

Ampicillin/sulbactam-induced Kounis syndrome with cardiogenic shock

Anaphylactic cardiogenic shock is a complex and extremely dangerous complication of anaphylaxis; it involves complex patho-physiological mechanisms, and its treatment remains unclear to date.

During anaphylactic shock, the main contributors to coronary hypoperfusion, leading to myocardial damage, are systemic vasodilatation, reduced venous return, leakage of plasma and volume loss due to increased vascular permeability, and diminished cardiac output (1). However, experimental and clinical evidence has shown that the heart, particularly the coronary arteries, is the main target of anaphylaxis. The experimental evidence of a rapid increase in left ventricular end-diastolic pressure during the initial phase of anaphylactic shock is attributed to coronary vasoconstriction than to leakage of plasma and volume loss (2). This is supported by clinical evidence that anaphylactic cardiogenic shock does not always respond to fluid replacement but needs anti-allergic and myocardial infarction protocol treatment (3).

An interesting report has been published in *Anatol J Cardiol* 2016;16: 893-4. Keskin et al. (4) entitled "Kounis syndrome presenting with acute inferior wall myocardial infarction and cardiogenic shock secondary to intravenous ampicillin/sulbactam administration" about a 44-year-old male patient who developed Kounis syndrome and cardiogenic shock following the intravenous administration of ampicillin/sulbactam. Although this patient did not present with any cutaneous manifestations, he exhibited severe hypotension, electrocardiographic signs of inferolateral myocardial ischemia, increased serum tryptase levels and cardiac biomarkers, diffuse constriction of the left anterior descending and left circumflex arteries, and total occlusion of the right coronary artery in coronary arteriography, suggesting a type I variant of Kounis syndrome progressing to acute myocardial damage. With the initiation of prednisolone, ranitidine, diphenhydramine, and intracoronary nitroglycerin treatment and change in the antibiotic to ciprofloxacin, the patient had an uneventful recovery. Adrenalin was not administered.

Indeed, this report raises several issues that need to be commented on:

1. Anaphylactic cardiovascular collapse with shock can occur immediately without skin or respiratory symptoms in about 30% of patients (5). This is attributed to the sequestration of blood histamine and other released mediators in the third

body space (transcellular), resulting in non-availability to the skin and causing flush, rash, or urticaria. Therefore, caution should be taken when diagnosing anaphylactic cardiac collapse, and the authors correctly diagnosed this patient.

2. Ampicillin/sulbactam was replaced by ciprofloxacin without any sequelae. While fluoroquinolones are generally considered well-tolerated antibiotics and their consumption is continuously increasing, they can also induce allergic reactions and are now most frequently involved in allergic drug reaction medicines after β -lactams (6). Kounis syndrome has been induced not only by ciprofloxacin and levofloxacin but also by the original quinolone cinoxacin (7). In cases of respiratory infections, macrolides are also considered safe. Therefore, extreme caution should be taken during antibiotic use in such cases.
3. Although adrenalin is a life-saving drug, it may prove dangerous, and the authors therefore did not administer adrenalin in the described patient. Exogenous adrenalin administration increases the platelet production of thromboxane B₂, thereby promoting platelet aggregation. Further, it promotes heightening in platelet sensitivity to ADP and promotes thrombin-induced binding of platelet to fibrinogen (8). Moreover, every commercially available preparation of adrenalin usually contains sodium metabisulfite which is a strong allergen, as a preservative. Fortunately, sulfite-free adrenalin (epinephrine) is available today (American Regent Inc, USA) for patients sensitive to sulfites.

Indeed, in sulfite-sensitized patients who suffer from anaphylactic shock, this situation poses a therapeutic dilemma that only few physicians are aware of. Although the described patient was not on any cardiac medication, it should be known that adrenalin may be ineffective in patients receiving β -blockers and may induce more vasospasm due to an unopposed α -adrenergic effect.

In conclusion, Kounis syndrome cases are increasingly appearing in clinical practice and some of them are fatal with aborted sudden cardiac death (9); therefore, diagnostic and therapeutic criteria concerning this condition need to be established.

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Accepted Date: 22.11.2016

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 DOI:10.14744/AnatolJCardiol.2016.7612



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