Oncologic Emergencies

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KEYWORDS

• Hypercalcemia • Hyperviscosity • Malignant airway obstruction
• Malignant spinal cord compression

Cancer patients are at risk for several life-threatening emergencies, including metabolic, cardiologic, neurologic, and infectious events. Many of these high-risk situations can be prevented or effectively managed if promptly recognized and urgently treated. This review addresses the more commonly encountered emergencies in cancer patients.

HYPERCALCEMIA

Hypercalcemia is one of the most common oncologic emergencies. The reported incidence varies widely, and may occur in up to 30% of all cancer patients at some time in their disease course.[1]

Hypercalcemia in patients with cancer can be mediated by several different mechanisms, including humoral-related factors, such as parathyroid hormone-related peptide (PTHrP), parathyroid hormone (PTH) oversecretion, overproduction of vitamin D, or direct osteolytic effect of tumor on bone.[2]

PTHrP-mediated hypercalcemia (also termed humoral hypercalcemia of malignancy [HHM]), is by far the most common mechanism, accounting for 80% of all cases.[2] PTHrP works much like PTH, causing increased resorption of calcium from the bones and enhancing renal retention of calcium.[3] Tumors most commonly associated with PTHrP production are of squamous histology and usually arise from the lung, esophagus, head and neck, and cervix.

Ovarian, endometrial, and renal carcinoma may also produce hypercalcemia through this mechanism. Serum measurement of PTHrP is feasible, but of little to no clinical significance, so is not routinely recommended.

Tumors that overproduce PTH itself, rather than PTHrP, are rare. Only a few patients are known who have hypercalcemia because of high PTH levels.[2,4]

About 15% of cancer patients with hypercalcemia have tumors that lead to an overproduction of the active form of vitamin D. Lymphomas are particularly adept at

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secreting the active form of vitamin D, which leads to increased bone resorption and increased efficiency of intestinal absorption of calcium, leading to hypercalcemia.[5]

Cancers that have a tendency to metastasize to the bone may lead to local osteolytic cell activation and produce hypercalcemia.[6] Local production of any one of several cytokines facilitates local bone resorption. Included in these cytokines is PTHrP. Common examples of tumors producing hypercalcemia from local bone effects include breast cancer, multiple myeloma, and many lymphomas.[7] Other tumors that have a high predilection for bone metastases, such as prostate cancer, are only rarely associated with hypercalcemia, reinforcing the dependence not just on the presence of the bony metastases, but the unique characteristics and cytokine production of the tumor itself.

Clinical Presentation

The clinical manifestations of hypercalcemia are vague and nonspecific, often confused with many other comorbid conditions present in patients with advanced cancer.[8] The rate of increase of the calcium level is more important than the absolute calcium level in determining the appearance of symptoms. High levels may be well tolerated if the rate has been slow and prolonged. The most common symptoms are constipation, lethargy, abdominal pain, and polyuria. Electrocardiograph (ECG) may show a shortened QT interval and arrhythmias may occur. Acute renal failure, seizures, coma, and death may also occur if corrective measures are not taken.

Diagnosis

The best way to diagnose hypercalcemia is to obtain an ionized calcium level. Total calcium level measurement may not be as accurate, because of changes in plasma proteins, particularly albumin, which affect the level considerably. Although formulas for correction for calcium according to albumin levels are widely used, they only help in making approximations.

Although PTHrP is the most common mechanism for hypercalcemia in patients with cancer, coexistent primary hyperparathyroidism is not a rare entity and must be considered in the differential diagnosis.[2,9] PTHrP and PTH levels can be measured, but there can be no strong recommendation to check either, as most of these patients have obvious widely metastatic cancer, and the management of the patient is unlikely to be effected. In patients with minimal metastatic disease, or in tumors that are rarely associated with hypercalcemia, PTH levels are reasonable to check, especially for those with more indolent tumors, whose survival may be prolonged.

Management

Patients with clinically significant hypercalcemia are almost always intravascularly volume depleted. (**Table 1**) This, in turn, leads to a decreased glomerular filtration rate, further decreasing excretion of calcium by the kidneys. Thus, the cornerstone of the management of hypercalcemia is adequate hydration. Normal saline is immediately started, generally at rates between 200 and 300 mL/h, depending on the patient's cardiovascular status. Once adequate intravascular volume repletion has been achieved, loop diuretics should be used to facilitate calcium excretion. Thiazide diuretics should be avoided, as they worsen hypercalcemia.

