ACUTE STROKE IN THE CANCER PATIENT

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Seven percent of patients with metastatic cancer experience a clinically evident stroke during the course of their illness and twice that number have autopsy evidence of stroke. Cancer patients have traditional risk factors for stroke (hypertension, smoking, diabetes, atrial fibrillation) as well as cancer-specific risk factors such as hematologic abnormalities, hypercoagulability, radiation induced vasculopathy, direct compression of vessels by tumor and certain anti-neoplastic medications.

Stroke in hematologic malignancies often presents as **intracranial hemorrhage (ICH)**. Thrombocytopenia is a major risk factor for ICH and may result from chemotherapy or infiltration of bone marrow by tumor. A platelet transfusion is indicated and if thrombocytopenia is secondary to tumor growth, treatment of the underlying malignancy will improve platelet counts. Disseminated intravascular coagulation (DIC) can be seen in patients with acute promyelocytic leukemia and may produce both ischemic and hemorrhagic events. Hyperleukocytosis in patients with acute leukemia produces leukostasis and predisposes to the development of microhemorrhages in the brain. In patients with solid tumors, brain hemorrhages are most likely to be the result of hemorrhage into a parenchymal metastasis. Hemorrhage into brain metastases can be treated surgically if the patient has clinically significant symptoms and the lesion is surgically accessible.

Cancer patients with high risk for development of venous thrombo-embolism are at risk of **cerebral venous sinus thrombosis**. Anti-coagulation is the treatment of choice. Hyperviscosity syndromes (Waldenström's macroglobulinemia), sepsis and dehydration can also predispose cancer patients to develop cerebral venous sinus thrombosis. Tumor invasion of the venous sinus from bony metastases (prostate cancer, breast cancer) can result in venous infarcts and increased intracranial pressure. Treatment of the underlying metastases with radiation can help in re-establishing proper venous outflow.

Arterial strokes in cancer patients are typically associated with DIC or nonbacterial thrombotic endocarditis (NBTE). NBTE is characterized by the development of sterile platelet-fibrin vegetations on heart valves. The clinical syndrome is characterized by multifocal neurologic deficits of acute onset, or occasionally, by diffuse encephalopathy. The value of anticoagulation in patients with NBTE and/or DIC in cancer patients has not been determined. Treatment of the underlying malignancy may help but prognosis is usually poor.

Radiation exposure to the head and neck produces accelerated atherosclerotic disease in the cervical or cerebral vessels within the radiation ports. This is usually a delayed effect and occurs 5-10 years after treatment. Radiation-induced carotid and vertebral stenosis may be amenable to the same treatments applied to atherosclerotic cerebrovascular disease. Cranial radiation can result in a radiation induced vasculopathy. A syndrome of subacute migraine like attacks after radiation therapy (SMART syndrome) occurs more than several years after radiation. Patients present with headaches, focal findings that last hours to days and an unusual pattern of enhancement on an MRI. Treatment with calcium channel blockers can prevent recurrence.

Chemotherapeutic agents including cisplatin, high dose methotrexate and bevacizumab have also been associated with stroke syndromes. Bevacizumab can result in arterial strokes in 1-3% of treated patients. Cerebral venous thrombosis is a relatively common complication of treatment with L-asparaginase. Treatment of arterial or venous thrombosis directly related to chemotherapy is best treated with cessation of the offending agent. Anthracyclines can cause cardiomyopathy and long term survivors are at higher risk of cardio-embolic stroke.

Acute Interventions such as TPA are relatively contraindicated in cancer patients. Sudden onset of symptoms may herald the discovery of new brain metastases rather than an acute stroke and cancer patients require contrasted neuro-imaging to rule this out. Patients with brain metastases are at high risk for seizures and

presentation can be in the setting of post-ictal paralysis and an unwitnessed convulsion. The pathophysiology of cancer related strokes are often distinct from more common strokes and the use of TPA will often not address the underlying condition. Finally, a patient's pre-stroke performance status and their prognosis in regards to their cancer need to be ascertained immediately after presentation. The risk of intervention may outweigh any benefit if a patient has a limited life expectancy.

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