Atherosclerosis and Colorectal Carcinogenesis: Shared Risk Factors or Common Pathogenesis?

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In this issue of *Digestion*, Kim and colleagues demonstrate a significant association between the detection of carotid artery stenosis (defined here as greater than 50% luminal narrowing) and the presence of one or more colorectal adenomas in nearly 1,900 middle-aged Korean men undergoing routine health screening who were not taking aspirin or a statin [1].

Carotid artery stenosis was more frequently detected in individuals harbouring a colorectal adenoma(s) compared with those without a colorectal neoplasm [1]. These data add to a growing literature that demonstrates a link between atherosclerotic disease and the presence of colorectal neoplasia [2]. One explanation is the existence of many shared risk factors for vascular disease and development of colorectal neoplasia such as tobacco smoking, obesity, metabolic syndrome and type II diabetes mellitus [3]. However, an alternative explanation, as pointed out by Kim et al. [1], is a possible shared pathogenic factor; chronic inflammation.

The inflammatory process is now understood to be central to atherosclerosis [4]. Less well-recognised is the role of inflammation in so-called 'sporadic' colorectal carcinogenesis, as opposed to colorectal neoplasia developing on a background of longstanding inflammatory bowel disease. Several strands of indirect evidence link 'sporadic' colorectal carcinogenesis and chronic inflammation including the association between raised C-reactive protein levels and incident colorectal cancer [5], the

consistent protective effect of regular use of non-steroidal anti-inflammatory drugs [6] and the important role of several pro-inflammatory cytokines during carcinogenesis [7]. Interestingly, the cyclooxygenase-2 enzyme, which is established as an effective chemoprevention target, is present predominantly in stromal cells, including macrophages, in 'sporadic' colorectal adenomas, reminiscent of a chronic inflammatory cell infiltrate [8].

Moreover, shared molecular mechanisms in atherosclerosis and colorectal carcinogenesis are now being uncovered. For example, the pro-inflammatory cytokine macrophage migration inhibitory factor (MIF) has been discovered to play a role during atherogenesis [9] and the early stages of colorectal carcinogenesis [10].

Further epidemiological studies of the relationship between atherosclerotic disease and colorectal neoplasia, particularly in non-Asian populations, and greater understanding of the role of chronic inflammation during atherosclerosis and colorectal carcinogenesis, as well as elucidation of the link with predisposing pro-inflammatory states such as obesity [11], should prompt evaluation of the role of inflammation biomarkers such as CRP and serum cytokine levels as predictors of future neoplastic risk in the colorectum in at-risk groups such as the obese. 'Anti-inflammatory' therapy in its broadest sense (of which aspirin can be thought of as an example) is an attractive strategy which could combine cancer prevention and vascular prophylaxis.

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