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# Oncologic Emergencies and Urgencies

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Notes & Additional Readings

## Summary and Key Points

1. Cancer patients are at risk for oncologic and metabolic crises. These effects may be caused by the cancer, the treatment provided to cure or palliate the cancer, and/or other medical conditions. They may occur at initial presentation, as a first sign of disease or during the disease course.
2. Oncologists divide these crises into emergencies and urgencies, depending on the severity of the consequences of delay in treatment**.**
3. Table 1. Emergencies versus urgencies

| Emergencies | Urgencies |
|---|---|
| Spinal Cord Compression & Cauda Equina Syndrome | Superior Vena Cava Syndrome |
| Cardiac Tamponade | Respiratory Compromise |
| Uncal Herniation | Brain Metastases |
| Metabolic Emergencies | Carcinomatous Meningitis |
| Hypercalcemia | Deep Venous Thrombosis |
| Acute Tumor Lysis Syndrome | Pain |
| Hyponatremia | Tumor Bleeding |
| Febrile neutropenia | Pulmonary Embolism |
| Seizures | Anemia & dehydration |

4. Remember that any one of these conditions may be the first clinical evidence of an undiagnosed cancer.

## Introduction

The American Cancer Society estimates in 2014 more than 1.6 million Americans will be diagnosed with cancer and almost 600, 000 will die[1]. This excludes Americans with basal and squamous cell skin cancers. Almost 14 million people were alive after a diagnosis of cancer on January 1, 2012[1]. Therefore, every health care provider should be aware of the signs and symptoms of oncologic urgencies

and emergencies and initial management.

Any of these conditions can occur at any point in the course of illness. It is particularly important to remember that one of these conditions may be the first clinical evidence of an undiagnosed cancer.

## Oncologic Emergencies

### Spinal Cord Compression (SCC) and Cauda Equina Syndrome

Presentation

SCC typically is a syndrome with a long prodrome, which is back pain. If the symptom is not attended to, it will predictably progress to paralysis. The pain can be localized in the central back, or may radiate out laterally on one or both sides (unilaterally or bilaterally). A change in the nature or severity of pre-existing back pain in a patient known to have a malignancy should be considered a warning sign. Often, patients will report that they have had progressive pain over the preceding two weeks by the time they are paralyzed. However, patients with SCC may present with chronic back pain. Because back pain is such a common presenting complaint, it is appropriate to consider obtaining radiographic studies on patients with back pain accompanied by a neurologic deficit. When SCC is suspected, plain radiographs and bone scans are not definitive; the patient should go directly to spine MRI (Figure 1).

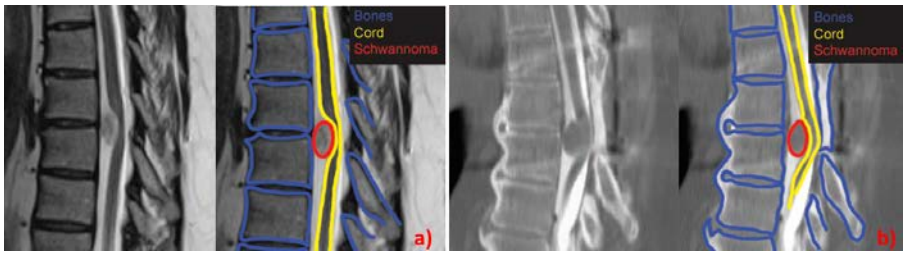


Figure 1a. A 56 yo female presents with progressive lower extremity weakness, numbness, and spasticity and worsening bowel and bladder function. MRI of the thoracic spine demonstrates a mass resulting in severe compression of the spinal cord. Figure 1b. Resection of this lesion yielded a schwannoma. Two years later, the patient presents with recurrent

symptoms. A CT myelogram was performed. Contrast injected into the thecal sac outlines a focal mass causing severe compression of the spinal cord, representing recurrence of the schwannoma at the same site. University of Massachusetts Medical School, Department of Radiology.

Patients may experience a Brown-Seguard like pattern of numbness. The pain may mimic the pain of shingles, as a single dermatome will often be affected. The pain level provides a clue to the vertebral level involved. It must be remembered that the nerve roots actually arise several levels superior to the egress foramen, so the anatomic level may be above the symptomatic dermatome. Spinal tenderness and up-going toes indicating upper motor neuron compression are useful additional clues to the presence of spinal metastasis with cord involvement.

If the condition is diagnosed and treated before paralysis sets in, patients may continue to walk. Once motor paralysis and particularly once autonomic dysfunction sets in, the process is almost always irreversible. Autonomic dysfunction initially causes constipation and urinary retention, but will progress to incontinence of urine and stool. This catastrophic outcome is a reason that spinal cord compression is considered a true medical emergency.

**Cauda Equina Syndrome**

Compression of the cauda equina, which is below L1 in most adults, causes identical signs and symptoms, has the same etiology and is managed identically to SCC. It is referred to as cauda equina syndrome.

Mechanism & Etiology

Etiology

Compression of the spinal cord or cauda occurs when:

- Tumor within a vertebra grows into the spinal canal or a pathologic fracture drives bone fragments into the cord.

- Paraspinal tumor grows through the vertebral openings into the epidural foramen.
- Metastatic tumor grows through the epidural space and impinges on the dura.

Tumors can cause spinal cord compression in several ways. The most common is a bony metastasis growing out of bone as soft tissue extension into the canal or pushing bone fragments into the neural structures (Figures 2 & 3.). While the neural foramen may be compressed similarly and may cause symptoms, this compression alone will cause pain, but not paralysis. A paravertebral mass may, however, grow through a foramen into the canal without involving the bone. Epidural or parenchymal metastases may cause compression. Pain from an epidural lesion is usually in a dermatome distribution.

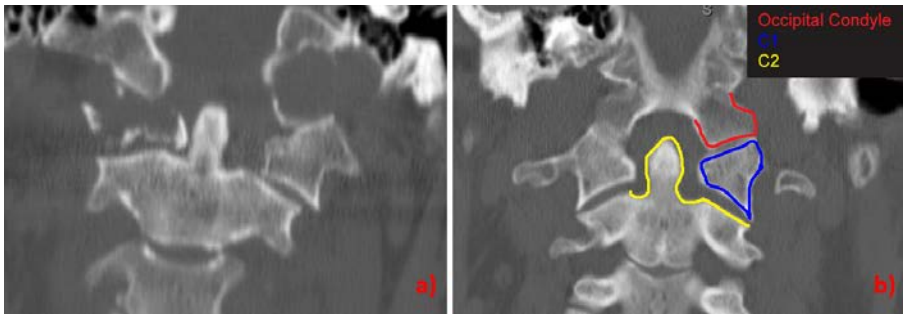


Figure 2a. A 64 yo male presents with severe acute onset neck pain with both upper and lower extremity weakness and numbness. Coronal CT reformat demonstrates lytic metastasis to the left occipial condyle and right lateral mass of C1. Weaking of the bone has resulted in a pathologic fracture of the right lateral mass of C1 with loss of vertebral height. On further workup, a lung mass was identified and biopsy returned non-small cell lung cancer. Figure 2b is provided as comparison of normal anatomy. University of Massachusetts Medical School, Department of Radiology.

