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Macrophage, eosinophil, and mast cell extracellular traps (METs, EETs and MCETs) participate in coronary thrombus evolution after acute myocardial infarction

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Background

Extracellular traps generated by neutrophils (NETs) play important roles in the formation and propagation of the atherothrombotic mass following coronary plaque disruption, and are thus presumed to contribute to the ensuing onset of acute myocardial infarction. However, other cells such as macrophages, eosinophils and mast cells, may also capable of releasing extracellular traps, which are called as METs, EETs and MCETs, respectively. The generation of these extracellular traps also marks a distinct form of cell death namely etosis.

Purpose

The aim of this study was to investigate the formation of NETs, METs, EETs and MCETs in human coronary thrombectomy specimens of myocardial infarction (AMI) patients, in relation to the age of the thrombus.

Method

Thrombectomy specimens obtained from 48 AMI patients were available in paraffin sections for this study. Using HE-stains, they were classified as either 25 fresh (<1 day old, intact erythrocytes and granulocytes), 25 lytic (1-5 days old, lytic changes) or 19 organised (>5 days, fibrocellular ingrowth) thrombi. Immunohistochemistry was performed to identify neutrophils (MPO), macrophages (CD68), eosinophils (EMBP) and mast cells (tryptase). NETs, METs, EETs and MCETs were visualised in double-immunostains using the cell specific antibodies in combination with anti-citrullinated histone-3 (CitH3) antibody. Single and double-immunostained cells were counted as number/mm² and calculated as the average numbers/mm² for each thrombus category.

Results

NETs, METs, EETs and MCETs were present in all different thrombus age. Fresh thrombi contained more NETs (167/mm²), followed by METs (43/mm²), EETs (10/mm²) and MCETs (4/mm²)(p<0.05); lytic thrombi had more NETs (120/mm²) and METs (101/mm²) compared to EETs (2/mm²) and MCETs (2/mm²)(p<0.05); and organised thrombi contained more METs (37/mm²), followed by NETs (25/mm²), MCETs (8/mm²) and EETs (2/mm²) (p<0.05).
Conclusion

Not only neutrophils, but also macrophages, eosinophils and mast cells are able to generate extracellular traps and undergo etosis during the evolution of coronary thrombosis. Their relative participation depends on the organisation stage of the thrombus.