Cytomegalovirus Infection and Coronary Restenosis

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There are several possible pathophysiological mechanisms by which CMV might affect the restenotic process. CMV infection of endothelial cells can induce procoagulant activity or the expression of endothelial-leukocyte adhesion molecules. CMV infection of SMCs can increase proliferation and decrease apoptosis; this may be related, at least in part, to inhibition of the p53 tumor-suppressor gene product, an inhibitor of cell cycle progression. Alternatively, a systemic low-grade inflammatory response in CMV-infected patients, rather than reactivation of local coronary infection, might increase the risk of restenosis.

In this issue of Circulation, Manegold and colleagues analyze the impact of prior CMV infection on restenosis at 6-month angiographic follow-up in 92 patients with successful balloon angioplasty. Sixty-five percent of patients were positive for anti-CMV IgG; 35% had no evidence of prior CMV infection. Restenosis was assessed with quantitative coronary angiography. The extent of restenosis was similar in CMV-positive and CMV-negative patients; minimal lumen diameter, percent diameter stenosis at follow-up, late loss, and the loss index did not differ between groups.

These negative results do not support an important role for prior CMV infection in the risk of coronary restenosis after balloon angioplasty. However, as is the case for all negative studies, one has to wonder whether the study was adequately powered to detect a reasonable difference between groups. The study by Manegold et al included only 92 patients and probably lacked sufficient statistical power to definitely exclude a relationship between CMV status and restenosis after balloon angioplasty. The fact that diabetes, which has been found to be a risk factor for restenosis after balloon angioplasty, was not shown by multivariate analysis to be a significant predictor in their study (P = 0.90) also underscores the relatively small size of the study population. The negative results of Manegold et al are supported, however, by the results of independent studies. As shown in the Table, these studies are remarkable for the constant proportion of seropositive patients and by the lack of impact of CMV status on restenosis.

Why would prior CMV infection be a risk factor for restenosis after coronary atherectomy but not after balloon angioplasty? As pointed out by Manegold et al, the acute gain obtained with coronary atherectomy is higher than with balloon angioplasty; this may be associated with a higher degree of wall injury and a potentially higher degree of CMV reactivation. Another explanation may be related to the mechanisms of restenosis. Although restenosis after coronary atherectomy or balloon angioplasty involves both vessel remodeling and neointimal hyperplasia, it has been suggested that SMC proliferation may be more important after coronary atherectomy than after balloon angioplasty; in this setting, CMV inhibition of p53 would be more likely to affect
the risk of restenosis. To test this hypothesis further, it would be important to analyze the impact of prior CMV infection on restenosis after coronary stenting. Stent implantation is associated with a high acute gain; in addition, because vessel remodeling is virtually abolished, in-stent restenosis, if it occurs, is mainly the consequence of neointimal hyperplasia.\(^1\) In-stent restenosis would thus appear to be an excellent model to test the impact of prior CMV infection on SMC proliferation and migration.

Identification of patient-related risk factors for restenosis would be especially important in clinical practice because they affect all lesions treated in an individual patient. Patient-related factors, however, are not limited to infectious factors. As stated above, diabetes has been associated with a very high restenosis rate in different studies.\(^2,3\) More recently, related factors, however, are not limited to infectious factors. They affect all lesions treated in an individual patient. Patient-related factors in the pathophysiology of coronary artery disease in restenosis and give further insights into the role of systemic factors in the pathophysiology of coronary artery disease in general.

References


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