

ACUTE ENCEPHALOPATHY IN A CANCER PATIENT

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A workup of encephalopathy in cancer patients should include investigation of common causes including infections, medications, electrolyte abnormalities and metabolic disorders as well as evaluation of risk factors such as frailty, underlying cognitive disorders and substance withdrawal. **Supportive care medications** in cancer patients including high doses of narcotics, anti-emetics and corticosteroids, can all cause mental status changes and medication lists need to be carefully examined. Cancer patients with cachexia or malnutrition may be more prone to nutritional deficiencies. **Wernicke's encephalopathy** should be a consideration in these patients and treated emergently. Patients with cancer are at risk for seizures related to brain metastases, medications or electrolyte abnormalities. In a cancer patient with unexplained mental status changes, an EEG should be performed to rule out **non-convulsive status epilepticus** (NCSE). NCSE is the underlying cause of altered mental status in up to 10% of patients with cancer and can be a presenting sign of new brain metastases.

Brain and Leptomeningeal Metastases are most common in patients with lung cancer, melanoma, metastatic breast cancer, renal cell cancer, acute leukemia and high grade lymphomas. Multiple small brain metastases can result in mental status changes in the absence of other focal findings. Emergent whole brain radiotherapy can be considered to improve mentation in solid tumor patients and chemotherapy regimens may benefit patients with hematologic malignancies. **Obstructive Hydrocephalus** can be a consequence of a single brain metastasis near the 4th ventricle or foramen of Monro and requires placement of an external ventricular drain to rescue neurologic function. Obstruction of CSF reabsorption can also occur in the setting of leptomeningeal metastases and an MRI may show only hydrocephalus with no visualization of an obstructive lesion. An urgent high volume lumbar puncture should be performed to check opening pressure, evaluate fluid and to reduce intracranial pressure.

Cytotoxic chemotherapeutic drugs can cause encephalopathy. Ifosfamide encephalopathy is one of the most common and may improve with administration of methylene blue. High dose chemotherapy regimens are associated with increase blood brain barrier penetration of drugs resulting in global CNS dysfunction. Although rare, encephalopathy has been reported with high dose regimens of methotrexate, etoposide, cytarabine and taxanes. **Intrathecal chemotherapies** such as methotrexate or liposomal cytarabine can cause aseptic meningitis. Patients can present with mental status changes, but also have meningeal signs, headaches, neck pain, nausea or vomiting. Urgent IV steroids can improve symptoms quickly and prophylactic intrathecal steroids can prevent recurrence with future administration. **Monoclonal Antibodies** such as bevacizumab and rituximab can cause a reversible posterior leukoencephalopathy syndrome (RPLS) that requires management of hypertension and discontinuation of the drug. In patients receiving rituximab or alemtuzumab, progressive multifocal leukoencephalopathy should be considered in the differential of patients with new CNS symptoms.

Exposure to **whole brain radiotherapy** (WBRT) can result in an acute encephalopathy especially in elderly patients or patients with an underlying dementia. Some patients can present several months after WBRT with a static encephalopathy and evidence of leukoencephalopathy on an MRI. Treatment consists of minimizing aggravating factors and supportive care. **Stereotactic Radiosurgery** (SRS) is a highly localized form of radiation that is delivered to patients with 3 or fewer solid tumor brain metastases. SRS can result in significant cerebral edema around the treatment target as well as radiation necrosis. Patients can develop encephalopathy, focal findings or seizures. Treatment with IV corticosteroids can produce immediate relief.

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