

## COMPLICATIONS AND EMERGENCIES IN ONCOLOGIC PATIENTS

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### Neurological complications

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#### Abstract

Patients with neurological malignancies are subject to developing a unique set of complications that require emergent evaluation and treatment. With the increasing incidence of cancer in the general population and improved survival, these emergencies will be more frequently encountered. Physicians must be able to recognize these conditions and institute appropriate therapy after a focused initial evaluation. The approach to definitive therapy is commonly multidisciplinary, involving surgeons, radiation oncologists, medical oncologists, and other medical specialists. Prompt interventions can be lifesaving and may spare patients considerable morbidity and pain. In neuro-oncology, there are some more specific complications and emergencies. The more general complications are not reviewed here.

**Keywords:** *Complications; emergencies; brain tumors; oncology.*

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#### Introduction

Patients with neurological malignancies are subject to developing a unique set of complications that require emergent evaluation and treatment. With the increasing incidence of cancer in the general population and improved survival, these emergencies will be more frequently encountered. Physicians must be able to recognize these conditions and institute appropriate therapy after a focused initial evaluation. The approach to definitive therapy is commonly multidisciplinary, involving surgeons, radiation oncologists, medical oncologists, and other medical specialists. Prompt interventions can be lifesaving and may spare patients considerable morbidity and pain<sup>[1]</sup>.

In neuro-oncology, there are some more specific complications and emergencies. The more general complications are not reviewed here. The important complications and emergencies frequently encountered include:

- acute ischemic stroke (AIS)
- intracranial hemorrhage

- subarachnoid hemorrhage (SAH), subdural hemorrhage (SDH) or extradural hemorrhage (EDH)
- increased intracranial pressure mass effect
- hydrocephalus
- infection
- cystic mass – cerebrospinal fluid (CSF) breach and leaks
- surgical devices/cavity
- local/general toxicity
- metabolic posterior reversible encephalopathy syndrome (PRES)/paraneoplastic encephalitis
- spinal cord compression

#### Acute ischemic stroke

AIS can occur in the setting of malignancy secondary to a hypercoagulable state. In neuro-oncology, however, vascular compression can occur due to mass effect from a large intracranial mass. Mass effect and shift of structures can occlude the anterior cerebral arteries with significant midline shift. Transtentorial herniation can

result in posterior cerebral artery occlusion. In the post-operative setting there can sometimes be transient ischemia in the surgical bed, which usually resolves. Diffusion-weighted imaging is a useful sequence to exclude acute ischemia<sup>[2,3]</sup>.

### **Intracranial hemorrhage: subarachnoid hemorrhage (SAH), subdural hemorrhage (SDH) or extradural hemorrhage (EDH)**

Some malignancies have a propensity to hemorrhage in the brain. Lesions that are very vascular, including brain metastases, in particular metastatic renal, thyroid, choriocarcinoma and melanoma, can hemorrhage. Vascular malformations, even though technically not tumors obviously can hemorrhage. In the post-operative setting blood products are often seen in the surgical cavity. Computed tomography (CT) imaging is an excellent modality for detecting acute blood products in the subarachnoid, subdural or extradural space. More recently, gradient echo imaging on MR and susceptibility weighted imaging (SWI), a high resolution gradient echo sequence, are even more sensitive in detecting subtle blood products in the brain<sup>[4,5]</sup>.

### **Increased intracranial pressure and mass effect**

Elevated intracranial pressure is a common complication and emergency in neuro-oncology. This is typically secondary to a combination of vasogenic edema and with primary gliomas, a degree of infiltrating edema as well. The increase in pressure and mass effect could result in acute ischemic stroke as described above. Besides surgical decompression, elevated intracranial pressure is most commonly treated with steroids, specifically dexamethasone, because it is the most lipid soluble of all the steroids. A commonly used regimen consists of an initial dose of 16–24 mg intravenously, followed by 4 mg every 6 h. Lower doses (4 mg/day) may be as effective as higher doses and associated with fewer adverse effects. Asymptomatic patients may not need corticosteroids. Seizures are treated with anticonvulsants<sup>[1]</sup>.

