AntiVEGF therapy: hidden changes on heart and vessels

VEGF (Vascular endothelial growth factor) is a protein normally present in our organism that promotes the growth of new blood vessels, a process known as angiogenesis. Cancer cells produce this substance in large quantity, obtaining a continuous supply of nutrients from the new vassels necessary to meet the increased metabolic request.

Starting from the idea to ??attack tumors by removing their supplying, the researchers developed the so-called angiogenesis inhibitors (or anti-VEGFR), drugs that, blocking the VEGF action, prevent tumors from creating new vessels, arresting in this way, or at least, slowing, their growth.

Since VEGF is produced also by the healthy cells, with an important role in the homeostasis of the vascular system, it is easy to figure out that this class of drugs has a strong effect on the cardiovascular district.

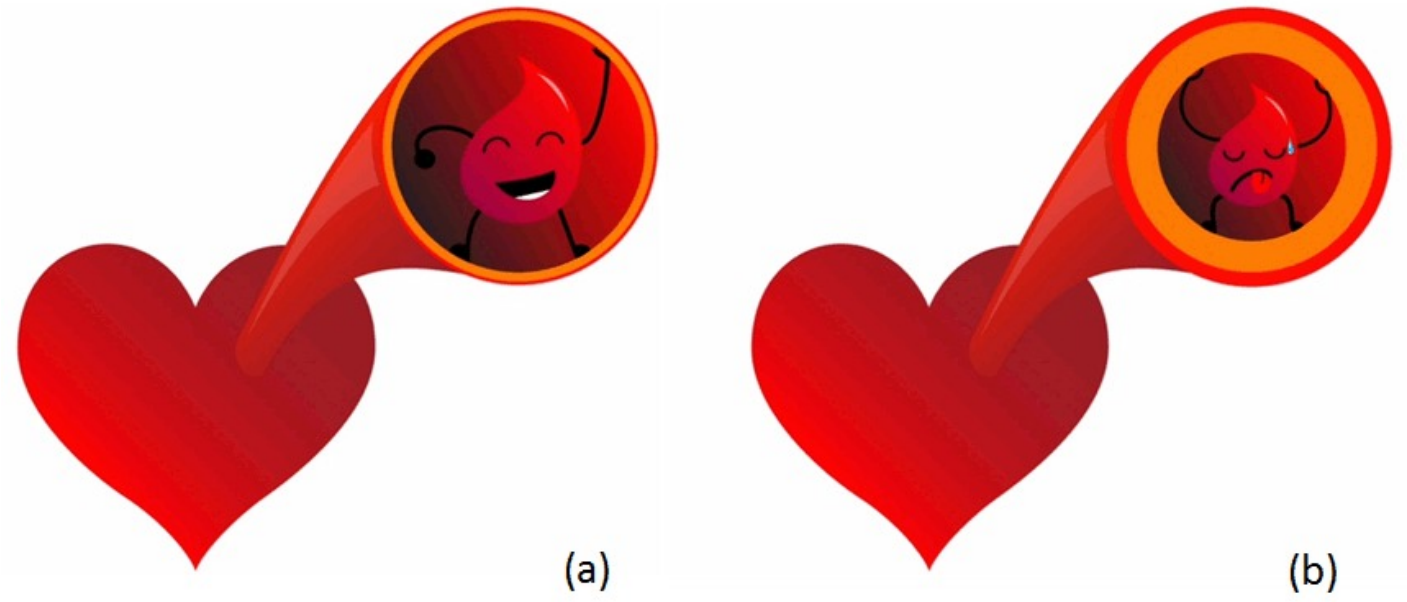

Fig 1. Elastic artery (a) versus stiff artery (b), effect of the anti-VEGFR treatment on the cardiovascular system.

We have studied cardiac and vascular function of 29 patients with cancer under treatment with anti-VEGFR drugs through non-invasive arterial investigation and echocardiography. The measurements have been made at three different times: before starting treatment (T0), after 2 weeks (T1) and 6 weeks (T2) from the beginning. We have found that these individuals have a significant increase in blood pressure, both brachial and central. Furthermore, we have seen an

early increase of the so-called stiffness (expressed with the Pulse wave velocity, PWV), i.e. vessels, during drug treatment, become more stiff. The alterations were not limited to a vascular level. Even at the cardiac level, an initial alteration of cardiac function has been found, both systolic (i.e. the contractility of the cardiac muscle, investigated with a specific parameter, the global longitudinal strain, GLS), both diastolic (i.e. the ability of the heart to relax and fill with blood). It is also interesting to note that adverse cardiovascular effects appear already after only two weeks, so early, and are maintained in patients who continued treatment, while disappear/decrease in patients whose treatment is stopped. This last observation shows how the adverse cardiovascular effects of angiogenesis inhibitors are early, but reversible. Hence the hypothesis that these alterations are "functional", whose origin may be due to a reduced secretion of nitric oxide (an endogenous vasodilator substance) and to an increase of the tone of smooth cells of the arterial wall. Lastly our study has important clinical implications. First, the adverse effects of anti-VEGFR treatment are even greater than previously believed. Two, the possibility that the parameters we found early altered (such as the PWV and GLS) could play a role in the oncology outcome. A focused cardio-vascular staging could integrate the oncologic one and permit a real patient-oriented therapy and, in parallel, an early and intensive correction of eventual cardio-vascular toxicity.

Publication

Effects of Cancer Therapy Targeting Vascular Endothelial Growth Factor Receptor on Central Blood Pressure and Cardiovascular System.
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