

Letter to the Editor

Serum tryptase levels and Kounis syndrome

N.G. Kounis

Medical Sciences Department, Patras Highest Institute of Education and Technology, 7 Aratou street, Queen Olga's Square 26221 Patras, Greece

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Tryptase is a preformed neutral protease which has been estimated to constitute approximately 20% of the total cellular protein of human mast cells [1]. Mast cells constitute the sole source of tryptase, although negligible amounts of tryptase are found in human basophils (0.04 pg per basophil) [2]. In the paper by Kervinen et al. [3], published recently in IJCA, serum tryptase levels were found to be normal in patients suffering from acute coronary syndromes (ACS) despite of the increased amounts of degranulated mast cells normally found at the actual sites of plaque erosion or rupture of such patients [4].

However, other recent reports [5–7] have shown that tryptase levels are significantly raised in non-allergic patients suffering from acute myocardial infarction, unstable angina and in patients with significant coronary artery disease. Based on these reports, it has been suggested that tryptase may be a potential new marker characterizing the unstable plaque, a novel way of identifying asymptomatic patients with coronary artery disease and a new biomarker of therapeutic efficacy in these patients.

Kounis syndrome [8] is the concurrence of ACS with conditions associated with mast cell degranulation and it is caused by mediators released during degranulation. Tryptase is a key mediator incriminated for plaque erosion or rupture. Tryptase, like pancreatic trypsin, preferentially cleaves peptide and ester bonds of the carboxyl side of basic aminoacids [9], although unlike trypsin, has a quite restricted range of natural substrates. Relatively few protein substrates have been identified, but the ability of tryptase to activate stromelysin [10] and urokinase plasminogen activator [11], to cleave 72-kDa gelatinase and fibronectin [12] and type IV collagen [13] would be in

keeping with participation in processes of tissue destruction and remodelling.

The important questions which arise following the above contradictory reports on serum tryptase levels and measurements after ACS is about the suitable time for taking blood samples after the onset of symptoms and whether tryptase is released through the classical mast cell degranulation or by piecemeal or intragranular activation or differential or selective release [8].

Tryptase, like other inflammatory mediators, is short lived and has a half-life of about 90 min [14]. It must be emphasized that tryptase in immunoreactive form is stable, but as an enzyme has a half-life less than 3 min in physiologic buffers [15]. Based on the above, it has been suggested [14] that “the best time to obtain samples for tryptase determinations is 1–2 h after the precipitating event but, depending on the magnitude of the initial response, elevated levels of tryptase may be present in the circulation for several hours”. However, patients with ACS do not show evidence of any initial anaphylactic response with large amount of tryptase release and therefore the tryptase measurements should be restricted to the time range of 1–2 h after the onset of symptoms. In the second process of piecemeal degranulation or intragranular activation or differential or selective release, mast cells seem to undergo ultrastructural alterations of their electron dense granules indicative of secretion but without overt degranulation and therefore the quantity of tryptase, if any, is not sufficient to be detected by measuring tryptase concentration in the systemic circulation as it has been stated by Kervinen et al. [3].

Kervinen et al. seemed to have collected blood specimens too late after the onset of symptoms (in some patients 2–5 h and on average 7.3 ± 5.0 h). The same applies to another paper [16] with normal tryptase levels which Kervinen et al. are referring to.

E-mail address: ngkounis@otenet.gr.

Until the process of mast cell activation in ACS is elucidated, we suggest that blood samples for tryptase measurements should be taken early enough after the onset of symptoms. The best time for the first specimen seems to be half an hour after the initial symptoms and 30 min thereafter during the following 2 h.

We have a study in progress correlating tryptase levels, in ACS, with cardiac enzymes, troponins and C-reactive protein, and the preliminary results seem to corroborate the above suggestion.

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