It is important to note that following whole brain radiation or some chemotherapeutic agents, edema can also result in increased intracranial pressure.

### **Hydrocephalus**

Hydrocephalus can be an obstructive non-communicating hydrocephalus, typically from obstruction at the foramen of Monroe (from a central neurocytoma or colloid cyst), at the aqueduct (from a tectal or brainstem lesion), at the fourth ventricle or its outlet foramen (from a cerebellar lesion). MR imaging is critical in this setting

to determine the cause of the obstruction. Surgical decompression by placement of a ventricular catheter is important in the emergent setting to avoid significant shift and mass effect. In the more semi-emergent setting, third ventriculostomies can be performed. With diffuse leptomeningeal metastases, the arachnoid granulation can also be obstructed. This will result in a communicating type hydrocephalus. This can be a difficult diagnosis to confirm without clear evidence of leptomeningeal enhancement or drop metastases in the spine. Typically up to 3 lumbar punctures are performed with cytology to make the diagnosis.

### **Infection**

Infection can occur in neuro-oncology either de novo or in combination with steroid and other immunosuppressive therapies. Patients on immunosuppression are prone to developing fungal and some viral infections. Again it is important to recognize these entities on imaging and make a diagnosis so that correct therapy can be instituted in a timely manner. Post-operative infection is uncommon as sterile surgical technique is closely adhered to. Again diffusion-weighted imaging (DWI) has proven to be a useful technique in detecting bacterial infections in the brain<sup>[6–8]</sup>.

### **Cystic mass: CSF breach and leaks/surgical devices/cavity**

Cystic masses in the brain can pose a challenge in neuro-oncology. Fortunately most cystic masses such as pilocytic astrocytomas and hemangioblastomas are more benign lesions. However, treating these lesions surgically can sometimes result in a breach in the CSF, communication with the ependymal surface of the ventricles and cerebrospinal fluid leaks. There are also some novel surgically implantable devices now for the delivery of local radiation and chemotherapeutic agents, which can also cause local complications and emergencies.

### **Local/general toxicity metabolic PRES/paraneoplastic encephalitis**

The paraneoplastic limbic encephalitis is an unusual and hard to diagnose entity, which can easily be misdiagnosed as a psychiatric disorder. Early diagnosis and treatment is very important to avoid non-reversible neuronal damage. Paraneoplastic encephalitis can occur in patients with brain tumors. Most of these syndromes are caused by substances secreted by the tumor, that mimic natural hormones, or interfere with plasma proteins. The incidence of paraneoplastic syndromes with neurological manifestations is less than 0.5/100,000 per year, and affects about 0.01% of cancer patients. The pathogenesis of neurological paraneoplastic syndromes is attributed to

humoral autoimmunity, due to antibodies causing various neurological findings. The absence of antibodies does not exclude a neurological paraneoplastic syndrome, just as antibodies may be found without a neurological paraneoplastic syndrome. The characteristic symptoms of paraneoplastic limbic encephalitis are confusion of acute onset, mood changes, hallucinations, loss of short-term memory, and seizures; these symptoms generally develop in days or weeks, but may present suddenly. MR imaging, CSF evaluation, and serologic tests are the most useful in diagnosing a neurological paraneoplastic syndrome. The treatment requires two different approaches. The first is the suppression of the immune response generated by neurological damage. The second is by removing the tumor as the source of the antigen. The latter is often the only effective treatment. The paraneoplastic limbic encephalitis is an unusual and hard to diagnose entity, which can easily be confused with psychiatric problems. An early diagnosis and treatment is very important to avoid non-reversible neuronal damage<sup>[9]</sup>.

