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Vasa Vasorum Activities in Human Carotid Atherosclerosis is Associated with Plaque Development and Vulnerability

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Introduction

Carotid endarterectomy (CEA) has been shown to be beneficial in patients with high-grade symptomatic carotid artery stenosis. Subintimal and intraplaque hemorrhages are frequently seen during CEA in the absence of any visible breach in the intima, as these changes are derived from the vasa vasorum system rather than from blood in the vessel lumen. Imaging modalities to characterize unstable, vulnerable plaques are strongly needed for better risk stratification in these patients. The aim of this study was to investigate the correlation between the activities of the carotid vasa vasorum and carotid plaque vulnerability using indocyanine green-video angiography (ICG-VA) during CEA, focusing on how the carotid artery vasa vasorum is depicted.

Methods

Sixty-nine patients (mean age, 68.5 ± 2.5 years; mean degree of stenosis, 78.9 ± 3.8) who underwent CEA were enrolled prospectively from September 2013 to December 2014. ICG was injected intravenously as a bolus before and after resecting the atheroma during CEA. We also performed immunohistochemistry using CD68 (macrophage), CD117 (mast cell), CD4 (T-cell), and CD8 (T-cell) antibodies for resected plaque specimens.

Conclusions

The early appearance of VVE on ICG-VA was strongly associated with unstable carotid plaque and many microvessel channels that provided nutrients to the developing and expanding intima and potentially created an unstable hemorrhagic environment prone to rupture. Macrophages and mast cells were involved in the formation of microvessels in the atherogenic plaque and accelerated plaque progression into an unstable plaque phenotype.

Results

Active vasa vasorum density was observed in all patients on ICG-VA (n = 69). The vasa vasorum externa (VVE) and interna (VVI) were seen in 11 (16%) and 57 patients (82.6%), respectively. The types of VVE were strongly associated with preoperative angiographic instability (90.0%, $p = 0.005$) and carotid plaque vulnerability (100%, $p = 0.007$) macroscopically. In contrast, the types of VVI were less associated with angiographic instability (36.1%) and plaque vulnerability (49.1%, $p = 0.003$). CD86- and CD117-stained macrophages and mast cells were observed more frequently in unstable plaque, compared to those in stable plaque ($p < 0.0001$, $p = 0.002$, respectively).

Learning Objectives

By the conclusion of this session, participants should be able to understand 1)The activities of vasa vasorum play an important role in the development of human carotid atherosclerosis. 2)Unstable carotid plaque is strongly associated with vaso vasorum externa pattern

3)Innate immunity such as macrophage and mast cell is an important player in the development of unstable carotid plaque

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