

Venous Thromboembolism and Gliomas: The Need for Increased Vigilance

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Brain tumors, particularly malignant gliomas, have a high incidence of venous thromboembolism (VTE), but current guidelines do not support primary VTE prophylaxis for ambulatory patients with brain tumors. The often subtle presentation of VTE warrants increased vigilance for early diagnosis and treatment. This article presents a case study of a patient with VTE and offers suggestions for future research.

Mrs. X, a 55-year-old woman, initially presented with a one-month history of worsening cognitive and memory deficits. Magnetic resonance imaging revealed a right frontal enhancing lesion. A craniotomy was performed, and the pathology confirmed a glioblastoma multiforme (grade IV glioma). Perioperatively, Mrs. X received intermittent pneumatic compression and was ambulating to baseline at discharge 72 hours after surgery. Her discharge medications included dexamethasone 4 mg twice daily for management of intracranial swelling. Four weeks post-surgery, Mrs. X began a six-week course of radiation therapy with concomitant temozolamide oral chemotherapy. Six weeks postsurgery, she presented with a report of occasional left leg cramps. At this time, she was walking daily and using a stationary bike three times a week. She had no erythema, edema, or localized tenderness.

Mrs. X underwent a venous ultrasound, which was positive for deep vein thrombosis. She was managed as an outpatient with 60 mg enoxaparin twice daily. Several weeks after initiation of anticoagulation, her local primary care physician changed her treatment to warfarin because of the high out-of-pocket expense for enoxaparin. Several months later, she experienced increased neurologic symptoms from both tumor progression and an intratumoral hemorrhage. Warfarin treatment for primary venous thromboembolism (VTE) in

patients with cancer is associated with increased rates of recurrent VTE and bleeding complications when compared to patients without malignancy (Gerber, Grossman, & Streiff, 2006); therefore, warfarin was discontinued. The decision also was made to remain off VTE treatment since she had completed six months of therapy.

Venous Thromboembolism

VTE includes both deep vein thrombosis and pulmonary embolism. According to Virchow's triad, three broad categories contribute to thrombus formation: a hypercoagulable state, venous injury, and venous stasis (Lyman & Khorana, 2009). Cancer itself confers additional risks because of multiple pathophysiologic mechanisms, including increased procoagulant expression (Lyman & Khorana, 2009).

VTE is related to significant morbidity and mortality in patients with cancer. Patients with cancer have a fourfold to sevenfold increased risk of developing VTE (Streiff, 2009), a threefold

increased risk of recurrent VTE, and a threefold to sixfold increased risk of major bleeding complications related to anticoagulation compared to the general population (Carrier & Lee, 2009). In addition, VTE is a leading cause of death among patients with cancer (Lyman et al., 2007), and a diagnosis of VTE can prolong hospitalization, delay cancer treatments, and increase healthcare costs (Lyman & Khorana, 2009).

Other than cancer, risk factors for VTE include patient characteristics and comorbidities similar to those found in patients without cancer. The factors include advanced age, renal or pulmonary disease, obesity, and prior history of VTE. The primary site of cancer (e.g., brain, pancreas, ovary, kidney, stomach, bladder, lung, blood), cancer diagnosis within three months, increased biomarkers (e.g., tissue factor, D-dimer, prechemotherapy leukocytes, platelets), and cancer treatments all are associated with an increased risk of VTE (Connolly & Khorana, 2010) (see Figure 1).

Patients with brain tumors (particularly gliomas, which arise from the supporting cells of the brain) have one of

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