Allergic acute coronary syndrome (Kounis syndrome): report of 3 cases secondary to oral amoxicillin use

N. Lombardi[1,2], A. Pugi[1,2], V. Maggini[1,2], M. Moschini[1,2], M.C. Lenti[1,2], E. Gallo[1,2], E. Lucenteforte[1,2], A. Mugelli[1,2], E. Cecchi[2,3], A.Vannacci[1,2]

[1]Dept. of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, Centre for Molecular Medicine (CIMMBA), University of Florence, Florence
[2] Tuscan Regional Centre of Pharmacovigilance, Florence
[3] Prato Hospital Emergency Department, Prato

Background

The concurrence of acute coronary syndrome with allergy or hypersensitivity as well as with anaphylactic reactions is increasingly encountered in daily clinical practice. Mast cell activation with acute cardiovascular (CV) events is described as Kounis syndrome (KS), an 'allergic angina', progressing to 'allergic myocardial infarction' [1]. Possible triggers include drugs, foods, animal or insect bites, and even drug-eluting stents or endovascular devices [1].

Description

We present three cases of 57 (1), 58 (2) and 64-year-old (3) men who were admitted to Prato hospital emergency department with thoracic pain and dyspnea. In patients 1 and 2 the symptoms recurred after taking only one pill of amoxicillin/clavulanic acid (875/125 mg) for periodontal disease. The third patient reported being treated with oral amoxicillin (1000 mg) as a preventive measure before dental treatment. He had taken a total of 5 pills and he stopped the medication a day before hospital admission because of intermittent epigastric pain. After the hospitalization, in keeping with analytical parameters (troponin I increase: 3.78 ng/ml (1); 0.14 ng/ml (3)) and electrocardiographic abnormalities (ST segment elevations (1-2)), all patients were diagnosed with unstable angina or acute myocardial infarction during anaphylaxis to antibiotic drug. An emergency coronary angiogram, performed for all patients, showed abnormal coronary arteries only in the 64-year-old man (3). All patients recovered without complications and were discharged on their third, second and sixth day of hospitalization, respectively.

Discussion

From an analysis of medical literature and validated databases (Micromedex®; Farmadati®) emerged that KS due to amoxicillin or amoxicillin/clavulanic acid use is a rare event in the adults [2]. In the present cases the temporal relationship between the event and drug assumption strongly suggested a role of amoxicillin in the occurrence of 'allergic angina'. The causal relationship of amoxicillin in patients 1 and 2 might be confounded by concomitant use of other drugs (atorvastatin (1); nebivolol/hydrochlorothiazide, doxazosin and tapazole (2)). Therefore the three reports were graded as 'possible' according to the objective causality assessment [3].

Conclusion

The presentation of three cases of Kounis syndrome in a single hospital emergency department during about three months period (between December 2011 and February 2012), suggests that this case might not be as rare as previously believed. Clinicians should be aware of this contingency when treating patients with acute cardiovascular symptoms taking drugs known to induce allergic reactions.