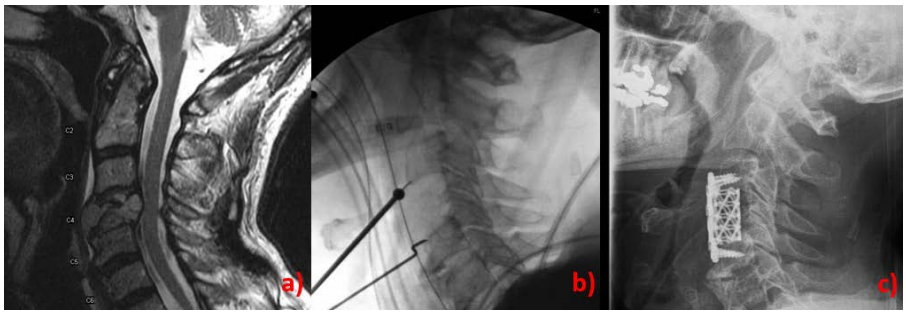


Figure 3a. A 54 yo female presents with progressively worsening neck pain over several weeks. Sagittal T2 weighted MRI sequence demonstrates an

unstable pathologic fracture of the C4 vertebral body. Figure 3b from an intraoperative radiograph shows that this lesion has essentially replaced the vertebral body. Figure 3c is a postoperative radiograph after placement of an interbody spacer in the cavity created by removing the tumor. An anterior plate with anterior fixation screws span C3-C5 stabilizes these levels. Tissue sampling of this lesion was consistent with renal cell carcinoma. University of Massachusetts Medical School, Department of Radiology.

Treatment

Management of spinal cord compression requires decreasing pressure on cord. The first step is dexamethasone to decrease swelling. The mainstay of treatment for spinal cord compression has been radiotherapy, with chemotherapy reserved for chemo-sensitive tumors, such as lymphomas. Surgery has traditionally been used when diagnosis is required, or symptoms progress during radiotherapy or after full dose radiation to the volume, or if bone fragments are seen to be involving cord. With recent improvements in surgical techniques, more patients are benefitting from early surgical decompression, usually followed by postoperative radiotherapy.

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**Neoplastic Cardiac Tamponade**

Suspect neoplastic cardiac tamponade in any oncology patient presenting with dyspnea and hypotension. This is not common, however, tamponade must be thought of emergently, so that lifesaving pericardiocentesis is not delayed. Neoplastic cardiac tamponade may result from post-radiation pericarditis (acute or up to a year after treatment), fibrosis, or pericardial metastases. It may also result from the physical encroachment of benign tumors on the heart and resultant fluid buildup. Clinical suspicion can be supported by ultrasound, chest x-ray showing the classic “water bottle” heart, EKG showing low voltage QRS complexes, and/or the finding of pulsus alternans.

Management

Consult cardiothoracic surgery if available, or general surgery. Treatment involves pericardiocentesis and may require creation of a pericardial window.

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### Uncal Herniation

The brain is confined in the rigid skull. As a result, additional tissue or swelling in the brain can increase intracranial pressure. Either primary brain cancers or metastases in the brain can cause brain tissue to press into the base of the skull and protrude through the foramen magnum. Temporal lobe pressure can transmit laterally and force the uncus, which contains the respiratory drive center, into the foramen magnum. The patient will have impaired brainstem function, rapid loss of consciousness and respiratory drive. Pressure on other areas of the brain can present with a myriad of other symptoms such as headache, vomiting, hiccups, and mental status changes.

Management

Immediate treatment is directed at airway protection for ventilatory support, and mannitol, up to 1g/kg IV, to reduce intracranial pressure

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## Metabolic Emergencies

### Hypercalcemia (>14 mg/dl)

Etiology

- Direct Tumor Destruction of Bones
- Parathyroid Hormone-Related Protein
- Increased Vitamin D synthesis in some tumors, especially Hodgkin's lymphoma

Presentation

Table 2 lists the malignant diagnoses that can result in hypercalcemia. It is important to appreciate, that most non-malignant

causes of hypercalcemia produce a relatively slow rise in plasma calcium levels compared to hypercalcemia of malignancy. Signs and symptoms of hypercalcemia present much more acutely in the setting of cancer. These clinical findings include delirium, stupor, coma, muscle weakness, anorexia, constipation, cardiac arrhythmias, and renal failure.

Table 2. Malignant Conditions That May Result in Hypercalcemia

| |
|---|
| Renal Cell Carcinoma |
| Lymphoma |
| Breast Cancer |
| Myeloma |
| Non-small Lung Cell Carcinoma |

Prostate cancer, despite its propensity to metastasize to the bones, is rarely associated with hypercalcemia because bone metastases from prostate cancer are usually blastic, not lytic.

Mechanism

Two general mechanisms have been identified by which cancers can cause hypercalcemia. A number of solid tumors (e.g., non-small cell lung cancer, renal cell carcinoma) can secrete hormones that increase bone resorption in the absence of overt bone metastases. These hormones include parathyroid-related peptide. This is a para-neoplastic phenomenon. In addition to using humoral factors, some cancers (e.g., myeloma, breast cancer) can also directly invade bone and cause osteolysis.

Ninety-nine percent of total body calcium is stored in bones, which are constantly being remodeled. Osteoclasts resorb established bone and osteoblasts lay down new bone. Hypercalcemia of malignancy is due to an imbalance in the remodeling process. There is almost always an increase in bone resorption resulting in release of calcium from bone into extracellular fluids. Osteoblasts may also

be inhibited from utilizing calcium to mineralize bone. Although the kidneys are usually able to respond to elevations in plasma calcium, they are overwhelmed in the setting of massive calcium mobilization. Hypercalcemia itself can impair renal function by causing nephrocalcinosis or volume depletion.

