

Accumulation of eosinophils, mast cells, and basophils in the spleen and the coronary arteries in anaphylactic deaths: is the Kounis hypersensitivity associated syndrome present?

Nicholas G. Kounis · George D. Soufras ·
George Hahalís

Accepted: 2 September 2013 / Published online: 17 October 2013
© Springer Science+Business Media New York 2013

In a very interesting study published in *Forensic Science, Medicine, and Pathology* [1] it was found that measurement of eosinophils and mast cells in the spleen combined with serum tryptase measurement could diagnose anaphylaxis and anaphylactic death with a high degree of certainty. The authors stated that anaphylactic death cannot be diagnosed by autopsy alone or by counting mast cells in the lung and airways because these methods have failed to give consistent results. The search for other tissues infiltrated by allergic inflammatory cells could prove of paramount importance in diagnosing anaphylactic sudden death. They recommended that splenic tissue should be sampled for immunohistochemical examination in all cases of unwitnessed sudden death.

Eosinophils, mast cells, and basophils are important effector cells in the allergic response and they have been implicated in the pathogenesis of anaphylaxis. While diagnosing the cause of sudden death is a challenging task for both physicians and forensic pathologists, anaphylactic etiology is rarely suspected. Frequently, sudden death cases are attributed to myocardial involvement, but unrecognized

anaphylaxis may accompany up to 13 % of sudden unexpected deaths in adults [2]. There is experimental and clinical evidence that anaphylaxis is frequently associated with myocardial involvement due to coronary artery spasm and thrombosis manifesting as Kounis type I and Kounis type II variant [3]. Some experiments have shown that anaphylactic cardiac damage is not due to peripheral vasodilation but is the result of the action of anaphylactic mediators on the coronary vasculature [4]. Clinically, there are patients with anaphylactic cardiac shock who do not respond to fluid replacement but need anti-allergic and current myocardial infarction protocol treatment, thus denoting that the heart and especially the coronary arteries are primarily affected [5, 6]. However, differentiating global myocardial hypoperfusion from a primary cardiac myocardial suppression due to mast cell mediator action is clearly challenging and combined myocardial suppression and peripheral vasodilatation might occur simultaneously.

There are reports of sudden death due to coronary artery spasm in which the coronary arteries are involved. In a patient with repeated episodes of coronary spasm, who died suddenly following cessation of his treatment, the number of adventitial mast cells was found to be increased [7]. In this patient, histologic sections in all three major coronary arteries, including the area of spasm, were stained with toluidine blue and showed increased mast cells. In the same report, two additional subjects with sudden cardiac death also had increased mast cells in their coronary arteries with the highest counts in atherosclerotic and hemorrhagic plaques. Furthermore, coronary arteries of cardiac patients are hyper-reactive and contain stores of amines deriving from inflammatory cells that are the main culprits in inducing coronary spasm [8]. Type I and type II variants of the Kounis syndrome have led to coronary artery spasm and sudden death in two patients with drug-eluting stents. It is

N. G. Kounis (✉)
Department of Medical Sciences, Patras Highest Institute
of Education and Technology, 7 Aratou Street, Queen Olas
Square, Patras 26221, Greece
e-mail: ngkounis@otenet.gr

G. D. Soufras
Department of Cardiology, 'Saint Andrews' State
General Hospital, Patras, Greece
e-mail: gasouf@gmail.com

G. Hahalís
Department of Cardiology, University of Patras Medical School,
Rio, Patras, Greece
e-mail: hahalig@yahoo.com

known that drug-eluting stent components include a metal strut which is made from stainless steel containing nickel, the polymer coating and the eluted drugs all of which have antigenic properties [6]. In these patients histological examination of the left anterior descending coronary artery and Giemsa stain for mast cells with positive controls showed occasional scattered mast cells in the tunica adventitia [9, 10].

Therefore, histologic examination of the heart, and 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 sudden death.

References

1. Edston E. Accumulation of eosinophils, mast cells, and basophils in the spleen in anaphylactic deaths. *Forensic Sci Med Pathol*. 2013. doi:[10.1007/s12024-013-9468-9](https://doi.org/10.1007/s12024-013-9468-9).
2. Schwartz HJ, Yunginger JW, Schwartz LB. Is unrecognized anaphylaxis a cause of sudden unexpected death? *Clin Exp Allergy*. 1995;25:866–70.
3. Kounis NG, Mazarakis A, Tsigkas G, Giannopoulos S, Goudenos J. Kounis syndrome: a new twist on an old disease. *Future Cardiol*. 2011;7:805–24.
4. Felix SB, Baumann G, Berdel WE. Systemic anaphylaxis separation of cardiac reactions from respiratory and peripheral vascular events. *Res Exp Med*. 1990;190:239–52.
5. Shah G, Scadding G, Nguyen-Lu N, Wigmore T, Chenzbraun A, Wechalekar K, et al. Peri-operative cardiac arrest with ST elevation secondary to gelofusin anaphylaxis—Kounis syndrome in the anaesthetic room. *Int J Cardiol*. 2013;164:e22–6.
6. Kounis NG, Davlouros P, Hahalis G, Mazarakis A. The heart seems to be the primary site and the target of anaphylaxis resulting in the development of Kounis syndrome. *Intern Emerg Med*. 2012;7(Suppl 2):S119–20.
7. Forman MB, Oates JA, Robertson D, Robertson RM, Roberts LJ II, Virmani R. Increased adventitial mast cells in a patient with coronary spasm. *N Engl J Med*. 1985;313:1138–41.
8. Kalsner S, Richards R. Coronary arteries of cardiac patients are hyperreactive and contain stores of amines: a mechanism for coronary spasm. *Science*. 1984;223(4643):1435–7.
9. Kounis NG, Kounis GN, Soufras GD. Kounis syndrome: a potential cause of simultaneous multivessel coronary spasm and thrombosis after drug-eluting stent implantation. *J Invasive Cardiol*. 2007;19:200–1.
10. Brott BC, Anayiotos AS, Chapman GD, Anderson PG, Hillegass WB. Severe, diffuse coronary artery spasm after drug-eluting stent placement. *J Invasive Cardiol*. 2006;18:584–92.