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Increased neutrophil extracellular trap (NET) formation in uremia is associated with chronic inflammation and prevalent coronary artery disease

Jwa kyung KIM, Mi jin PARK , Hyung seok LEE, Young rim SONG , Hyung jik KIM, *Sung gyun KIM

Internal medicine, Hallym University Sacred Heart Hospital, Korea,South

Objectives : Neutrophils are involved in the pathogenesis of atherosclerosis by neutrophil extracellular traps (NETs) formation. We evaluated that the NETs formation of neutrophils might be changed in end-stage renal disease (ESRD) patients, explaining their higher incidence of cardiovascular diseases.

Methods : A cross-sectional study was performed in 60 maintenance hemodialysis (MHD) patients, 30 age- and sex-matched healthy individuals (HV, negative control), and 30 patients with acute infection (positive control). Neutrophil activation and function were measured with reactive oxygen species (ROS) activity, degranulation, NET formation and phenotypical changes. And Western blot was performed with antibodies against citrullinated histone H3 (Cit H3) and histone 3 (H3).

Results : Compared with HV, neutrophils extracted from MHD patients displayed significantly increased levels of basal NET formation, ROS production and degranulation, suggesting spontaneous activation in uremia. Also, an increase in Cit H3 was detected in this group compared to the HV. And neutrophils from HV were normal CD16bright/CD62Lbright cells; however, neutrophils from MHD were CD16bright/CD62Ldim, similar to those from patients with acute infections. Interestingly, baseline NET formation was strongly associated with the prevalent coronary artery disease (CAD), circulating neutrophil count, and various inflammatory markers. Multivariate analyses identified the prevalent CAD and neutrophil counts as independent determinants of baseline NET formation (β=0.323, p=0.016 and β=0.369, p=0.006, respectively).

Conclusions : In this explorative study, uremia-associated increased NET formation may be a sign of in vivo inflammatory conditions and the burden of atherosclerosis.

Keywords : neutrophil extracellular traps, uremia, cardiovascular, atherosclerosis, inflammation