Circulating microparticles from Crohn's disease patients cause endothelial and vascular dysfunctions

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BACKGROUND: Microparticles (MPs) are small vesicles released during cell activation or apoptosis. They are involved in coagulation, inflammation and vascular dysfunction in several diseases. We characterized circulating MPs from Crohn’s Disease (CD) patients and evaluated their effects on endothelial function and vascular reactivity after in vivo injection into mice.

METHODS: Circulating MPs and their cellular origins were examined by flow cytometry from blood samples from healthy subjects (HS) and inactive or active CD patients. MPs were intravenously injected into mice. After 24 hours, endothelial function and vascular reactivity were assessed.

RESULTS: Circulating MP levels did not differ between HS and inactive CD patients except for an increase in leukocyte-derived MPs in CD. Active CD patients compared to HS displayed increased total circulating MPs, pro-coagulant MPs and those from platelets, endothelium, erythrocytes, leukocytes, activated leukocytes and activated platelets. A significant correlation was found between total levels of MPs, those from platelets and endothelial cells, and the Harvey-Bradshaw clinical activity index. MPs from CD, but not from HS, impaired endothelium-dependent relaxation in mice aorta and flow-induced dilation in mice small mesenteric arteries, MPs from inactive CD patients being more effective than those from active patients. CDMPs induced vascular hypo-reactivity in aorta that was prevented by a nitric oxide (NO)-synthase inhibitor, and was associated with a subtle alteration of the balance between NO, reactive oxygen species and the release of COX metabolites.

CONCLUSIONS: We provide evidence that MPs from CD patients significantly alter endothelial and vascular function and therefore, may play a role in CD pathophysiology, at least by contributing to uncontrolled vascular-dependent intestinal damage.

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