### Spinal cord compression

Malignant spinal cord compression (MSCC) is a relatively common problem and a true oncologic emergency. At our institution it is the only indication for an emergent after hours magnetic resonance imaging (MRI) scan. Early diagnosis is extremely important to prevent further neurologic compromise and to maintain functional status and quality of life. Between 2.5% and 6% of patients with cancer have MSCC as a complication of their disease. All cancers can cause MSCC, but breast, lung, and prostate cancers account for almost two-thirds of all cases. Survival after the diagnosis of MSCC is poor, especially if paralysis is present or there is no clinical response to therapy. The neurologic status at diagnosis and the time to development of symptoms are important prognostic factors for outcome. Functional outcome is better if the development of symptoms is slow. Overall survival depends on the tumor type, and patients with hematologic malignancies have better survival than patients with solid tumors. Patients with lung cancer have an especially poor prognosis.

Most spinal cord compressions develop from tumors metastatic to the vertebral bodies that subsequently erode into and encroach on the spinal cord. The thoracic spine is the most common location for metastases that cause MSCC. Less commonly, tumors such as lymphomas, sarcomas, and lung cancers that occupy the paraspinal space may enter the spinal canal through the intervertebral foramen and cause cord compression.

The mechanism of injury to the spinal cord from an epidural tumor is due to direct compression of the neural elements interrupting axonal flow or a vascular mechanism. Venous plexus obstruction can cause marked cord edema, whereas tumor occlusion of the arterial blood supply to the spinal cord creates an acute infarction,

leading to abrupt and irreversible cord ischemia. Multiple inflammatory mediators and cytokines can increase the edema and the ischemia. The ischemia finally results in irreversible neuronal injury. Ninety percent of patients with MSCC have back pain. Eighty percent of all cases of MSCC occur in patients with a preceding diagnosis of malignancy. Back pain in a patient with known cancer should be considered secondary to MSCC until proved otherwise. Other symptoms include radicular pain, motor weakness, gait disturbance, and dysfunction of bladder and bowel function. Because neurologic deficits may not improve with treatment, it is imperative to not wait until neurologic dysfunction develops before considering the possibility of spinal cord compression. Multiple and synchronous spinal metastases are common, occurring in up to one-third of patients. MRI is the imaging study of choice in diagnosing MSCC. CT myelography can be used if MRI is contraindicated or not available. Plain radiographs of the spine and radionuclide bone scans have limited sensitivity and specificity and are therefore less useful than MRI or CT in suspected cases of cord compression. Plain radiographs are easy to obtain in most hospitals and emergency departments and may provide valuable information because abnormal findings have been reported in more than 80% of patients with symptomatic spinal metastases.

Therapy should be initiated as soon as possible but preferentially after the imaging studies have been obtained. Glucocorticoids should be given immediately if there is a delay in performing the imaging studies. Dexamethasone is the most commonly used corticosteroid and is typically given as an initial intravenous dose of 10–16 mg followed by 4 mg every 4 h. Higher doses of dexamethasone (up to 100 mg) may be associated with slightly better outcome but have a higher incidence of adverse effects. Patients without motor deficits or massive invasion of the spine on imaging studies may do well without corticosteroids. Radiation therapy has been the mainstay of the treatment, but recent studies have challenged that belief. Several radiation regimens are available, but there is no evidence that one is superior to the others. A recent study by Patchell *et al.*<sup>[10]</sup> showed that in patients who present with neurologic deficits, functional outcome, including the ability to ambulate and maintain continence, is better in patients who undergo radical tumor resection followed by radiation compared with patients who receive radiation therapy alone. Despite the findings of that study, the indications for surgical treatment continue to be debated and have to be carefully considered for each case. It seems reasonable to consider surgery in highly selected cases, especially in patients who maintain a good performance status, including the ability to withstand an extensive operation; when there is gross instability of the spine, rapidly progressive symptoms, or progressive symptoms during radiation therapy; or when tissue for diagnosis is needed.

A surgeon experienced in spinal surgery should be consulted if there is any doubt regarding the need for a surgical intervention. Surgery may become even more feasible with the advent of minimally invasive surgical techniques<sup>[1]</sup>.

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