Calcium homeostasis is maintained by intricate hormonal regulation involving calcitonin, parathyroid hormone, and vitamin D (1,25-dihydroxyvitamin $D_3$). A normal level of ionized calcium in extracellular fluids is critical for proper nerve and muscle function. Hypercalcemia due to malignancy can result in very high plasma levels of calcium and can be life-threatening.

Management

Treatment of hypercalcemia of malignancy is directed at prompt reduction of calcium levels. This is particularly important for patients who are symptomatic or who have calcium levels above 13.5 mg/dl. Elimination of factors that can contribute to hypercalcemia (thiazide diuretics, calcium and vitamin D supplements) is important. Most patients will be severely volume depleted and aggressive hydration with normal saline is a cornerstone of treatment.

Bisphosphonates have now become the pharmacologic agents of choice in the treatment of hypercalcemia of malignancy. Pamidronate and zoledronic acid are both given intravenously and will result in normocalcemia in up to 90% of patients. Zoledronic acid does appear to be slightly superior to pamidronate. Other drugs that may be used in patients who do not respond to bisphosphonates include gallium nitrate, calcitonin, and glucocorticoids. Recently the anti-RANK ligand antibody denosumab has been reported to correct hypercalcemia of malignancy in patients previously treated with bisphosphonates. However, the use of denosumab in this setting

remains experimental.

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## Tumor Lysis Syndrome (TLS)

Etiology

TLS is caused by the rapid breakdown of tumor with:

- Increased K+ and PO4 into circulation
- Increased Urate from DNA breakdown
- Urate and CaPO4 precipitation in renal tubules

Presentation

Cell death results in the loss of cell membrane integrity and the release of intracellular contents into the extracellular space. These contents undergo metabolism and eventual excretion primarily via the kidneys. If a large number of cells suddenly die, the ability of the kidneys to clear the products of cell necrosis may be compromised. TLS refers to the host of metabolic abnormalities that can result from cell death. Though it can be observed in patients with rapidly growing tumors, TLS is most commonly seen after chemotherapy treatment of bulky drug-sensitive tumors.

It can also be seen after initiation of radiotherapy for bulky, radiosensitive tumors. The malignancies with the highest risk of TLS after treatment include the acute leukemias and high-grade non-Hodgkin lymphomas.

Patients at highest risk of TLS are those within the first five days of the start of chemotherapy or radiotherapy for rapidly growing tumors. Risk increases with volume of tumor and with the presence of hyperurecemia or preexisting renal insufficiency. There is a correlation between elevated lactate dehydrogenase (LDH) and development of TLS.

Mechanism

Potassium, phosphate, and purines are all released by cells after death. Purines are metabolized to uric acid, which is poorly soluble in acidic urine and so can precipitate in urine and cause an obstructive uropathy. The subsequent renal damage can make the hyperkalemia and hyperphosphatemia resulting from cell lysis worse by impairing the ability of the kidney to clear these substances. Hyperkalemia can cause cardiac arrhythmias and conduction disturbances. Muscle weakness, cramping and paresthesia can also arise from hyperkalemia. Hyperphosphatemia causes a secondary hypocalcemia as a result of precipitation of calcium phosphate. Hypocalcemia can cause muscle spasms, mental status changes, hypotension, and may worsen the cardiac conduction abnormalities caused by hyperkalemia. Cardiac arrhythmias and renal failure could be fatal.

Management

TLS is best prevented rather than treated. Patients at risk should receive aggressive intravenous hydration prior to starting anti-cancer therapy. They should also receive allopurinol, an inhibitor of xanthine oxidase, to block the conversion of xanthine and hypoxanthine to uric acid. Fluids used for hydration could contain sodium bicarbonate in order to alkalinize the urine to increase the solubility of uric acid, though alkaline urine may increase the risk of precipitation of calcium-phosphate salts. Oral phosphate binders can be given to lower the risk of hyperphosphatemia.

If TLS does occur, aggressive hydration should be continued to maintain good urinary output. Allopurinol should also be continued and recombinant urate oxidase (rasburicase) can be given to patients with hyperuricemia. A single dose of rasburicase is generally sufficient. Hyperkalemia should be treated with oral cation exchange

resins, loop diuretics, and sodium bicarbonate. Patients who develop acute renal failure should receive hemodialysis.

It is important to appreciate that the cancers most likely to develop TLS are potentially curable, so aggressive supportive care in the acute treatment setting can prove to be life-saving.

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## Hyponatremia

### Etiology

Table 3. Conditions that May Cause Hyponatremia

| |
|---|
| (SIADH) Syndrome of inappropriate antidiuretic hormone secretion: Common Malignancies: Small cell lung cancer |
| CNS tumors: Glioblastoma, Metastatic Disease |
| Chemotherapy drugs: Cyclophosphamide, Vinca Alkaloids |
| Adrenal gland insufficiency: Addison's disease |
| Underactive thyroid: Hypothyroidism |
| Dehydration |
| Kidney problems |

### Presentation

Sodium is the principle cation in extracellular fluid. The concentration of sodium will affect nerve conduction and muscle function. As serum sodium levels fall below 125 mEq/L, patients can develop generalized weakness, anorexia, altered mental status, seizures, and coma. Hyponatremia can occur for a variety of reasons in patients with cancer. Table 3 lists some of the causes of hyponatremia. In patients with cancer, SIADH should be considered.

### Mechanism

Antidiuretic hormone (ADH, arginine vasopressin, AVP) is synthesized in neurons in the hypothalamus and migrates down the axons of those neurons to be released into the bloodstream in the posterior pituitary. ADH binds to renal collecting duct cells and

makes the kidney permeable to water. SIADH can occur when there is ectopic production of ADH or when there is dysregulation of production of ADH from the hypothalamus. In cancer patients, SIADH can be a paraneoplastic syndrome resulting from the ectopic production of ADH by tumor cells. This occurs most commonly in patients with lung cancer, especially small cell lung cancer. SIADH can also be a complication of treatment. A number of chemotherapy drugs, including cyclophosphamide, vinca alkaloids, and some drugs used for supportive care, such as opiates and phenothiazines, can cause SIADH.

Management

Patients with severe hyponatremia (serum sodium less than 115 mEq/L) should be treated with normal or hypertonic saline hydration. Care should be taken not to correct the hyponatremia too rapidly– there is an increased risk of long-term neurologic damage from central pontine myelinolysis with overly aggressive correction of hyponatremia. Patients with less severe hyponatremia can frequently control their sodium levels with moderate restriction of water intake. The oral antibiotic demeclocycline, which blocks the effect of ADH on the renal tubule, can also be used to control sodium levels in patients with SIADH. Recently, two ADH receptor antagonists, conivaptan and tolvaptan, have also been approved for the treatment of SIADH.

