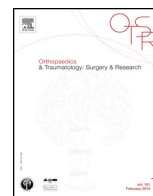




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Letter to the editor

Shoulder arthroscopy and ATA (adrenaline, Takotsubo, anaphylaxis, and Kounis hypersensitivity-associated syndrome)[☆]

In the very interesting report published in *Orthopaedics & Traumatology: Surgery & Research* [1], a 48-year-old woman subjected in acromioclavicular resection and partial supraspinatus tear and labrum tear debridement via arthroscopy developed repeated cardiac arrests. Coronary angiography showed normal coronary arteries, ejection fraction at 25%, and apical ballooning of the left ventricle, suggesting Takotsubo syndrome. Despite intense cardio-respiratory resuscitation efforts she finally succumbed. Disseminated intravascular coagulation and multiorgan failure due to catecholamine cardiomyopathy was the final diagnosis. The authors of this report correctly wondered about a hypersensitivity reaction to epinephrine that may have been precipitated by the beta-blocker treatment.

However, this case raises additional important questions concerning the various medications she received, the repeated doses of epinephrine and the cause of death:

- adrenaline contains, as preservative, according to Drug facts and comparisons (a standard pharmacy reference published by Wolters Kluwer and updated monthly) sodium metabisulfite. Sodium metabisulfite is commonly used as an antioxidant in food and pharmaceutical industries. Anaphylactic shock has been reported during epidural anesthesia for caesarian section in which the responsible agent was metabisulfite an additive agent of adrenaline containing local anesthetic [2]. Only few physicians are aware of such a treacherous association in sensitized patients. Fortunately, nowadays, free sulfite adrenaline is commercially available for use in sulfite sensitive patients (American Regent Inc, USA) [3];
- the patient received 6 different drugs as premedication namely acebutolol, alprazolam, cimetidine, ropivacaine, lidocaine and clonidine and 4 additional drugs during general anesthesia including sufentanil, propofol, cisatracurium and repeated doses of epinephrine during the cardiac arrest. All these 10 drugs could have acted as potential antigens able to induce anaphylactic cardiogenic shock. Clinical studies indicate that sensitized patients simultaneously exposed to several antigens have more symptoms than monosensitized individuals. On the other hand, IgE antibodies with different specificities can have additive effects and small, even subthreshold numbers of them can

join forces and trigger the cells to release their mediators [4];

- the autopsy was interpreted as catecholamine cardiomyopathy. It has been suggested [5] that histological examination, especially, of coronary arteries, could reveal the presence of inflammatory cells such as mast cells and eosinophils, which may help in elucidating the cause of cardiogenic shock. Such an examination was not stated to have taken place. Epinephrine administration has already induced acute thrombosis inside stented arteries, a manifestation of type III variant of Kounis hypersensitivity associated syndrome that affects the coronary arteries with mast cell and eosinophil coronary artery infiltration [6];
- the patient received repeated doses of epinephrine which is drug of choice for cardiogenic shock, but excess doses might induce transient takotsubo syndrome through direct myocardial stunning. Takotsubo cardiomyopathy or apical ballooning syndrome, named from a Japanese pot for catching octopus-like appearance of the heart on left ventriculography is associated with partial dilatation of apical cardiac cavities [7]. This clinical entity has been excessively discussed nowadays but there are many questions regarding its etiology, pathophysiology and treatment, which still remain unanswered. Administration of epinephrine for hemodynamic support could also increase the plasma catecholamine level and perpetuate this vicious cycle. It has been emphasized recently that adrenaline, takotsubo, anaphylaxis, and Kounis hypersensitivity-associated coronary syndrome (ATA) constitute a challenging contemporary complex [8].

We, therefore, believe that “attacking” on the above complex would elucidate the pathophysiology of contemporary administration of epinephrine and anesthetic medications and would help in applying proper diagnostic, preventive and therapeutic measures.

Disclosure of interest

The authors declare that they have no competing interest.

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