The Role of Platelets in Atherothrombosis

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Abstract

Platelets have evolved highly specialized adhesion mechanisms that enable cell-matrix and cell-cell interactions throughout the entire vasculature irrespective of the prevailing hemodynamic conditions. This unique property of platelets is critical for their ability to arrest bleeding and promote vessel repair. Platelet adhesion under conditions of high shear stress, as occurs in stenotic atherosclerotic arteries, is central to the development of arterial thrombosis; therefore, precise control of platelet adhesion must occur to maintain blood fluidity and to prevent thrombotic or hemorrhagic complications. Whereas the central role of platelets in hemostasis and thrombosis has long been recognized and well defined, there is now a major body of evidence supporting an important proinflammatory function for platelets that is linked to host defense and a variety of autoimmune and inflammatory diseases. In the context of the vasculature, experimental evidence indicates that the proinflammatory function of platelets can regulate various aspects of the atherosclerotic process, including its initiation and propagation. The mechanisms underlying the proatherogenic function of platelets are increasingly well defined and involve specific adhesive interactions between platelets and endothelial cells at atherosclerotic-prone sites, leading to the enhanced recruitment and activation of leukocytes. Through the release of chemokines, proinflammatory molecules, and other biological response modulators, the interaction among platelets, endothelial cells, and leukocytes establishes a localized inflammatory response that accelerates atherosclerosis. These inflammatory processes typically occur in regions of the vasculature experiencing low shear and perturbed blood flow, a permissive environment for leukocyte-platelet and leukocyte-endothelial interactions. Therefore, the concept has emerged that platelets are a central element of the atherothrombotic process and that future therapeutic strategies to combat this disease need to take into consideration both the prothrombotic and proinflammatory function of platelets.
Platelet adhesion, activation, and aggregation at sites of vascular endothelial disruption caused by atherosclerosis are key events in arterial thrombus formation. Platelet tethering and adhesion to... Platelet-endothelial cell interactions during ischemia/reperfusion: the role of P-selectin. Blood 1998; 92: 507–15. PubMedGoogle Scholar. 71. 5. Role in coagulation. Platelets contribute substantially to thrombin generation, which further induces additional platelet activation. In addition, platelet thrombus stabilization requires local fibrin generation that depends on thrombin generation. When platelets are stimulated by strong agonists, the negatively charged phospholipids on the inner leaflet of the platelet plasma membrane are “flipped” to the outer leaflet. This reorganization may be mediated by the calcium activated scramblase TMEM16F. [33] Translocation of negatively charged phospholipids forms a stage upon which coagulation Platelets exhibit a major role in development and progression of atherothrombosis. The normal function of platelets is to secure hemostasis at sites of vascular injuries. Abnormal endovascular structure may result in excessive platelet function with consequence of progressive or acute reduction in vascular lumen and cessation of blood flow. Obviously, decrease in platelet count is accompanied by reduction in platelet function that manifests clinically at low critical count. It is important to emphasize that platelet dysfunction may be present despite normal platelet count.