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**Febrile Neutropenia**

Infection is a leading proximal cause of cancer deaths. Neutropenia is a common side effect of chemotherapy, Remember that most fevers have an infectious etiology, but tumor necrosis, homeostatic imbalance from CNS dysfunction, and various medical interventions may also result in elevated temperature.

Management

Evaluate the patient carefully for a source of infection, especially all lines and ports, then obtain blood cultures, and immediately start broad-spectrum antibiotics.

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## Oncologic Urgencies

### Pain

Presentation

Pain from cancer tends to have a typical presentation despite variation in the pathophysiology due to different etiologies. Although there are exceptions, the pain tends to present gradually. Cancer pain is usually continuous, progressively more severe, and unlike any previous pain the patient has experienced. Pain from increased intracranial pressure is an exception, as it tends to be worse in the morning. Pain is subjective and severity must be patient reported.

Mechanism

It is important to realize that, although the public perception of cancer is that it is always very painful, only about 50% of cancer patients will experience physical pain during the course of their illness. In addition, even for patients who do experience pain, most of the course of their illness will be pain free. Essentially all cancer patients experience psychological or emotional pain, and many experience physical or emotional pain from treatment side effects. Psychic and spiritual pain often exacerbates physical pain.

Management

Treatment of the underlying malignant cause may relieve the pain. For a responsive tumor, chemotherapy may cause enough response to palliate pain in certain circumstances. Surgery may be required to palliate pain in situations where the pain is due to an impending or

actual fracture, or to place a stent to relieve obstruction. Most frequently, however, radiation therapy is the treatment with the greatest likelihood of relieving pain, especially bone pain and from Glisson's capsule distention around an enlarged liver. While the response rates for palliation by radiotherapy vary a bit by tumor histology, roughly 2/3-3/4 of patients will have significant relief. In at least 50% of responders, the relief will be durable. Injections, nerve blocks, and neuraxial infusions may be useful in selected cases.

For most patients and for the interval until the above treatments can become effective, the cornerstone of medical pain management is pharmacological, utilizing the WHO pain pyramid.

It is well documented that pain management is inadequate far too often, even among patients who are actively undergoing treatment on a regular basis. This may be due to inadequate pain assessment, failure to prescribe analgesic, or patient or provider fear of addiction or legal problems.3 However, pain is considered the fifth vital sign, to be assessed and managed at every visit.

On occasion, pain becomes so severe that it is referred to as a pain crisis; this is a true medical emergency, and should lead to a palliative medicine consult, if available, and continuous physician supervision of medical pain intervention until relief is achieved.

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**Tumor Bleeding**

Presentation

Tumor bleeding can present dramatically as massive hemoptysis, vaginal, rectal or urinary bleeding or it can be quite subtle, presenting as unexplained anemia. Anemia that arises gradually as the result of a tumor that is slowly oozing blood will frequently be due to iron deficiency as the result of chronic loss of iron. In this case, red cells

will typically be microcytic. Unexplained microcytic anemia due to iron deficiency should be considered a gastrointestinal malignancy until proven otherwise.

Occasionally tumors within the central nervous system may bleed into themselves, presenting as a cerebrovascular accident.

Mechanism

The most common physiology is bleeding from friable, abnormal tumor vasculature. But on rare occasions, a tumor may invade through a blood vessel wall. If the affected vessel is a major artery, the bleeding may be massive and rapidly fatal. On the other hand, if the affected vessel is a minor vein, the bleeding may look just like bleeding from abnormal tumor vessels.

Treatment

The treatment of tumor bleeding depends on the location of the tumor and the anatomy of the normal structures surrounding it. Volume replacement support and consideration of transfusion is the first step. It may be possible for an interventional radiologist to block the feeding vessels, provided that would not damage vital surrounding tissue. Similarly surgical ligation of these feeding vessels would stop the bleeding. If it is possible to resect the tumor, that would be the most rapid intervention. For chemo-sensitive tumors, chemotherapy may work.

Most commonly radiation therapy is used. For brain lesions, it is usually the only option. For tumors elsewhere in the body, it is usually the most cost effective and least invasive treatment available. With conventional fractionation bleeding usually takes about two weeks to stop (and it almost always does stop). However, a single large radiotherapy dose will usually work much more rapidly. Unfortunately such a large fraction may make it difficult to deliver

definitive radiotherapy to a tumor, so it is rarely done in the United States, as most American radiation oncologists are accustomed to conventional fractionation. British and Canadian physicians are more likely to use large fraction sizes in this situation.

While exsanguination can be a terminal event, if a patient is minimally symptomatic and a blood bank is available, tumor bleeding usually is treated routinely rather than emergently.

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## Pulmonary Embolism

### Etiology

Pulmonary embolism occurs when a blood clot in a large vein, usually in the lower legs or pelvis, breaks free and moves through the right heart into the pulmonary arteries. Cancer patients are at particular risk of developing thromboses. (See Paraneoplastic Syndromes chapter). Though not actually described by the eminent German pathologist Rudolf Virchow, conditions now known as Virchow's Triad increase the risk of developing a clot. These are damage to blood vessel walls, stasis of venous blood flow, and hypercoagulability of blood. Cancers can lead to all three of these situations. Tumors can damage vessel walls. Cancer patients, especially late in the course of the disease, like long distance airline passengers, are relatively immobile, with extended periods sitting or lying in bed, which can lead to venous stasis. And some malignancies, for uncertain reasons, can cause hypercoagulability and migratory thrombophlebitis.

### Presentation

Patients with pulmonary embolism can present with the abrupt onset of shortness of breath or chest pain These symptoms can be severe. Large pulmonary emboli which obstruct a large fraction of the cardiac

output from the right side of the heart and cause hypotension and even sudden death. Most symptomatic pulmonary emboli arise from veins in the pelvis or thighs. Complaints of pain, swelling, redness, or warmth along a lower extremity should raise the possibility of a venous thrombus in the affected limb.

Diagnosis

If there is concern that a patient may have a deep vein thrombosis in the pelvis or a lower extremity, Doppler ultrasound (Figure 4.) to assess flow in the large veins of the extremity and pelvis should be performed. Patients with severe chest pain and shortness of breath could be evaluated with a CT of the chest with IV contrast on a pulmonary embolism protocol (Figure 5).

