

Q: Should a patient with a brain tumor receive anticoagulation for a thromboembolic event?

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A: ALTHOUGH PATIENTS with brain tumors are prone to develop thrombosis, many physicians are reluctant to use anticoagulation, for fear it will increase the risk of intracranial hemorrhage in the tumor. We believe that anticoagulation is appropriate in many of these cases, as long as physicians are careful to exclude those with contraindications to anticoagulation. Although many physicians believe that inferior vena cava (IVC) filters are safer and more effective than anticoagulation, the data do not bear this out.

■ THE RISK: THROMBOSIS, BLEEDING

Patients with brain tumors are prone to thromboembolic events for several reasons, including the hypercoagulable state of malignancies, advanced age, immobility, hemiparesis, and neurological deficits.^{1,2} These thrombotic events include pulmonary embolism, deep vein thrombosis of an extremity, hepatic or portal vein thrombosis, Trousseau syndrome, disseminated intravascular coagulation, nonbacterial thrombotic endocarditis, and microvascular arterial thrombosis.³

On the other hand, another complication of brain tumors is spontaneous intracranial bleeding. The reason for bleeding inside an intracranial mass is not well understood, and depends on the type of malignancy and the location of the mass.¹ In metastases, the bleeding mainly occurs at the periphery of the mass, possibly related to the necrosis of the adjacent parenchyma caused by the expansion of the metastases. When the bleeding is central, the reason might be central necrosis and rupture of the newly formed vessels.

Types of tumors especially prone to cause intracranial hemorrhage include melanoma, renal-cell carcinoma, thyroid cancer, choriocarcinoma, and germ-cell tumors.^{2,4} The risk of spontaneous intracranial hemorrhage is less than 1% for metastases from breast cancer and less than 5% for metastases from lung cancer.¹

■ WHAT PHYSICIANS BELIEVE

Many physicians are reluctant to give anticoagulation to patients with either a primary or metastatic intracranial tumor who have a thromboembolic event. Some believe this to be an absolute contraindication.

■ WHAT THE DATA SHOW

Nevertheless, intracranial hemorrhage resulting from anticoagulant therapy in patients with brain tumors is not as common as some physicians think. In fact, several studies suggest that the risk of intracranial hemorrhage with well-controlled anticoagulant therapy is no higher than the risk of bleeding without anticoagulation.

Ruff and Posner⁵ reviewed the cases of 103 patients with high-grade gliomas and deep vein thrombosis who received anticoagulation. The target prothrombin time was less than 2.5 times the control value. Patients were followed for 14 weeks, during which time only two hemorrhagic complications and 1 death occurred.

Altschuler et al⁶ reported a series of 23 patients with brain tumors who received anticoagulation after a thromboembolic event, with no intracranial hemorrhagic events. The prothrombin time was maintained at 1.25 times control for 6 months.

Schiff and DeAngelis⁷ reported the cases of 42 patients with brain tumors and thrombotic events who received anticoagulation.

Anticoagulation is not absolutely contraindicated in patients with brain tumors

Three experienced serious cerebral hemorrhages: one was receiving supratherapeutic doses of heparin, another was receiving excessive doses of warfarin (the prothrombin time was 4.8 times control), and the third was receiving heparin within the therapeutic range.

Choucair et al³ did not find any complications in a group of patients receiving a non-standard regimen of subcutaneous unfractionated heparin twice a day for at least 3 months.

■ MISCONCEPTIONS ABOUT IVC FILTERS

It is widely believed that inferior vena cava (IVC) filters are safer and more effective than anticoagulant therapy when treating deep vein thrombosis in a patient with a brain tumor. However, Olin et al,⁴ in a case series of 50 patients treated with either an IVC filter or anticoagulation, found that anticoagulation was associated with no increase in intracranial hemorrhagic complications compared with IVC filters. Overall survival was the same with either therapy, and all the deaths that occurred were due to the malignancy and not from complications of the therapy used.

Furthermore, IVC filters are not completely effective or free of complications. Complications include filter migration and malpositioning, cellulitis or hematoma at the insertion site, erosion of the filter through the IVC wall, air embolism, and pneumothorax.^{2,4} In a series of 42 patients with IVC filters, Levin et al² reported that 12% had a recurrent pulmonary embolism, 26% had either filter or IVC thrombosis (3% had both), 21% had a recurrent deep vein thrombosis, and 9% developed the postphlebotic syndrome.

IVC filters assist in thrombosis management in the short run by preventing acute propagation of lower extremity clots and dislodgment into the pulmonary vasculature.

■ ANTICOAGULATION CONTRAINDICATIONS

Contraindications to anticoagulation in patients with brain tumors include:

- Preexisting intracranial hemorrhage
- High risk for falling or other injury
- Poor compliance with medical therapies
- Immediate postoperative status

- Serious thrombocytopenia (ie, a platelet count $< 50 \times 10^9/L$), due to either tumor involvement or chemotherapy, or expected serious thrombocytopenia due to future chemotherapy.

Caution should be observed in giving anticoagulation to patients with malignancies well known for their propensity to cause intracranial hemorrhage, eg, renal cell carcinoma, thyroid cancer, choriocarcinoma, and germ cell tumors. A relative contraindication to anticoagulation is a short life expectancy in a patient with various comorbid factors.

■ RECOMMENDATIONS

- Anticoagulation is the preferred therapy for thromboembolic complications in patients with brain tumors, as long as care is taken to exclude patients with contraindications to this therapy.
- Perform a brain CT scan to make sure there is no intracranial bleeding and no intratumoral hemorrhage.
- Reserve use of an IVC filter for situations such as when a patient with thromboembolism also has bleeding or recurrent emboli despite adequate anticoagulation.■

■ REFERENCES

1. Graus F, Rogers L, Posner JB. Cerebrovascular complications in patients with cancer. *Medicine* 1985; 64:16-35.
2. Levin JM, Schiff D, Loeffler JS, Fine HA, Black PM, Wen PY. Complications of therapy for venous thromboembolic disease in patients with brain tumors. *Neurology* 1993; 43:1111-1114.
3. Choucair AK, Silver P, Lenin VA. Risk of intracranial hemorrhage in glioma patients receiving anticoagulant therapy for venous thromboembolism. *J Neurosurg* 1987; 66:357-358.
4. Olin JW, Young JR, Graor RA, Ruschhaupt WF, Beven EG, Bay JW. Treatment of deep vein thrombosis and pulmonary emboli in patients with primary and metastatic brain tumors. *Arch Intern Med* 1987; 147:2177-2179.
5. Ruff RL, Posner JB. The incidence and treatment of peripheral venous thrombosis in patients with glioma. *Ann Neurol* 1983; 13:334-336.
6. Altschuler E, Moosa H, Selker RG, Vertosick FT Jr. The risk and efficacy of anticoagulant therapy in the treatment of thromboembolic complications in patients with primary malignant brain tumors. *Neurosurgery* 1990; 27:74-77.
7. Schiff D, DeAngelis LM. Therapy of venous thromboembolism in patients with brain metastases. *Cancer* 1994; 73:493-498.

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