

Neostigmine-induced coronary spasm: Beware of Kounis syndrome

We read with great interest the article – Neostigmine induced coronary artery spasm: A case report and literature review.^[1] Neostigmine-induced coronary artery spasm is a very rare and fatal complication. It is worth knowing about such a disastrous perioperative complication. The authors have mentioned acetylcholine to be responsible for coronary vasospasm in diseased arteries. However, we would like to mention Kounis syndrome as one of the main differential diagnosis. Kounis syndrome is an allergic angina syndrome with manifestation of coronary artery vasoconstriction in the settings of anaphylactic reactions. Neostigmine was reported to be the cause of anaphylactic reaction.^[2] It was confirmed by demonstrating neostigmine-specific IgE, serum tryptase level, and positive skin prick test. However, the patient had generalized rash, bronchospasm, and periorbital edema apart from hemodynamic instability. It is essential to note that the present case did not present any cutaneous, respiratory or hypotensive features of anaphylaxis or anaphylactic shock.

Anaphylaxis with hypertension

Initially, mast cells were described as widely distributed in different tissues particularly skin, lung, and gastrointestinal tract.^[3] In the early 1990s, cardiac mast cells were extensively studied and found to be associated with intramural and epicardial blood vessels. Mast cells react to IgE-mediated stimuli by releasing large quantities of mediators.^[4] Apart from this, cardiac mast cells, unlike skin and lung mast cells, are also activated by other stimuli such as substance P, anaphylatoxins (C3a and C5a), eosinophilic cationic proteins, and certain drugs.^[3] Compared with lung or skin mast cells, cardiac mast cells release unusually large quantities of chymase or mediators. It has been recently studied that mast cells in human heart secrete significant quantities of renin.^[5] This causes activation of cardiac local renin angiotensin system (RAS). Angiotensin I is converted to angiotensin II by not only interstitial angiotensin converting enzyme (ACE) but also by chymase. Angiotensin II promotes local secretion of noradrenaline by stimulating AT1 receptors expressed on sympathetic nerve endings. These findings suggest that cardiac mast cells are fully capable of activating adrenergic system by stimulating cardiac RAS. This adrenergic activity during anaphylaxis may be responsible for myocardial ischemia

and hypertension. Human hearts obtained from transplant recipients were studied, and it was found that cardiac tissue in patients with dilated or ischemic cardiomyopathies contains a significant amount of mast cells compared to hearts from normal individuals who died accidentally.^[3]

Accordingly, cardiac tissue from patients with heart diseases contains and liberates numerous mast cell-derived mediators upon activation.^[3] These observations explain why cardiac manifestations of anaphylaxis are more severe in patients with degenerative or ischemic heart diseases.

It is essential to be aware of the potential allergenicity of neostigmine. Even though the case reported by Kolker *et al.* did not demonstrate classical features of anaphylaxis, clinical presentation did not completely rule out the possibility of anaphylaxis with hypertensive response in the light of recent studies. We agree with the possible mechanism of coronary spasm by neostigmine mentioned by the author, it is always imperative to be aware of Kounis syndrome in such scenario. Kounis syndrome is an underrated phenomenon in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Kolker S, Tzivoni D, Rosenmann D, Meyler S, Ioscovich A. Neostigmine induced coronary artery spasm: A case report and literature review. *J Anaesthesiol Clin Pharmacol* 2017;33:402-5.
2. Seed MJ, Ewan PW. Anaphylaxis caused by neostigmine.

- Anaesthesia 2000;55:574-5.
3. Triggiani M, Patella V, Staiano RI, Granata F, Marone G. Allergy and the cardiovascular system. *Clin Exp Immunol* 2008;153(Suppl 1):7-11.
 4. Marone G, Patella V, de Crescenzo G, Genovese A, Adt M. Human heart mast cells in anaphylaxis and cardiovascular disease. *Int Arch Allergy Immunol* 1995;107:72-5.
 5. Mackins CJ, Kano S, Seyedi N, Schäfer U, Reid AC, Machida T, *et al.* Cardiac mast cell-derived renin promotes local angiotensin formation, norepinephrine release, and arrhythmias in ischemia/reperfusion. *J Clin Invest* 2006;116:1063-70.

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