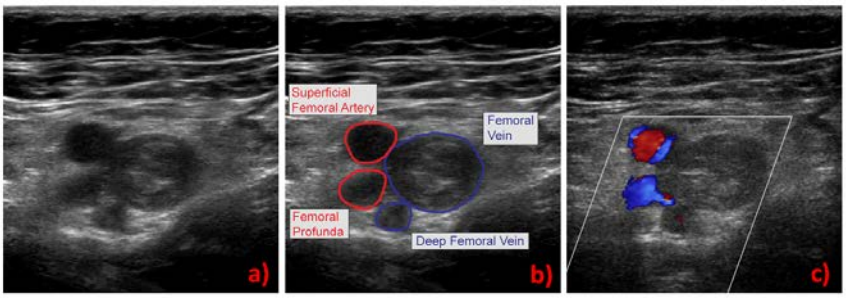


Figure 4. Ultrasound of the right lower extremity was obtained due to asymmetric leg swelling. Figures 6a and 6b demonstrate abnormal heterogeneously increased echogenicity in the femoral vein and deep femoral vein when compared with the adjacent arteries. Figure 6c a color Doppler, shows vascular flow in the arterial system (mixture of red and blue colors) and no flow in the venous system. This is deep venous thrombosis. University of Massachusetts Medical School, Department of Radiology.

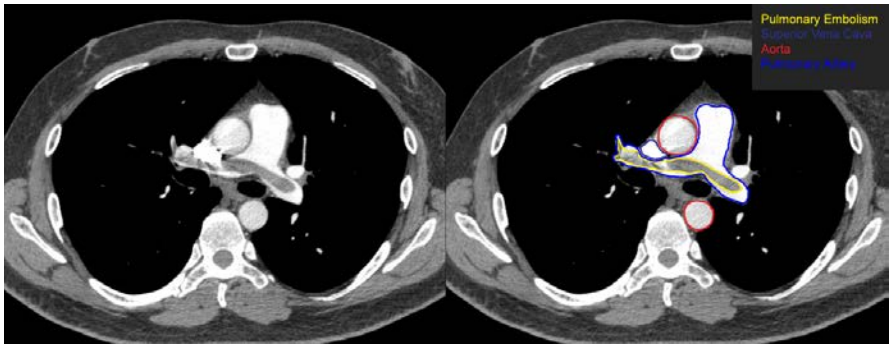


Figure 5. A 45 yo male with a known history of renal cell carcinoma

presents with acutely worsening shortness of breath. CT angiography was performed and a large pulmonary embolus was found. The unique location of the pulmonary embolus draped across the bifurcation of the main pulmonary artery is known as a saddle embolus. University of Massachusetts Medical School, Department of Radiology.

Management

The foundation of management of pulmonary embolism or deep vein thrombosis is anticoagulation. Patients with active malignancies may benefit from long-term anticoagulation, as their risk of recurrent clot is very high if anticoagulation is stopped.

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## Respiratory Compromise

Etiology

Malignancy can cause respiratory distress through three primary mechanisms (Table 4). While most of the time, respiratory compromise is a medical emergency, for oncologists, after initial stabilization, it is only urgent. The reason for this statement is that, if the patient is in severe distress, intubation and ventilation is required. Once that is accomplished and the airway is secure, there is time for whatever treatment required to be delivered. On the other hand, if this cannot be accomplished or is ineffective, the patient is usually beyond help. One exception would be an exquisitely sensitive tumor, which will respond rapidly to radiotherapy or chemotherapy. A second exception would be a situation where bronchoscopic suction or a laser resection will relieve the obstruction.

Table 4. Etiologic Mechanisms of Malignant Respiratory Distress

| Primary Mechanism | Airway Obstruction | Damage to Lung Parenchyma | Lung Collapse |
|---|---|---|---|
| | Mucous plug | Direct tumor destruction | Pleural effusion |
| | Intrinsic tumor | Post-obstructive pneumonia | Pneumothorax |
| | Extrinsic compression | Pulmonary embolism (Figure 5) | |

Airways may be blocked in three ways. The most common cause of blockage is a mucous plug, which can be mechanically dislodged. Most lung cancer patients have some form of chronic obstructive pulmonary disease, which places them at increased risk of mucous plugs. Tumor within the trachea or main stem airways causes intrinsic compression. Tumor outside can collapse the airways causing extrinsic compression.

Any of these pathophysiologies can trigger post-obstructive pneumonia. Bacteria, which normally are swept out by the cilia of the normal lung epithelium, become trapped behind the obstruction, and infect the parenchyma of the lung distal to the obstruction. Tumor growth can also destroy enough lung tissue to push already compromised lung function over the edge. Lung collapse due to reactive or malignant pleural effusion or pneumothorax can push even healthy lungs into dysfunction.

Presentation

The patients tend to present tripoding and sitting bolt upright, with a history of sleeping in a chair for a few days. They are laboring to breathe with severe dyspnea at rest. If the tumor is in the upper airway, the presentation may be dominated by stridor. Once intubated, or once they have undergone tracheotomy, they re-oxygenate rapidly, unless the blockage is distal to the tip of the endotracheal tube.

Management

If the problem is caused by a mucous plug, then suction may relieve the symptoms. If the issue is intrinsic compression, and the bronchoscope can be passed through the stenosis, laser may be used to unblock the tube, and/or perhaps a stent may be placed. But then the tumor must be treated, or it will often rapidly re-grow and re-

obstruct. Extrinsic compression may, in unusual circumstances, be amenable to a stent. Usually the symptom will only respond to a treatment which actually shrinks the tumor, either chemotherapy or more usually, radiotherapy. Intrinsic obstruction may be amenable to endoluminal brachytherapy; but the dose from this procedure will not reach out to effectively treat a tumor causing extrinsic compression.

Patients with stridor and upper airway blockage can be readily treated by tracheotomy, and any physician may find it necessary to perform this lifesaving procedure.(Figure 6). If the tumor compressing the trachea is in the low anterior neck, for example anaplastic cancer of the thyroid, attempting tracheotomy is extremely dangerous. Cutting through the tumor can cause significant bleeding, and may then allow the tumor to grow down into the trachea. In this circumstance, even biopsy may be dangerous, and tracheotomy should not be attempted.

