Peripheral Artery Disease and Stroke

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Authors

Concetta ZitoEmail authorRoberta ManganaroScipione CarerjFausto J. PintoBijoy J. Kandheria

Abstract

Peripheral artery disease (PAD) and stroke can occur as vascular complication of anticancer treatment. Interruption of vascular endothelial growth factor (VEGF) inhibitor signaling (i.e., bevacizumab) is associated with vascular toxicity and clinical sequelae such as hypertension, stroke, and thromboembolism beyond acute coronary syndromes. However, BCR-ABL tyrosine-kinase inhibitors (TKIs), used for the treatment of chronic myeloid leukemia (CML), are the main antineoplastic drugs involved in the development of PAD. In particular, second- and third-generation TKIs, such as nilotinib and ponatinib, while emerging as a potent arm in contrasting CML, are associated with a higher risk of PAD development rather than imatinib. Factors favoring vascular complication are the presence of traditional cardiovascular risk factors (CVRF) and predisposing genetic factors, high doses of BCR-ABL TKIs, longer time of drug exposure, and sequential use of potent TKIs. In addition, circulating concentrations of VEGF are reduced by cyclophosphamide administered at continuous low doses, which might underpin some of the observed vascular toxicity, as seen in patients treated with VEGFIs. This alkylating agent is therefore associated with vascular complications including stroke. The risk of stroke is also increased after treatment with anthracyclines that can induce endothelial dysfunction and increase arterial stiffness. Head and neck radiotherapy is associated with a doubled risk of cerebrovascular ischemic event, especially if exposure occurs in childhood. The mechanisms involved in radiation vasculopathy are represented by endothelial dysfunction, medial necrosis, fibrosis, and accelerated atherosclerosis. An accurate cardiovascular risk stratification is strongly recommended in patients candidate to anticancer treatment associated with higher risk of vascular complication, in order to correct CVRF and select appropriate patient tailored strategy of treatment. Then a clinical follow-up, eventually associated to instrumental evaluation through vascular ultrasound, should be performed.

Keywords

Endothelial dysfunction Atherosclerosis Arterial stiffness Thrombosis Prevention