One of the most useful pharmacologic agents for treatment of hypercalcemia are the bisphosphonates.[10] Pamidronate or zoledronic acid may be used, although studies show that zoledronic acid is slightly more efficacious.[11] Zoledronic acid requires a shorter infusion time, but is more expensive. Calcitonin can be used in the first 12 to 24 hours, but its effects are modest and tachyphylaxis occurs quickly.

Table 1
Treatment of hypercalcemia

Medication	Usual Dose	Points to Remember
Normal saline	Rapid infusion 200–300 mL/h until euvolemic	Caution in patients with heart failure
Furosemide	20–40 mg IV	Only after adequate hydration
Pamidronate	60–90 mg IV	Caution if renal insufficiency present
Zoledronic acid	4 mg IV	Adjust dose for renal insufficiency
Calcitonin	4–8 IU/kg SQ or IV	Tachyphylaxis occurs quickly
Steroids	Hydrocortisone 100 mg every 6 h; or prednisone 60 mg/d by mouth	Role usually limited to lymphomas
Mithramycin/gallium nitrate		Of historical interest only

Abbreviations: IU, international units; IV, intravenous; SQ, subcutaneous.

However, it may be particularly useful in those severe cases in which the calcium level requires immediate lowering, such as in patients with seizures or arrhythmias. Because of the rapid tachyphylaxis, calcitonin should never be used as a single agent in treating hypercalcemia.

In the rare cases in which vitamin D_3 is responsible for the hypercalcemia, such as some lymphomas, steroids are useful. Agents such as mithramycin and gallium nitrate are rarely, if ever, used, as bisphosphonates tend to be effective with fewer side effects. These are largely of historical interest at this point (for a summary of the treatment of hypercalcemia, see **Table 1**).[12]

HYPONATREMIA

Hyponatremia is common in cancer patients and is defined as a serum sodium concentration of less than 136 mmol/L.[13] The most common cause is the syndrome of inappropriate secretion of antidiuretic hormone (SIADH); however, it is important to recognize that volume depletion can also be associated with hyponatremia.

Hyponatremia can be classified as mild if the sodium level is between 135 and 131 mmol/L, moderate if the level is 130 to 126 mmol/L, and severe if less than 125 mmol/L.[14] Severe hyponatremia can be life-threatening, especially if the onset is acute.

Causes of SIADH in Cancer Patients

SIADH may ensue from the tumor itself or the chemotherapy that is used to treat it. Many different tumors can actively produce antidiuretic hormone (ADH), but it is most classically associated with small cell lung cancers. Other lung tumors and duodenal, pancreatic, genitourinary, and head and neck cancers can lead to ectopic ADH production. Rare cases of SIADH have been reported with lymphomas, sarcomas, and thymomas.[14]

Certain chemotherapy drugs, notably cisplatin,[15] ifosfamide, and vincristine, can stimulate excessive ADH production or enhance its activity. These drugs are also nauseating, and nausea in itself is a potent stimulus for ADH release; the SIADH and resultant hyponatremia from these drugs can be severe.

Symptoms

Mild hyponatremia may manifest as excessive tiredness, difficulty concentrating and remembering, headache, and muscle cramps. A peculiar but uncommon symptom of hyponatremia is dysgeusia. More severe hyponatremia may manifest with diffuse neurologic symptoms including confusion, hallucinations, seizures, coma, and death.

Diagnosis

SIADH is diagnosed when a clinically euvolemic patient with normal adrenal and thyroid function has a decreased effective serum osmolality of less than 275 mOsm/kg and an increased urinary osmolality of more than 100 mOsm/kg of water. In addition, urine sodium should be greater than 40 mmol/L when the dietary sodium is not excessive.[14] Other findings may include serum uric acid less than 4 mg/dL[16] and blood urea nitrogen less than 10 mg/dL. Fractional excretion of sodium is typically greater than 1%, and that of urea greater than 55%. Levels of ADH should not be routinely checked, but are typically elevated.

