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Letter to the Editor

A new classification of Kounis syndrome

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I read with great interest an article entitled “Kounis syndrome: A manifestation of drug-eluting stent thrombosis associated with allergic reaction to contrast material” published by Kogias et al. describing a 48-year-old man with drug-eluting stent thrombosis [1].

Kounis syndrome was described in 1991 as the concurrence of acute coronary events with allergic or hypersensitivity reactions as well as anaphylactic or anaphylactoid reaction [2]. There are several causes that have been reported as capable of inducing Kounis syndrome [2–6]. These include a number of conditions, several drugs, foods, insect stings, etc.

Two variants of Kounis syndrome have been described so far [7]. The type I variant (*coronary spasm*), which might represent a manifestation of endothelial dysfunction or microvascular angina, includes patients with normal coronary arteries without predisposing factors for coronary artery disease in whom the acute release of inflammatory mediators can induce either coronary artery spasm without increase of cardiac enzymes and troponins or coronary artery spasm progressing to acute myocardial infarction with raised cardiac enzymes and troponins. The type II variant (*coronary thrombosis*) includes patients with culprit but quiescent pre-existing atherosclerotic disease in whom the acute release of inflammatory mediators can induce either coronary artery spasm with normal cardiac enzymes and troponins, plaque erosion, or rupture manifesting as acute myocardial infarction.

In recent years, an association between Kounis syndrome and Tako-tsubo cardiomyopathy [8], and drug-eluting coronary stent thrombosis [9] is argued.

Although the pathophysiology of drug-eluting stent thrombosis is multifactorial and has not been fully elucidated, allergic reactions to

stent components may be one of the capable causes of this catastrophic entity. The use of bare metal stent is not associated with allergic reactions. However, all the components of the drug-eluting stent (nickel strut, polymer and impregnated drug) can induce allergy either separately or synergistically [9]. Concomitant drugs such as clopidogrel and aspirin may also act as potential antigens. Although allergic reactions are now recognized as key components of stent thrombosis, the incidence, especially of subclinical cases, is likely under-reported.

Recent case reports and studies show that coincidence of hypersensitivity reaction following implantation of drug-eluting stents and stent thrombosis may be considered as a manifestation of Kounis syndrome. In light of recent reports I would like to propose herewith a type III variant (*drug-eluting stent thrombosis*) which would include patients with stent thrombosis in whom thrombus harvesting and staining with hematoxylin–eosin and Giemsa shows the presence of eosinophils and mast cells respectively in the pathology specimens (Fig. 1).

Before considering for drug-eluting stent implantation, a thorough atopic history should be sought, with specific attention to previous Kounis syndrome or other allergic reactions. In atopic patients bare metal stents should be the first choice. However, when drug-eluting stents are indicated skin tests to stent components and desensitization strategies should be performed. Implantation of non-allergenic substances may also be the solution to this complication.

Acknowledgment

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

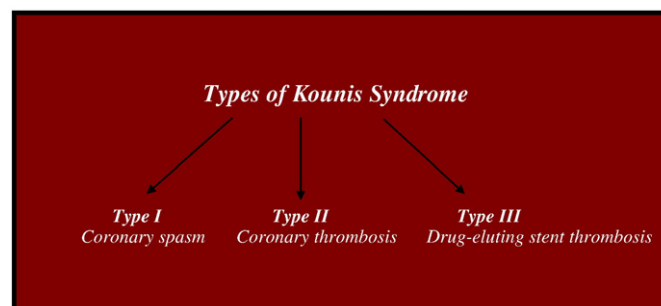


Fig. 1. Types of Kounis syndrome.

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