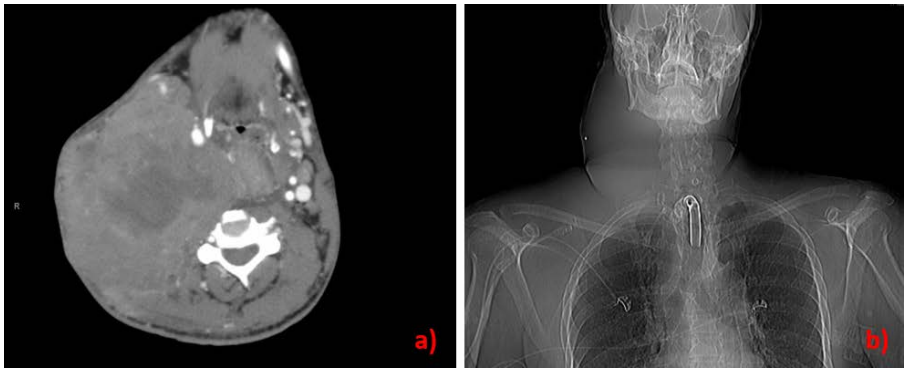


Figure 6. A 39 yo male with a rapidly enlarging mass in the right neck over a one month period presents with severe shortness of breath. Figure 5a is from a CT of the neck at presentation showing a large mass in the right neck with marked encroachment on the upper airway. This patient required an urgent tracheostomy as shown on Figure 6b. University of Massachusetts Medical School, Department of Radiology.

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## Superior Vena Cava Syndrome (SVC)

Etiology

Tumor growing in the thoracic inlet, can compress the lymphatic channels and great veins returning blood to the superior vena cava from the upper extremities and the head. As the flow slows, a clot may develop and extend down into the SVC (Figure 7a & b). The arteries are under sufficient pressure that they are rarely compressed, so fluid builds up in one or both arms and head. At this point, jugular venous distension develops, even when the patient is sitting perfectly upright, and the face and/or arm(s) swell (Figure 7c& d). Subsequently, intracranial pressure may increase; patients then complain of headache, and the ocular discs may bulge. As the condition tends to be sub-acute the small veins (collaterals) on the chest wall will dilate, to allow blood to return to the heart. The most dangerous acute complication is that the trachea, which has a membranous wall posteriorly, behind the partial cartilaginous rings, may become compressed, causing respiratory distress. If the airway does not become compromised, the condition tends to resolve over a period of several weeks as the vessels recannulate.

Presentation

SVC syndrome is most easily recognized when the patient presents with significant swelling of the arms, neck and head and with jugular venous distension even when the patient is straight upright. The initial symptoms may be as subtle as a swollen finger with difficulty removing a ring. The swelling may progress to a single extremity and then to the head. There is often a palpable mass in the supraclavicular fossa, sometimes in the anterior neck. As symptoms progress, signs of increased intracranial pressure may appear (See Increased Intracranial Pressure section of this chapter). Ultimately, a late sign is dilation of the subcutaneous veins on the chest. However, the most ominous symptom is respiratory distress from tracheal

compression. This is a late sign as well, but often occurs before the veins dilate (See Respiratory Compromise section in this chapter).

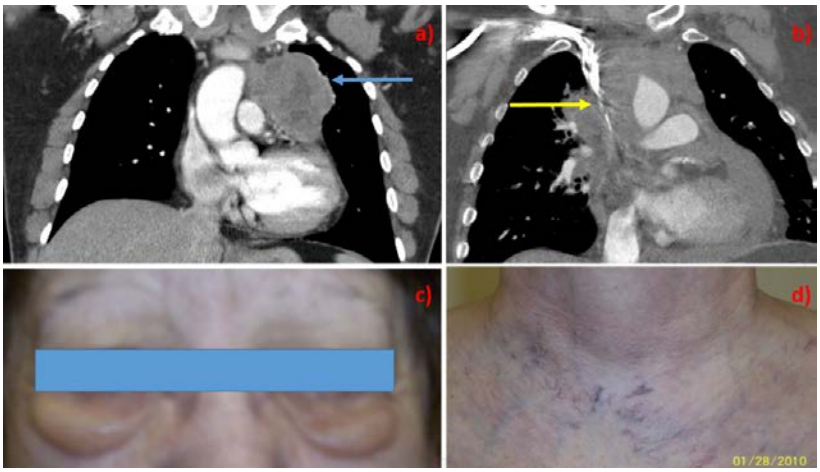


Figure 7. This is a 73 yo male complaining of headaches and dyspnea. Figure 7a demonstrates a left mediastinal mass. This mass infiltrates most of the upper mediastinum, surrounding and compressing the superior vena cava indicated by the yellow arrow on Figure 7b. Venous congestion results in facial edema as in Figure 7c, with edema of the lower eyelids. Figure 7d. Demonstrates venous distention in the neck and petechia from superficial capillary hemorrhages. University of Massachusetts Medical School, Department of Radiology

Treatment

In many instances, superior vena cava compression may be the first manifestation of a malignancy. It is imperative that a pathologic diagnosis of an underlying cancer be obtained before starting treatment. If the mediastinal mass is the only site of tumor, then that should be biopsied. In the past, there was concern that elevated venous pressure from the mass would increase the risks associated with biopsies. Reviews of mediastinal mass biopsies in patients with superior vena cava syndrome have not shown an increased risk of complications compared with similar biopsies done in patients without the syndrome.

Once a diagnosis is made, treatment should be directed at the underlying cancer. If the tumor is an untreated lymphoma or leukemia, chemotherapy has an excellent chance of providing

prompt tumor shrinkage. If the tumor is a solid malignancy (lung, breast, etc.), initial treatment should include radiation therapy.

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**Brain Metastases**

Seizure & status epilepticus: The most likely cause of seizure in a cancer patient is brain metastasis. The first step in management is to stop the seizure. Further evaluation should include a scan of the brain as well as appropriate studies to be sure that metabolic derangements are not contributing to the seizure. Anti-seizure medication should be continued to prevent further seizures.

Brain metastases are a relatively frequent complication of cancer; the annual incidence is almost 200,000 cases in the United States. About half of these cases arise from lung cancer; breast cancer is the next most common site of origin and melanoma is the third common malignancy. There is a concept called the fertile field; metastases from certain cancers tend to spread to particular organs, and the brain is particularly affected by metastases from lung, breast and melanoma. Any cancer can give rise to brain metastases and today, as patients are living longer with cancer, more patients are presenting with brain lesions from previously unusual primary sites.

Once brain metastases are discovered, life expectancy is typically measured in months, and uncontrolled lesions can cause rapid neurologic deterioration. After treatment, patients whose extra-cranial disease is controlled will do better than those whose disease is not, and good performance status patients will live longer than poor performance status patients.

Presentation

Patients with brain metastases tend to present with symptoms of increased intracranial pressure, (headache, nausea and possibly vomiting), mental status changes, focal motor weakness, visual field cuts, papilledema, symptoms of a cerebral vascular accident or seizure. While the initial workup in an emergency room almost always includes a CT scan (Figure 8), an MRI of the brain with gadolinium (Figure 9.) provides far more information as to the extent of disease. Definitive treatment decisions virtually require that an

MRI be obtained, so if an MRI is equally available and time permits, the CT may be omitted.

