrome and simultaneous multivessel acute coronary syndromes after successful drug-eluting stent implantation. *Int J Cardiol* 2008;127:146–8.
- [3] Patané S, Marte F, Di Bella G, Chiofalo S, Currò A, Coglitore S. Acute myocardial infarction and Kounis syndrome. *Int J Cardiol* 2009;134:e45–6.

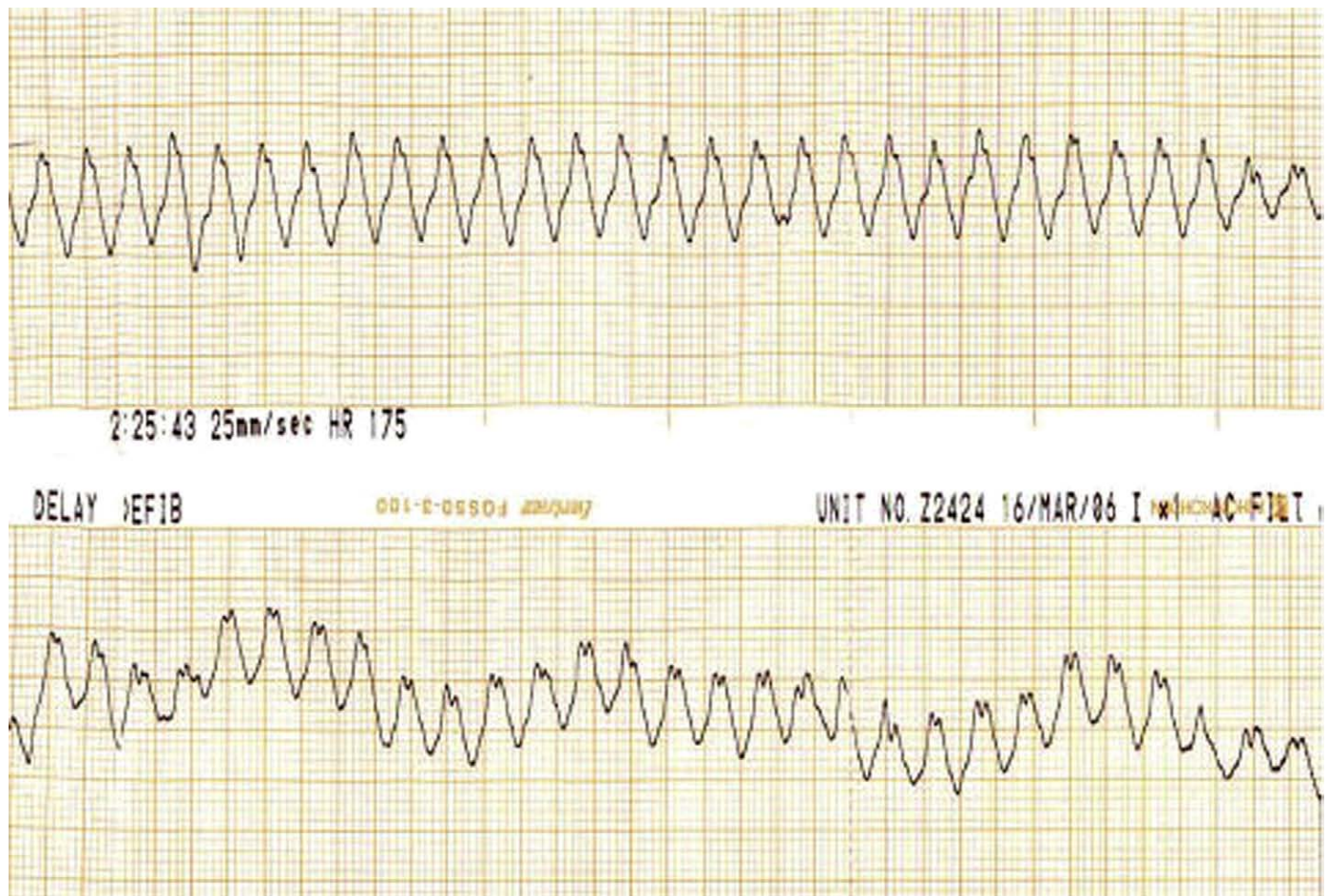


Fig. 2. Electrocardiogram during cardiogenic shock showing ventricular flutter.

- [4] Cook S, Ladich E, Nakazawa G, et al. Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis. *Circulation* 2009;120:391–9.
- [5] Barlis P, Virmani R, Sheppard MN, Tanigawa J, Di Mario C. Angiographic and histological assessment of successfully treated late acute stent thrombosis secondary to a sirolimus-eluting stent. *Eur Heart J* 2007;28:1675.
- [6] Minai-Fleminger Y, Levi-Schaffer F. Mast cells and eosinophils: the two key effector cells in allergic inflammation. *Inflamm Res* 2009;58:631–8.
- [7] Nakae S, Suto H, Likura M, et al. Mast cells enhance T cell activation: importance of mast cell costimulatory molecules and secreted TNF. *J Immunol* 2006;176:2238–48.
- [8] Kogias JS, Papadakis EX, Tsatiris CG, et al. Kounis syndrome: a manifestation of drug-eluting stent thrombosis associated with allergic reaction to contrast material. *Int J Cardiol* 2008, doi:10.1016/j.ijcard.2008.08.026 electronic publication ahead of print.
- [9] Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol* 2006;110:7–17.
- [10] Coats AJ. Ethical authorship and publishing. *Int J Cardiol* 2009;131:149–50 222.