Nerve growth factor levels and mast cell distribution in human coronary atherosclerosis

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Abstract

Nerve growth factor (NGF), in addition to its neurotrophic function, acts on a variety of non-neuronal cells including immune cells and vascular smooth muscle cells. The aim of the present study was to determine the NGF levels and the distribution of NGF and low-affinity NGF receptor (p75NGFR) and mast cells (MC) in human atherosclerotic coronary arteries. Specimens of human coronary arteries obtained from autopsy cases (n = 12, subjects with atherosclerotic lesions; n = 9, subjects without atherosclerotic lesions/controls) were used. The present study showed that in the atherosclerosis-lesioned arteries, the amount of NGF decreased, whereas the expression of p75NGFR immunoreactivity and the number, both of MC and vasa vasorum, particularly in the adventitia, significantly increased, compared with the control arteries. Cumulatively, our findings help to set the neurotrophic theory and its currently extended neuroimmune framework into the context of pathobiology of atherosclerosis, suggesting that altered presence of NGF, p75NGFR, and MC may play a role in neuroimmune mechanisms of human coronary atherosclerosis.

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1. Introduction

Basic and clinical studies indicate that atherosclerosis is an inflammatory-fibroproliferative disease initiated by endothelial dysfunction, and develops as a result of a complex interaction between various growth factors/cytokines and vascular smooth muscle cells (VSMC) and immune cells [1–6]. The mechanisms involved in these interactions have not been yet elucidated. Lymphocytes, mast cells (MC), VSMC, and myofibroblasts are known to secrete a variety of biologically active molecules, including nerve growth factor (NGF) [7–13]. Evidence published in the last few years seems to indicate that NGF and MC are implicated in various inflammatory diseases, such as rheumatoid arthritis, systemic sclerosis, and bronchial asthma [7–10] whose cellular mechanisms are in general no different from those in atherosclerosis [1]. NGF is a powerful endogenous mediator which plays a crucial role acting on sympathetic and sensory peripheral nerve cells [9,14,15] and also on a variety of non-neuronal cells, including lymphocytes and MC [7–9,16,17] and VSMC [18–20]. NGF, through vascular innervation, influences the artery physiopathology [13,21,22] and, through its autocrine/paracrine action, both MC growth and degranulation [10,16,17] and VSMC migration and growth [18,19]. Thus, NGF could be also involved in the process of atherogenesis. However, no evidence is available as to whether the coronary artery produces and/or is receptive to NGF, except, to the best of our knowledge, the recently-reported high levels of the early growth response gene-1, NGF-induced-A (NGFI-A), in human and mouse atherosclerotic lesions versus adjacent media [3] and an increased expression of NGF and its receptors in VSMC in the rat aortic model of vascular injury [18]. Since MC are able to produce