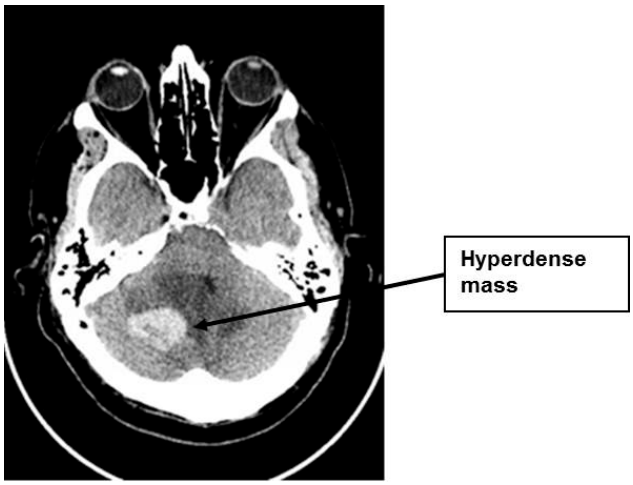


Figure 8. CT of the brain from a 63 year old man who presented with intractable nausea and vomiting demonstrates a hyperdense mass in the right cerebellum. Differential diagnoses include hematoma, hemorrhagic infarct, or neoplasm. University of Massachusetts Medical School, Department of Radiology

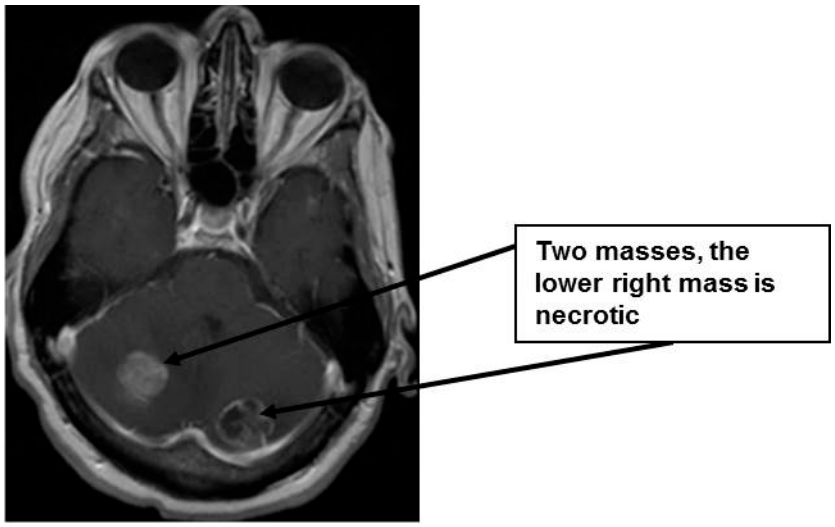


Figure 9. MRI of same patient as Figure 8 shows that there are actually two lesions in the cerebellum favoring the diagnosis of metastasis. This prompted a search for the primary site. The patient was found to have a colonic mass from adenocarcinoma. University of Massachusetts Medical School, Department of Radiology

Management

Initial management of brain metastasis is dexamethasone. This steroid decreases the peri-tumoral edema, thereby decreasing the intracranial pressure and mass effect. The patient's neurologic status will often improve rapidly after the initial administration of dexamethasone. Sometimes mannitol may be required to further decrease the intracranial pressure (ICP).

Patients who have presented with a seizure require effective anticonvulsant therapy. In the past, such therapy was initiated prophylactically to prevent seizures. This practice has been discouraged recently in patients who do not present with seizures. Randomized trials of prophylactic anticonvulsants in patients with brain metastases showed no reduction in the risk of developing seizures. Hence, prophylactic anticonvulsants provide no benefit and merely expose patients needlessly to side effects of the drugs. Nonetheless patients with brain metastases are at risk of sudden neurologic deterioration due to CVA, nausea or seizure. It is important that all such patients are instructed to stop driving, at least until their neurologic situation is clear and stable.

In patients for whom brain metastases are the presenting sign of malignancy, a search for a primary cancer is in order. This should not delay the start of treatment to the brain. If there is no preexisting diagnosis of malignancy, a biopsy is performed. Occasionally evidence of increased intracranial pressure or adverse medical condition may preclude this.

Today, management of brain metastases is a multi-disciplinary effort. Traditionally, surgery was restricted to biopsy of previously undiagnosed cancers presenting with brain metastases or sometimes proving metastatic status if the brain lesion is the first

known metastasis. Sometimes this biopsy would take the form of a resection of the lesion. However, the mainstay of treatment was palliative whole brain radiotherapy. The traditional palliative dose of radiation is radiobiologically insufficient to control bulk tumor deposits long term; it was adequate only because of the patient's short life expectancy.

For limited numbers of metastases (usually four or less), metastectomy or radiosurgery offers a chance of long-term control of the individual lesions. Which of these treatments is more effective has not yet been demonstrated. The role of post-operative or post radiosurgery whole brain radiotherapy is not yet clear. It does not extend survival, but does decrease the incidence of further brain metastases, and this appears to enhance quality of life, although it has also been demonstrated to impact memory. Whole brain radiation may be used prior to radiosurgery in selected patients.

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**Carcinomatous Meningitis**

Carcinomatous or lymphomatous meningitis is an unfortunate complication of malignancy. Seen most often in patients with breast cancer, lung cancer, acute leukemia, or non-Hodgkin, as well as certain pediatric tumors, any cancer diagnosis can give rise to this condition. It arises from cancer cells that have spread into the cerebrospinal fluid (CSF) and establish tumors on the meninges. This can occur anywhere in the central nervous system, from the outpouchings around the cranial nerves to the bottom of the cauda equina.

Presentation

Sometimes, it is an incidental finding on MRI of brain or spine, either at initial staging workup or while working up the symptoms described

above for brain metastases because the symptoms of nausea and headache can be identical. The classic sign that should make a physician consider the diagnosis is isolated or multiple cranial nerve deficits, especially those, which arise in patterns that cannot be explained, based on a single bony metastasis in the base of the skull. This is referred to as a non-anatomic pattern. Back pain or dermatome pain or numbness (Brown-Seguard Syndrome) may be symptoms of malignant meningitis. If untreated, patients may experience progressive loss of function in additional cranial nerves and these losses may be irreversible. Physical examination of the cranial nerves, which can be done very rapidly, is an important part of the examination of cancer patients.

