

Editorial Focus

Platelets play a direct role in sepsis-associated endothelial cell death

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Platelets are well known to be intimately associated with inflammatory events in addition to their obvious haemostatic functions. For example, during sepsis, circulating platelets can bind lipopolysaccharide via Toll-like receptors (TLR) causing their quick escape from the circulation and allowing them to present the bacterial product to, for example, tissue-associated neutrophils (1, 2). This event subsequently results in the rapid production of tumor necrosis factor- α (TNF- α) and generation of reactive oxygen species (ROS) ultimately leading to endothelial damage and vasculitis (1, 2). Alternatively, the phagocytosis of platelets by cells of the reticulo-endothelial system can be significantly altered by bacterial products and this may also be responsible for the platelets rapid clearance and their pro-inflammatory nature during sepsis (3). To date, however, few studies in septic hosts have examined whether bacterial products can evoke the platelets themselves to directly affect endothelial cell function.

In this issue of *Thrombosis and Haemostasis*, Kuckleberg et al. (4) have further shed light on how bacteria-activated platelets can bind with endothelial cells and mediate apoptotic cell death. They utilized the gram negative bacterium *Haemophilus somnus*

that causes respiratory and reproductive disease in domesticated cattle. They observed that bacteria-laden platelets directly interacted with endothelial cells and induced Caspase 8- and 9-mediated apoptosis via the generation of ROS, and this appeared to be independent of external FasL/Fas interactions. This novel mechanism of platelet-induced apoptosis via ROS production also did not appear to be related to the production of TNF- α . The authors proposed that platelet CD40L-endothelial cell CD40 interactions may be important in mediating these internal death events by perhaps bypassing FasL/Fas interactions.

What makes this study so intriguing is that it not only adds to a growing body of evidence supporting the concept that platelets are critical to bacteria-mediated inflammation during sepsis but also suggests that the platelets themselves can directly induce endothelial cell death. This novel platelet-dependent mechanism may directly contribute to vasculitis and thrombus formation by inducing endothelial cell apoptosis and exposing the underlying extracellular matrix. Further investigations of these complex platelet-bacteria-endothelial interactions in septic hosts may lead to a better understanding of how platelets mediate vascular complications during sepsis.

References

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