Cathepsin Enzymes and Cystatin C: Do They Play a Role in Positive Arterial Remodeling?

To the Editor:

We have read the impressive article recently published by Aoki et al.1 evaluating the cathepsin enzyme system in cerebral aneurysm formation. By using quantitative RT-PCR and immunohistochemistry, the authors have demonstrated increased expression of cathepsin B, cathepsin K, and cathepsin S in arterial wall of the cerebral aneurysms, whereas the expression of cystatin C was found to be decreased. These findings suggest an imbalance between cysteine cathepsins and their inhibitor. This imbalance may cause the excessive breakdown of extracellular matrix proteins in the arterial wall resulting in progressing arterial aneurysm formation. This conclusion was supported by the experimental use of the cathepsin inhibitor NC-2300.

Cystatin C is a ubiquitously expressed, secretory protein that inactivates members of the cathepsin family of cysteine proteases, and subsequently plays a role in protein catabolism, antigen presentation, bone resorption, hormone processing, and scavengers. Moreover, cystatin C shows an inverse correlation with the incidence of cardiovascular disease.2,3 Recently, decreased cystatin C levels have been shown in patients with coronary artery ectasia coexisting with obstructive coronary artery disease, when compared to patients with coronary artery disease alone.4 Moreover, patients with abdominal aortic aneurysm were shown to have higher levels of cathepsin enzyme activity and lower levels of cystatin C as compared to patients with obstructive abdominal aortic disease.5,6

It has already been demonstrated that dilated vascular segments are often not localized to a single vascular territory. Increased, several dilating vascular diseases such as abdominal aortic aneurysm,7 coronary artery ectasia,8 cerebral artery aneurysm9 and venous system dilatation10 may coexist, suggesting that a systemic abnormality may explain these vascular wall destructions.11 It is therefore reasonable to assume that the observed changes in cathepsin and cystatin C expression and activity may be the common denominator that may be found in patients with multiple manifestations of dilating vascular diseases.

Regarding the inhibitory effects of cystatin C on catabolic cathepsin enzymes, it is reasonable to expect increased vascular wall destruction leading to dilatation in involved segments. Beyond the possible inverse association between the atherosclerosis and cystatin C, it is becoming more and more obvious that decreased cystatin C expression level is associated with dilating vascular disease or positive arterial remodeling. As firstly proven by animal study of Aoki et al.,1 cathepsin enzymes and cystatin C may be good targets for novel therapeutic interventions aiming in decelerating or preventing the progression of aneurysmal disease.

Disclosures

None.

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References


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