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ABSTRACT N. PO26

NON-CANONICAL COAGULATION PLATELETS FUNCTION: MONOCYTE-PLATELET INTERACTION A BRIDGE BETWEEN INFLAMMATION AND COAGULATION.

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Background and Aims: Platelet activation leads to the release of various molecules with immunoregulatory functions. While these factors play a limited role in thrombosis, they have a significant impact on modulating host immune responses. Monocytes recognize microbial components and respond by producing different pro- and anti- inflammatory cytokines and chemokines. Importantly, their interaction with platelets can induced an anti-inflammatory phenotype. Studies have shown that activated platelets bind to monocytes predominantly via P-selectin and subsequently trigger downstream signalling pathways that alter monocyte phenotype. In the present study we aimed to assess platelets-monocytes interaction, as well as activity of platelets and monocytes, in patients with different bacterial infection and in healthy controls, using flow cytometry and fluorescence microscopy.

Methods: Ten patients with various bacterial infections—including tuberculosis and Whipple's disease—and ten healthy control subjects were enrolled in the study. Cytokine levels, specifically interleukin-6 (IL-6), were measured using the ELISA method. CytoFLEX SRT cytometry was performed on whole blood using the following antibodies CD41-PC7 and CD62P-selectin-PE (CD62P) to identify platelets; CD14-APC to identify monocytes; and the tetra-panel (CD45--FITC/CD4-RD1/CD8-ECD/CD3-PC5) to identify lymphocytes. Monocyte were identified on side scatter properties and positive CD14. Platelet–monocyte aggregates (MPAs) were assessed by double CD62P and CD14 positivity. Platelet activation were evaluated by expression of P-selectin and CD41 and their activity was compared between platelets aggregated with monocytes and those not aggregated. Immunofluorescence microscopy was performed on whole blood smear to visualize MPAs using the following CD41-FITC, CD62P-Alexa Fluor 647, and CD14-Alexa Fluor 594 antibodies.

Results: Whole blood CytoFLEX SRT cytometry proved to be an effective method for distinguishing MPAs of varying sizes from free circulating platelets. The level of MPAs showed a significant positive correlation with surface expression of P-selectin and was significantly lower in patients compared to healthy controls ($p < 0.001$). Interestingly, the proportion of activated platelets—defined as $CD41^{+}$- $CD62P^{+}$—was higher in patients than in controls ($p < 0.001$). Moreover, circulating IL-6 levels were elevated in the plasma of patients and showed an inverse correlation with MPAs formation, suggesting an increased inflammatory state. Platelet counts remained within the normal range in all study participants. Additionally, the number of MPAs did not correlate with the absolute platelet count, indicating that aggregate formation is independent of overall platelet levels.

Conclusions: MPAs formation was significantly reduced in patients with bacterial infections presenting with endotoxemia, highlighting the pro-inflammatory state. Increased binding of platelets to monocytes and elevated MPAs levels suggest a potential anti-inflammatory role. Although the sample size was limited, our results indicate that the level of MPAs could be a valuable biomarker for assessing the inflammatory status. Promoting the formation of MPAs, it may be possible to induce a shift in monocytes toward an anti-inflammatory phenotype, contributing to the long-term resolution of inflammation. A better understanding of the regulation network could be the basis of novel drug discovery and intervention approaches.

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