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Leucocyte activation in

References

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Leucocyte activation in coronary heart disease: but how and why?

Leucocytosis, a marker of inflammation, is associated with a greater cardiovascular risk. Thus, leucocyte myeloperoxidase (MPO) could serve as a biomarker of cardiovascular diseases, as shown by Morrow et al. But, they did not study as to why and how leucocyte activation occurs in coronary heart disease (CHD).

Infiltration of intima by leucocytes and macrophages is an early event to occur in atherosclerosis. Elevated low-density lipoprotein (LDL), hypertension, hyperglycaemia, and other systemic factors initiate and accelerate atherosclerosis. Despite the fact that the entire vascular endothelium is exposed to these systemic factors, atherosclerotic lesions occur in a patchy manner and develop preferentially at bifurcations, branch points, and inner curvatures of arteries, suggesting that local factors play a major role in the development of atherosclerosis. Haemodynamic forces induce the expression of pro-inflammatory genes that initiate and accelerate atherosclerosis at these points of shear stress. Normocholesterolemic C57Bl/6 mice and rabbits showed activation of NF-κB and elevated expression of VCAM-1 and ICAM-1, upregulation of pro-inflammatory genes IL-1, IL-6, MCP-1, as well as antioxidant genes glutathione peroxidase and glutathione-S-transferase in endothelial cells in atherosclerosis-susceptible regions of the ascending aorta. Intramural accumulation of LDL and its oxidation products preceded monocyte recruitment into early atherosclerotic lesions, suggesting that lipid accumulation triggers inflammatory response characterized by upregulation of the expression of chemokines and adhesion molecules in the lesion-prone areas in the intima that contributes to leucocyte accumulation and atherosclerotic lesion formation.

Healthy endothelial cells prevent excess expression of adhesion molecules, resist increases in LDL and cholesterol transport and retention, and abrogate the activation of NF-κB and the induction of expression of pro-inflammatory genes induced by haemodynamic forces at atherosclerosis-prone regions by producing factors that counter pro-atherosclerotic events. The patchy nature of atherosclerosis suggests that arterial walls undergo regional disturbances of metabolism that include the uncoupling of respiration and oxidative phosphorylation, which may be characteristic of blood vessels being predisposed to the development of atherosclerosis. Oxidative stress and abnormalities of uncoupling proteins produce smooth muscle contraction and cause hypertension, and respiratory uncoupling is increased in the aortae of experimental animals that are susceptible to atherosclerosis. Bemal-Mizrahi et al. showed that UCP-1 expression in aortic smooth muscle cells causes hypertension and increases atherosclerosis without affecting the cholesterol levels. This increase in UCP-1 expression enhanced superoxide anion production and decreased the availability of nitric oxide, suggesting that oxidative stress has been elevated. Thus, inefficient metabolism in blood vessels causes atherosclerosis.

One of the earliest signs of atherosclerosis is the development of abnormal mitochondria in smooth muscle cells. Arteries have marginal oxygenation, and hypoxia reduces the respiratory control ratio. Uncoupled respiration precedes atherosclerosis at lesion-prone sites but not at the sites that are resistant to atherosclerosis. Disease-free aortae have abundant concentrations of the essential fatty acid (EFA)-linoleate (LA), whereas fatty streaks are deficient in EFAs. EFA deficiency promotes respiratory uncoupling and atherosclerosis. Hence, local disturbances of EFA metabolism in the arterial wall could be responsible for atherosclerosis and vascular disease.

EFAs-linoleic acid (LA; 18:2 ω-6) and α-linoleic acid (18:3 ω-3) give rise to lipoxins (LXs), resolvin, and protectins in addition to forming precursors to various eicosanoids (reviewed in 3). Aspirin converts arachidonic acid (20:4 ω-6), eicosapentaenoic acid (20:5 ω-3), and docosahexaenoic acid (22:6 ω-3) to form aspirin-triggered 15 epimer LXs (ATLs) that inhibit inflammation on the vessel wall by regulating the motility of polymorphonuclear leukocytes (PMNs), eosinophils, and monocytes. LXs deficiency leads to an interaction between PMN and endothelial cells that result in endothelial damage, initiation, and progression of atherosclerosis. LXs, resolvin, and protectin inhibit cytokine generation, leucocyte recruitment, leucocyte diapedesis, and exudate formation, and suppress the production of pro-inflammatory cytokines. Hence, the local deficiency of LXs, resolvin, and nPD1 could initiate atherosclerosis. Furthermore, lipoxins suppress the production of MPO from activated leucocytes. Increased generation of MPO by leucocytes could be an indication of decreased formation of lipoxins, resolvin, and protectins by endothelial cells. This implies that enhancing the formation of endothelial LXs, resolvin, and protectins may suppress leucocyte activation and MPO generation, and prevent CHD.

References
3. Das UN. A defect in the activity of Δ⁶ and Δ⁵ desaturases may be a factor in the initiation and progression of atherosclerosis. Prostaglandins Leukot Essent Fatty Acids 2007;76:251–268.


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Blunt traumatic haematoma of the left anterior descending artery: intravascular findings

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A 27-year-old male was transferred to the Emergency Department after blunt chest trauma caused by motor cycle accident. Initial electrocardiogram showed a right bundle branch block (RBBB). On physical examination, the patient had non-severe facial injuries and anterior chest wall pain.

Transthoracic echocardiography demonstrated mild anterior hypokinesia with preserved global ejection fraction. Laboratory findings included T-troponins 0.51 ng/mL and CK-MB 31 ng/mL. Analgesia was started and the patient was monitored.

Twenty-four hours later, a transthoracic echocardiography demonstrated extensive anterior akinesia and myocardial damage markers peaked at T-troponins 3.18 and CK-MB 104. ECG showed RBBB resolution and T-wave inversion V1–V4. The patient was asymptomatic. Angiography revealed a single mid-left anterior descending artery lesion with hazy limits and TIMI 3 flow (Panel A). An intravascular ultrasound (IVUS) study showed a subintimal crescent-shape hypoechoic image, suggestive of intimal dissection with subintimal haematoma compressing the vessel lumen (Panel B). Optical coherence tomography (OCT) confirmed this findings with no intimal disruption (Panel C). A conservative management was planned with heparin and abciximab waiting for haematoma resolution to avoid stent deployment. For 1 week the patient remained asymptomatic, but a new angiography proved no resolution of haematoma. Thus, a direct stent was deployed with complete angiographic resolution (Panel D). IVUS confirmed correct stent apposition and haematoma exclusion (Panel E). OCT verified these findings with a final luminal diameter over 4 mm (Panel F). The patient made a good clinical recovery and was discharged 24 h later.

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