Management

The definitive treatment of SIADH in the cancer patient is removal of the underlying cause. If the hyponatremia is asymptomatic, it is appropriate to ascertain the cause before management is begun. It is often possible to remove the cause in cancer patients, such as resection of a tumor or discontinuation of the offending chemotherapy drug.

In case of symptomatic hyponatremia, prompt treatment is mandated. Treatment of symptomatic hyponatremia is associated with better outcomes even when the hyponatremia is chronic.[17] If symptoms are mild, fluid restriction to about 0.5 to 1 L of free water, along with increased intake of salt and protein, is usually sufficient.

In cases of more severe symptoms, the serum sodium should be restored using 3% saline cautiously. Over-rapid correction of hyponatremia, especially if long-standing, can result in central pontine myelinosis (CPM), a debilitating neurologic condition that manifests several days after the damage is done. It is characterized by spastic quadriparesis, pseudobulbar palsy, coma, or death.[18] Therefore, it is recommended that serum sodium be corrected by no more than 8 to 10 mmol/L in 24 hours, or less than 18 mmol/L in the first 48 hours.[19] If a patient has neurologic symptoms attributable to hyponatremia, it is reasonable to increase serum sodium by 1 to 2 mmol/L/h until the neurologic condition improves, and then return to the use of normal saline. The use of furosemide-induced diuresis is now considered controversial, and it is recommended that furosemide not be used along with 3% saline.

A single case has been reported in which reinduction of hyponatremia after excessive correction of serum sodium level apparently improved a patient's outcome.[20]

CARDIAC EMERGENCIES

Superior Vena Cava Syndrome

The superior vena cava (SVC) is easily compressed by tumors arising from the lung, mediastinal structures, or lymph nodes. Malignancies are the most common cause for superior vena cava syndrome (SVCS) but, as more and more indwelling central venous access devices are used, intrinsic thrombus is becoming a significant cause for SVCS,[21,22] accounting for as many as 20% to 40% of all cases.

Etiology

The leading cause of malignancy associated with SVCS is lung cancer, accounting for as many as 60% to 85% of all cases. The most common lung cancer type that is

associated with SVCS is non–small cell lung cancer (NSCLC), but that is only because NSCLC is far more common than small cell lung carcinoma (SCLC). It is estimated that 2% to 4% of all lung cancer patients will develop SVCS, but 10% of patients with SCLC will develop SVCS. The second most common cancer associated with SVCS is non-Hodgkin lymphoma, accounting for about 10% of all cases. Curiously, Hodgkin disease is rarely associated with SVCS even though it is often mediastinal in location.

Clinical presentation

SVCS causes edema in the upper body, particularly in the head and neck (**Fig. 1**). This edema may be significant enough to compromise the lumen of the larynx, causing dyspnea and stridor, and compromise of the pharyngeal lumen, causing dysphagia. There may be arm swelling and cutaneous venous dilatation as the venous return is shunted around the obstruction (**Fig. 2**). The most concerning symptoms are neurologic, such as headaches, confusion, or even coma, suggesting cerebral ischemia. Brain stem herniation and death can potentially occur.[23] However, the usual course of SVCS is that collaterals eventually develop, and symptoms tend to improve when this happens.[24]

Management

SVCS is not considered a true oncologic emergency unless neurologic symptoms are present. However, its presence is, in itself, a poor prognostic marker.[25] It is strongly recommended that, if a patient presents with SVCS without a prior tissue diagnosis of malignancy, every effort should be made to obtain biopsies and histologic diagnosis before any treatment decisions are made.[26]

If a true emergency exists, then a stent can be emergently placed in the SVC if the expertise to do so is available,[27,28] or radiation can be used. Stenting is now considered first-line treatment of SVCS from benign causes,[29] and many experts believe this can also be extrapolated to malignant causes.[30] Otherwise, therapy directed at the underlying cause should be used, and symptoms usually start improving rapidly if the tumor is responsive.

Although not a true emergency unless central nervous system (CNS) symptoms are present, the presence of SVCS at diagnosis does portend a poor prognosis in lung cancer and lymphoma, with overall median survival only 5 months.

