



Letter to the Editor

Postmortem diagnosis of drug-induced anaphylactic death



A B S T R A C T

Keywords:

Mast cells

Tryptase

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Postmortem biochemistry

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Kounis syndrome is defined as the concurrence of acute coronary syndromes including coronary spasm, acute myocardial infarction, and stent thrombosis, together with conditions associated with mast cell and platelet activation, involving interrelated and interacting inflammatory cells. Mast cells influence the inflammatory process decisively, though they are numerically inferior in this inflammatory cascade. Accumulation of eosinophils and mast cells in the splenic red pulp is frequently observed in anaphylactic deaths and can be considered a reliable finding for the postmortem diagnosis of this condition. Moreover, a high concentration of mast cell tryptase in serum and increased numbers of eosinophils and mast cells in the spleen make the diagnosis of anaphylactic death almost conclusive. Increased mast cell tryptase levels in postmortem serum, individually considered, do not allow the diagnosis of anaphylaxis-related death to be reached. On the other hand, neither does identification of mast cells and eosinophils within the coronary artery wall and the myocardium, individually considered, allow the hypothesis of anaphylaxis-related death to be formulated.

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Dear Sir,

We have read the letter by Kounis et al. with great interest.¹

Kounis syndrome is defined as the concurrence of acute coronary syndromes including coronary spasm, acute myocardial infarction, and stent thrombosis, together with conditions associated with mast cell and platelet activation, involving interrelated and interacting inflammatory cells. Mast cells influence the inflammatory process decisively, though they are numerically inferior in this inflammatory cascade.²

In this letter and other articles by the same authors, it has been rightly emphasized that the heart and the coronary arteries should be regarded as the main organs and primary targets of anaphylaxis. There is indeed 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 variants. According to the authors, postmortem investigations in suspected anaphylaxis deaths should always include histological examinations of the coronary arteries and Giemsa stain for mast cells, which might show scattered mast cells in the tunica adventitia.^{1,3}

In the case report discussed in the letter by Kounis et al. the coronary arteries revealed mild atheromatous disease without significant stenosis. Though unmentioned, exhaustive and thorough histological examinations of the coronary arteries and the myocardium were performed. These did not reveal any myocardial infiltration by eosinophils and/or mast cells.

Based on the conclusions of the studies by Edston⁴ and other authors, accumulation of eosinophils and mast cells in the splenic red pulp is frequently observed in anaphylactic deaths and can be considered a reliable finding for the postmortem diagnosis of this

condition. Moreover, a high concentration of mast cell tryptase in serum and increased numbers of eosinophils and mast cells in the spleen make the diagnosis of anaphylactic death almost conclusive.^{5,6}

In a former report, we found that increased postmortem serum levels of mast cell-derived tryptase can be measured, though not systematically, in cardiac deaths with coronary atherosclerosis disease of various severities. Likewise, mast cell accumulation at the site of atheromatous rupture can occasionally be identified in individuals with coronary artery thrombosis and myocardial infarction. Nevertheless, local mast cell activation in coronary atherosclerosis disease and acute coronary syndromes does not consistently turn into massive mast cell tryptase release and therefore cannot be ascertained by mast cell tryptase measurements in postmortem serum from femoral blood.⁷

It has been postulated that locally activated mast cells participate in both developing and weakening atherosclerotic plaques. Significant mast cell accumulation at the site of atheromatous erosion or rupture has been described by several authors, who subsequently established associations between blood mast cell tryptase levels and atherosclerotic plaque instability. Despite these findings, clinical observations from different research groups have reached diverging conclusions on the diagnostic relevance of mast cell tryptase levels and acute coronary syndromes. Hence, conclusive answers on this topic are unavailable at present.^{8–12}

Kounis and his research team have provided an extraordinary contribution to the understanding of the sequence of pathophysiological and cardiovascular events that characterize conditions associated with mast cell activation.

We share the conclusions made by Edston⁴ and other authors completely. They highlighted that the diagnosis of anaphylactic death

should be based on numerous elements including circumstantial evidence and medical history when available, morphologic findings (histological, histochemical and immunohistochemical identification of eosinophils and mast cells in the splenic red pulp) and biochemical investigation results (increased mast cell tryptase levels in postmortem serum above the proposed reference of 45 ng/ml).

At the same time, we strongly support the recommendations of Kounis et al. who emphasized that pathologists should always perform histological examination of the myocardium and the coronary arteries (using a suitable stain) in order to identify mast cells and eosinophils, thereby elucidating the pathophysiology of the death process.

It must be highlighted that increased mast cell tryptase levels in postmortem serum, individually considered, do not allow the diagnosis of anaphylaxis-related death to be reached. On the other hand, neither does identification of mast cells and eosinophils within the coronary artery wall and the myocardium, individually considered, allow the hypothesis of anaphylaxis-related death to be formulated.

Conflict of interest

None.

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