Neutrophil extracellular traps

Neutrophil extracellular traps (NETs) are networks of extracellular fibers, primarily composed of DNA from neutrophils, which bind pathogens.

Neutrophils are the immune system's first line of defense against infection and have conventionally been thought to kill invading pathogens through two strategies: engulfment of microbes and secretion of antimicrobials. In 2004, a novel third function was identified: the formation of Neutrophil extracellular traps (NETs). NETs allow neutrophils to kill extracellular pathogens while minimizing damage to the host cells.

Upon in vitro activation with the pharmacological agent phorbol myristate acetate (PMA), Interleukin 8 (IL-8), or lipopolysaccharide (LPS), neutrophils release granule proteins and chromatin to form an extracellular fibril matrix known as NET through an active process.

Neutrophil extracellular traps (NETs) play a major role in intrinsic immunity by limiting and killing pathogens. Recently, a series of studies have confirmed that NETs are closely associated with vascular injury and micro thrombosis. Furthermore, NETs play an important role in neuroinflammation after an ischemic and hemorrhagic stroke. Neuroinflammation and micro thrombosis after subarachnoid hemorrhage are key pathophysiological processes associated with poor prognosis, but their crucial formation mechanisms and interventions remain to be elucidated. Could NETs, as emerging and important pathogenesis, be a new therapeutic target after subarachnoid hemorrhage? [1)].

Severe carotid stenosis is a common cause of stroke. In addition, previous clinical studies revealed that patients symptomatic of carotid stenosis suffer from increased episodes of stroke compared with their asymptomatic counterparts. However, the mechanism underlying these differences in the recurrence of stroke remains unclear.

Objective: The present study aimed to evaluate the levels of neutrophil extracellular traps (NETs) in the plasma of patients with severe carotid stenosis and investigate whether NETs induced procoagulant activity (PCA) in severe carotid stenosis. The study also sought to investigate the interactions between platelets or endothelial cells (ECs) and NETs.

Methods: The levels of NETs in plasma were quantified using enzyme-linked immunosorbent assay (ELISA). In addition, NETting neutrophils and neutrophil-platelet aggregates were detected through flow cytometry. On the other hand, the morphology of NETs formation and endothelial cells were analyzed through confocal microscopy. Finally, the procoagulant activity (PCA) of NETs and endothelial cells were assessed through ELISA and fibrin formation.

Results: Patients with symptomatic carotid stenosis patients had significantly higher levels of NETs markers compared with their asymptomatic counterparts and healthy subjects. In addition, increased levels of neutrophil-platelet aggregates induced the generation of NETs in patients with symptomatic carotid stenosis. Moreover, NETs contributed to PCA through tissue factor (TF), in patients with carotid stenosis. Furthermore, NETs disrupted the endothelial barrier and converted endothelial cells (ECs) into PCA to enhance the PCA in patients with carotid stenosis.

The study revealed differences in the levels of NETs in the plasma of symptomatic and asymptomatic patients suffering from carotid artery stenosis. The study also uncovered the interaction between NETs and thrombogenicity in carotid stenosis. Therefore, inhibiting NETs may be a potential biomarker and therapeutic target for recurring stroke in severe carotid stenosis [2].

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2)
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