Malignant Pericardial Effusion

Cancer patients may develop fluid accumulations in the pericardial space as a result of metastases, various treatments, or direct extension of the tumor into the space

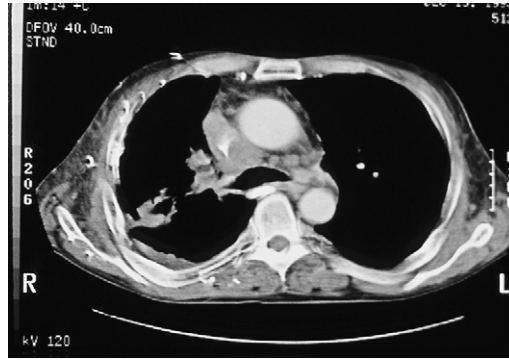

Fig. 1. CT scan demonstrating SVC compression.

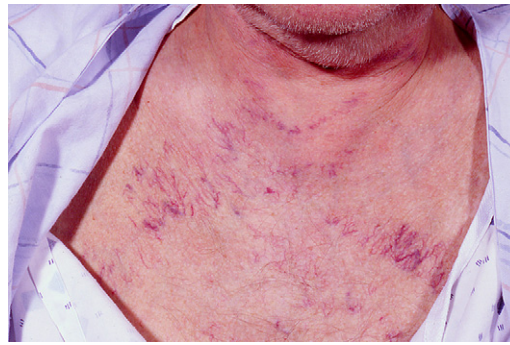

Fig. 2. Dilated collateral skin veins in patient with superior SVCS from small cell lung cancer.

(**Fig. 3**).[31] Primary malignancies of the pericardium are rare. Of these, mesothelioma is the most common, and is almost always unresectable and incurable at presentation.[32]

Most pericardial effusions are small and asymptomatic, although their presence does portend a poor prognosis, with median survival often less than 1 year.

Large effusions can be asymptomatic if they accumulate slowly, but rapidly accumulating effusions may lead to cardiac tamponade, even if small in amount.[33] It is estimated that, if an effusion occurs slowly, the pericardium may accommodate as much as 2 L of fluid without life-threatening compromise of ventricular filling.[34]

Signs and symptoms

The classic Beck triad of distended neck veins, silent precordium, and hypotension in cardiac tamponade is rarely seen in malignancy, as, more often, the fluid accumulation tends to be subacute rather than acute. Patients typically complain of shortness of breath, chest discomfort, and fatigue. Clinical examination reveals distant heart sounds, a narrow pulse pressure, and pulsus paradoxus.[35,36] An electrocardiogram (ECG) tends to show low-voltage complexes with nonspecific ST-T changes. Electrical alternans may be seen in patients with a large pericardial effusion, but this is not diagnostic for cardiac tamponade physiology (**Fig. 4**).[33]

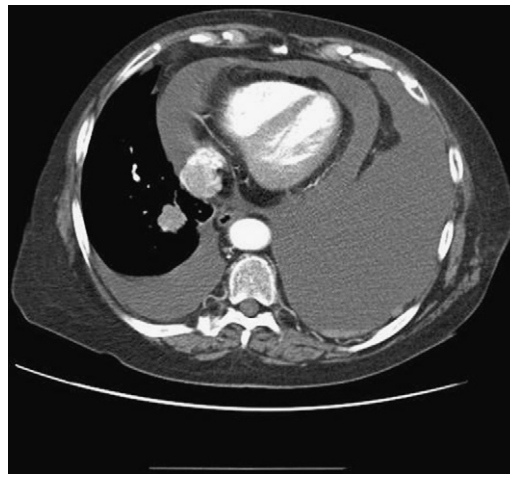

Fig. 3. CT scan showing large pericardial effusion and bilateral pleural effusions.

