Thromboembolic disease in patients with high-grade glioma.

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Abstract
Venous thromboembolism (VTE) is common throughout the course of disease in high-grade glioma (HGG). The interactions between the coagulation cascade, endothelium, and regulation of angiogenesis are complex and drive glioblastoma growth and invasion. We reviewed the incidence of VTE in HGG, the biology of the coagulome as related to glioblastoma progression, prevention and treatment of thrombosis, and the putative role of anticoagulants as anti-cancer therapy. VTE can be significantly reduced during the postoperative period with adherence to the use of mechanical and medical thromboprophylaxis. Activation of the coagulation cascade occurs throughout the course of disease because of a variety of complex interactions, including tumor hypoxia, upregulation of VEGFR expression, and increases in both tumor cell-specific tissue factor (TF) expression and inducible TF expression in numerous intrinsic regulatory pathways. Long-term anticoagulation to prevent VTE is an attractive therapy; however, the therapeutic window is narrow and current data do not support its routine use. Most patients with proven symptomatic VTE can be safely anticoagulated, including those receiving anti-VEGF therapy, such as bevacizumab. Initial therapy should include low molecular weight heparin (LMWH), and protracted anticoagulant treatment, perhaps indefinitely, is indicated for patients with HGG because of the ongoing risk of thrombosis. A variety of coagulation- and tumor-related proteins, such as TF and circulating microparticles, may serve as potential disease-specific biomarkers in relation to disease recurrence, monitoring of therapy, and as potential therapeutic targets.