Antivascular Endothelial Growth Factor-A Treatment: New Perspectives for High-Risk Plaque Stabilization

We would like to applaud the authors of the recent review in JACC (1) regarding the current status of clinical applications of vascular endothelial growth factors (VEGFs). As the investigators mentioned, VEGF therapy has tremendous potential in vascular therapeutics, although more clinical data are required to draw safe conclusions. In their comprehensive review, Ylä-Herttuala et al. (1) focused also on the possible role of VEGF-A in the "destabilization" procedure of atheromatic plaques via proinflammatory and angiogenic mechanisms. However, they also cite studies challenging the potential detrimental role of VEGF-A on plaque instability, as systemic gene transfer of VEGF-A did not alter plaque area, and local gene transfer inhibited neointimal growth in animal studies (1).

There is increasing evidence that vasa vasorum-derived microvessels nurture the atherosclerotic plaque, with an organized system regulated by sympathetic and hormonal stimuli (2). Recently, we investigated the potential therapeutic effect of local delivery of an antibody against VEGF-A on neovascularization and intimal hyperplasia in an experimental model. Specifically, we demonstrated that bevacizumab (Avastin, Genentech, South San Francisco, California), a monoclonal antibody for VEGF-A, delivered locally by a phosphorylcholine-coated stent is associated with less microvessel density and neointimal hyperplasia compared with the control segments. Moreover, the inflammation, endothelialization, and fibrin deposition scores were not affected by bevacizumab (3). These favorable experimental results were the stimulus to perform the first-in-man study, in which we included 20 patients treated by a bevacizumab-eluting stent (4). Angiographic and intravascular ultrasound examination at 6 months showed minimal late loss and neointimal hyperplasia area.

Ylä-Herttuala et al. (1) also mentioned that patients under systemic administration of bevacizumab for cancer treatment had an almost 5% increased risk of thromboembolic complications in addition to the more common side effects of hypertension and proteinuria (5). Thus, local delivery of bevacizumab is required to overcome the systemic side effects. In this first approach for plaque neovascularization inhibition we used a coated stent for the local delivery of bevacizumab. However, new means for local delivery of multiple inhibitors of VEGF-A are currently being investigated.

In conclusion, VEGFs may be important therapeutic targets in cardiovascular therapeutics. Local inhibition of VEGF-A needs to be further investigated as a new treatment strategy for "high-risk" plaque stabilization.

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