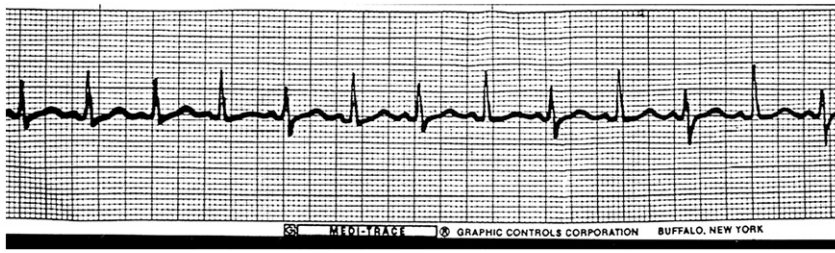

Fig. 4. ECG demonstrating electrical alternans in patient with pericardial tamponade.

Management

Echocardiography is useful in making the diagnosis of both effusions and demonstrating the physiology of tamponade, and also guides the drainage of the fluid to relieve symptoms.[37,38] There is probably no advantage to draining asymptomatic effusions, even if they are large.[39] A catheter may be left in place for a few days after drainage has been performed.

In the case of chemosensitive tumors, systemic chemotherapy may be useful. Intrapericardial installation of chemotherapy agents such as bleomycin,[40] carboplatin,[41] or mitomycin-C[42] has been studied in Japan and found to be safe. A recent study, also in Japan, found that overall survival is probably unchanged by such maneuvers.[43]

Surgical procedures, such as a subxiphoid pericardiostomy and percutaneous balloon pericardiotomy, are sometimes undertaken. These are low-morbidity procedures and usually can be accomplished under local anesthesia.[44] Subxiphoid pericardiostomy may be more appropriate for stable patients.[45] Video-assisted thoracoscopic (VATS) pericardial window is another safe and highly effective surgical alternative.[46]

Tumor Lysis Syndrome

Tumor lysis syndrome (TLS) results from rapid cell breakdown with the release of large amounts of nucleic acids, phosphorous, and potassium into the circulation. Although most commonly seen after administration of chemotherapy for highly sensitive tumors such as leukemias and lymphomas, spontaneous TLS has been reported to occur in a wide variety of tumors, most commonly those with a rapid growth pattern, the classic example being Burkitt lymphoma.

Nucleic acids are rapidly broken down into uric acid, which is not water soluble. Precipitation of uric acid crystals can occur in many organs, including the kidneys (causing renal failure), the cardiac conduction system (causing arrhythmias), and the joint spaces (causing an acute flare of gout). **Fig. 5** illustrates how nucleic acids are catabolized. Allopurinol inhibits the enzyme xanthine oxidase, thus decreasing uric acid production, whereas rasburicase is a recombinant form of the enzyme urate oxidase, which is not found in humans, and leads to the further degradation of uric acid into water-soluble allantoin. It is Food and Drug Administration (FDA)-approved for use in the pediatric population at high risk for the development of tumor lysis, and has also demonstrated efficacy in the adult population.[47–50] Risk factors for the development of TLS include intravascular volume depletion, rapidly growing malignancy, renal insufficiency, large tumor burden, and hyperuricacidemia.

Severe hyperphosphatemia can lead to renal failure by precipitation in the renal tubules of calcium phosphate crystals. This compound can deposit in the heart, causing arrhythmias. Acute, severe hyperkalemia can also produce life-threatening arrhythmia.

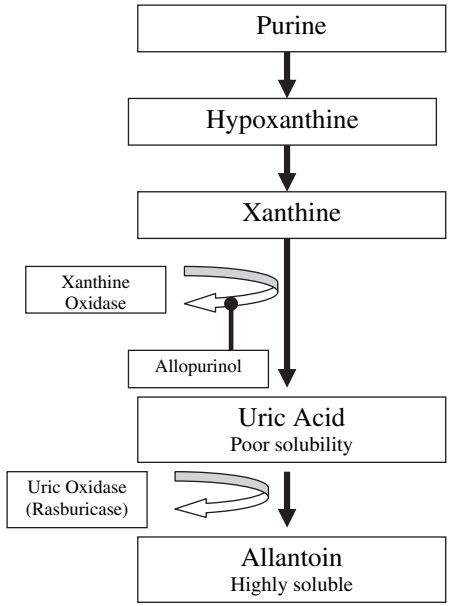

Fig. 5. Metabolism of uric acid with sites of action of allopurinol and xanthene oxidase.

TLS is defined by laboratory and clinical criteria. The Cairo-Bishop definition and grading is well accepted and recognizes laboratory and clinical parameters (**Box 1**).

