Letter

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Post mortem determination of (β)-tryptase for the diagnosis of anaphylaxis: looking for a reasonable cut-off

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Dear Editor,

Anaphylactic deaths represent a critical issue for forensic pathologists and its post-mortem diagnosis requires several steps in order to formulate a correct and reliable diagnosis, which is not always reachable in a forensic setting. This is the reason why, especially in deaths occurred out-of-hospital or in an unclear accidental manner, reliable diagnostic methods to confirm or exclude anaphylaxis would be of great value (1).

Mast cells are the main effectors of anaphylaxis, they are present throughout the body, but more abundant in the skin and around blood vessels, in the respiratory and intestinal mucosa, and in connective tissue. The content of granules contained into mast cells is excreted when these cells are stimulated; one of the components stored in granules is the neutral protease, tryptase. Tryptase exists in two isoforms, α and β; α-tryptase is constantly secreted from mast cells as an inactive pro-enzyme and it is used to quantify mast cells, the other isoform, β-tryptase, is activated through two proteolytic phases: the first phase occurs at acidic pH and when heparin or dextran sulphate are present and it includes an autocatalytic intermolecular cleavage, generating a monomer, significantly less active than the final tetramer. In the second phase following the removal of the remaining precursor dipeptide by dipeptidyl peptidase I, there will be the formation of the active tetramer (2,3).

When systemic anaphylaxis is enough severe to cause hypotension β-tryptase is released and its values increase in the serum. Tryptase concentrations generally above 11 μg/L have been detected in anaphylactic deaths by several authors, however higher values have also been found in other deaths, such sudden infant death syndrome (SIDS), heroin-related deaths, coronary atherosclerosis in sudden cardiac death, fatal traumas, amniotic fluid embolism etc (4-7). In addition also other types of death such as by asphyxia where other experimental approaches are used (8), can be explored and evidences needing further confirmation are emerging (9).

It is important to carefully evaluate all these aspects in assessing the role of β-tryptase as a reliable potential marker for the diagnosis of anaphylaxis in post-mortem setting. In addition, the circumstances in and around the time of death should also be evaluated for a proper interpretation of post-mortem values of β-tryptase (1).

We wish to draw the attention of the whole scientific community on the importance of the quantification of the isoform β-tryptase alone and not quantified together with α isoform. In addition, the assays for the measurement of tryptase should always be validated using internal and external quality controls.

The review of literature in this field highlights that β or α + β tryptase concentrations detected in post-mortem blood samples of anaphylactic cases fall in a very broad range from few μg to to 150.000 μg/L, making this marker alone not enough specific, taking also into consideration as above reported the raise of tryptase levels in others fatalities (1-3).

The forensic literature on anaphylactic deaths typically comprises numerous case studies and a few population-based studies (1,2), therefore we advocate for a systematic approach in order to clarify numerous issues surrounding (β)-tryptase, with the attempt to propose a reliable cut-off of this marker in post-mortem setting.

Finally, special attention must be given to the post mortem interval in order to better evaluate if it affects or not tryptase serum concentration.

Conflict of interest
None

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