Management

Initial management involves steroid therapy as for brain metastases. The patient must be assessed for increased intracranial pressure, as a lumbar puncture (spinal tap) to obtain cells to confirm diagnosis and injection of intrathecal chemotherapy is the next step. Radiotherapy to the whole brain, the base of the skull and the posterior half of the orbits, to encompass the entire outpouchings of the meninges around the cranial nerves is used to treat the cranial component of carcinomatous meningitis, since intrathecal chemotherapy is unlikely to effectively reach the outpouchings of the meninges around the cranial nerves . When intrathecal chemotherapy is utilized, it can be injected through a lumbar puncture. However, often an Ommaya reservoir is placed under the scalp, with a catheter extending into the lateral ventricle to deliver the therapy less traumatically and more effectively.

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## Conclusion

Every clinician must understand oncologic emergencies and

urgencies, because early diagnosis, appropriate treatment and consultation are critically important to preservation of function, quality of life and sometimes even preservation of life. Heightened suspicion for these conditions is required for any patient with even a remote history of malignant diagnosis. And any of these oncologic emergencies or urgencies can arise in patients with no prior history of malignancy as the first sign of cancer.

**Thought Questions**

1. A 27 year old woman comes to the emergency room extremely short of breath. A chest CT shows a large thoracic mass with compression of the trachea. A physician asks a radiation oncologist to radiate the mass.

   A. Why is this probably not the best thing to do at this point? Expert Answer

   B. What should be done before starting any tumor directed treatment? Expert Answer

2. A 67 year old woman is brought to the emergency room by her family because she has become increasingly lethargic. Initial labs in the ER show a calcium level of 16.3 mg/dl (normal 8.5-10.5).

   A. What information from a history and physical exam would be helpful at this point? Expert Answer

   B. What other laboratory information is needed? Expert Answer

   C. What therapy should be started immediately? Expert Answer

3. A 48 year old man comes to his doctor complaining of severe mid thoracic back pain. On exam he is hyperreflexive at his knees and ankles and has trouble supporting his weight. He had a melanoma removed from his arm four years ago.

   While waiting for a MRI of his spine, what treatment could you start?

Expert Answer

   B. How would your approach differ if he had a history of intravenous drug abuse and now was febrile?

Expert Answer

4. A 65 yo man presents with asymmetric sensorineural hearing loss and worsening facial droop on the right. Axial MRI images through the internal auditory canals (IACs) demonstrates a lesion in the right internal auditory canal.

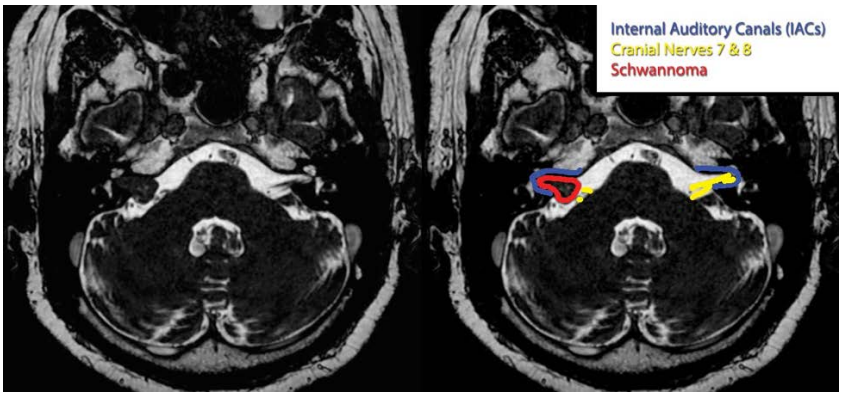


Figure 10. Axial FIESTA MRI sequence. University of Massachusetts Medical School, Department of Radiology.

Notice that the normal left side is filled with CSF which on this sequence is bright. Which cranial nerves run through the IACs?

Can this explain the cause of the symptoms?

Expert Answer

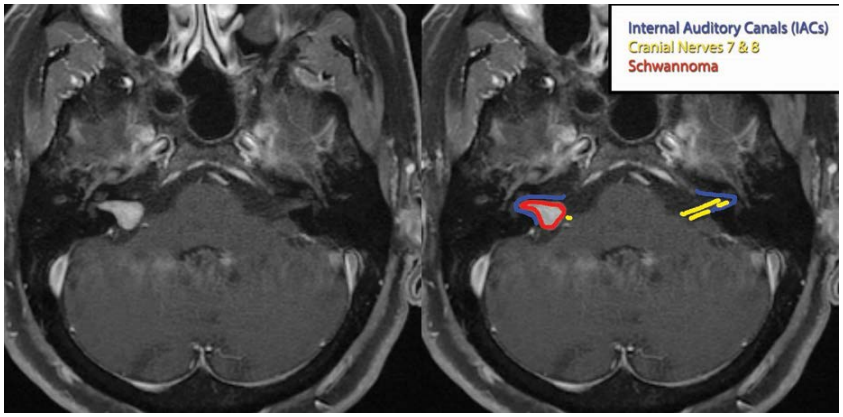


Figure 11. Axial T1 fat saturated MRI sequence post contrast. University of Massachusetts Medical School, Department of Radiology.

After administration of contrast, the lesion demonstrates homogeneous enhancement. This is most consistent with a vestibular schwannoma.

**Glossary**

Glisson's capsule- The fibrous covering of the liver

Radiosensitive– Tumors which shrink rapidly with radiation treatment

Paraneoplastic- Signs or symptoms related to a cancer but not due to a direct anatomic effect of cancer cells or tumors

Performance status– A measure of how functional a patient is at a point in time. Good performance status patients are active and can care for themselves; poor performance status patients may spend

most of their days in bed and require considerable support in activities of daily living.

RANK- RANK is the receptor for RANK-Ligand (RANKL) and helps regulate osteoclast differentiation and activation. It is associated with bone remodeling and repair, among many other functions.

Tripoding- Patient seated forward, hands on knees, chin extended, struggling to breathe.

**Reference**

1. American Cancer Society. Cancer Facts & Figures 2014. http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2014/. Atlanta: American Cancer Society; 2014.
2. Pieters RS, Niemierko A, Fullerton BC, Munzenrider JE. Cauda equina tolerance to high-dose fractionated irradiation. *Int J Radiat Oncol Biol Phys*. 2006; 64(1):251-7.
   PubMed Abstract
3. Janjan NA, Cleeland CS. Pain and suffering during cancer therapy: continued sins of omission. *Int J Radiat Oncol Biol Phys*. 2008; 72(1):6-8.
   PubMed Abstract