Can infective agents be respectable etiopathogenetic factors for acute coronary syndromes?

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A policeman sees a drunk man searching for something under a streetlight and asks what the drunk has lost. He says he lost his keys and they both look under the streetlight together. After a few minutes the policeman asks if he is sure he lost them here, and the drunk replies, no, that he lost them in the park. The policeman asks why he is searching here, and the drunk replies “this is where the light is”.

Atherosclerosis is a multifactorial disease and, among others, inflammation and activation of immune system play well established roles [1, 2]. In ACS, epicardial thrombosis with abrupt vessel occlusion is a crucial final event, initiated at the site of a “vulnerable plaque” [3]. Until recently, plaque rupture was considered predominantly mechanical, occurring at sites of vessel narrowing with turbulent blood flow [4]. However, removal of coronary stenosis has never proved to prevent ACS. On the other hand, exacerbation of inflammatory [5] and specific immune mechanisms has been implicated in platelet function modulation and thrombus formation in ACS [6, 7]. Therefore, pathophysiological pathways underlying the dynamic changes that ultimately cause coronary thrombotic occlusion represent an area of intense interest and research.

Inflammatory response in ACS includes systemic immune activation, local inflammation of the atherosclerotic plaque and immune reactions associated with the thrombotic event itself [8, 9]. Given the profound involvement of immune activation in ACS, infections and other systemic inflammatory reactions have also been proposed to increase the risk of ACS. Indeed, up to 30% of myocardial infarctions occur after upper respiratory tract infections [10], and chronic infectious agents such as Chlamydia pneumoniae or oral pathogens, initially linked to atherosclerosis, have been found to increase the risk of ACS [11–13]. In a very recent issue of Circulation, Pessi et al [14] assessed bacterial DNA in thrombus aspirates of 101 patients with STEMI and sought to determine the association between bacterial findings and oral pathology. They used real-time quantitative polymerase chain reaction with specific primers and probes to detect bacterial DNA from several oral species and C. pneumoniae. Bacterial DNA typical of endodontic infection was identified in 78.2% of thrombi, and periodontal pathogens were measured in 34.7%. In addition, bacteria-like structures (including whole bacteria) and monocyte/macrophage markers for bacteria recognition and inflammation were detected by transmission electron microscopy and immunohistochemistry analysis, respectively. In a subgroup of 30 STEMI patients examined with panoramic tomography, there was a significant association between periapical abscesses and oral viridans streptococci DNA-positive thrombi. The authors concluded that dental infection and oral bacteria, especially viridans streptococci, may be associated with the development of acute coronary thrombosis.

Such results are in line with another recent study, which also showed a lack of association between the severity of coronary atherosclerosis and periodontal...
bacteria [15]. A number of mechanisms that explain an infective etiology of atherosclerosis and ACS, including direct effects on vascular cells, circulating cytokines and inflammatory mediators, as well as initiation of autoimmune reactions have been proposed [16]. Returning to the above-mentioned study, the presence of bacterial DNA together with co-stimulation of immune-specific cells in the thoracic aspirates may suggest that these pathogens disseminate into systemic circulation, migrate to coronary plaques, and cause and/or maintain inflammation of the coronary artery [17].

At present the role of infective agents in ACS is not completely understood. Nonetheless, antimicrobial therapies have already been tested in ACS prevention trials [18–20]. Although treatment results have been contrasting, the objective evidence of bacterial particles in the coronary thrombi should further enhance research in this direction. Indeed, while technological progress has permitted continuous improvement in coronary artery plaque and thrombus removal, this should not prevent us from exploring other, maybe less evident, but probably as relevant causes of ACS.

REFERENCES