Signs and Symptoms

The signs and symptoms relate to the underlying electrolyte and metabolic abnormalities, and are not specific for this syndrome.

Management

TLS is best managed proactively, anticipating its occurrence and taking measures to avoid it. The most important measure is to ensure adequate hydration. The aim is to ensure a urine output of 100 mL/m^2 if there is no cardiac limitation. Alkalinization of the urine is believed to be beneficial, but may be harmful if only allopurinol is being used, because xanthine is even less water soluble in an alkaline environment, and may precipitate within the renal tubules.[51] Once adequate hydration is assured, loop diuretics may be used to increase urine output, if needed.

Allopurinol is routinely instituted in moderate-risk situations 2 to 3 days before starting chemotherapy, but in high-risk situations, or situations in which allopurinol may be of limited benefit (such as high uric acid at baseline, or high uric acid despite allopurinol use), it is recommended that allopurinol be omitted and the patient started on rasburicase instead[52] (**Table 2**). Allopurinol causes buildup of xanthine and hypoxanthine, compounds that are poorly water soluble, heightening the risk of renal failure in these situations. Rasburicase, facilitates the break down of uric acid into allantoin, which is easily excreted in urine. Although rasburicase is approved only in pediatric patients by the FDA in the United States, there is adult experience with its use in France.[53] An expert panel considered that the rationale and recommendations discussed earlier are equally applicable in adults.[52] **Table 3** shows general guidelines for starting allopurinol and rasburicase.

Box 1
TLS laboratory definition using Cairo-Bishop classification

Laboratory TLS

- Uric acid more than or equal to 8 mg/dL ($\geq$476 μmol/L) or 25% increase from baseline
- Potassium more than or equal to 6.0 mEq/L ($\geq$6 mmol/L) or 25% increase from baseline
- Phosphorus more than or equal to 6.5 mg/dL ($\geq$2.1 mmol/L) or 25% increase from baseline
- Calcium less than or equal to 7 mg/dL ($\leq$1.75 mmol/L) or 25% decrease from baseline

Clinical TLS

- Creatinine more than or equal to 1.5 times upper limit of normal
- Cardiac arrhythmia or sudden death
- Seizure

Note: Two or more laboratory changes within 3 days before, or 7 days after, cytotoxic therapy.
Data from Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol 2004;127(1):3–11.

Hyperphosphatemia is managed by placing the patient on a phosphorous-restricted diet, using oral phosphate binders, and, in extreme cases, dialysis.

Hyperkalemia is managed by using calcium gluconate, insulin and dextrose, and sodium polystyrene sulfonate, in addition to adequate hydration and diuresis as already mentioned. The accompanying table outlines the management of electrolyte abnormalities in TLS (**Table 4**).

MALIGNANT SPINAL CORD COMPRESSION

Malignant spinal cord compression (MSCC) is a devastating neurologic complication that occurs in approximately 1 in 12,700 cancer patients in the United States each

Table 2
Risk stratification forTLS

	Risk		
Type of Cancer	**High**	**Intermediate**	**Low**
NHL	Burkitt, lymphoblastic, B-ALL	DLBCL	Indolent NHL
ALL	WBC $\geq$100,000	WBC 50,000–100,000	WBC $\leq$50,000
AML	WBC $\geq$50,000 monoblastic	WBC 10,000–50,000	WBC $\leq$10,000
CLL		WBC 10,000–100,000 Tx w/fludarabine	WBC $\leq$10,000
Other hematologic malignancies (including CML and multiple myeloma) and solid tumors		Rapid proliferation with expected rapid response to therapy	Remainder of patients

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; B-ALL, Burkitt acute lymphoblastic leukemia; CML, chronic myeloid leukemia; DLBCL, diffuse large B-cell lymphoma; NHL, non-Hodgkin lymphoma; CLL, chronic lymphocytic leukemia; Tx, treatment.

Table 3
Treatment recommendations forTLS

Agent	Recommendation
Allopurinol	Dosing: 100 mg/m^2/dose every 8 h (10 mg/kg/d divided every 8 h) PO (maximum, 800 mg/d) or 200–400 mg/m^2/d in 1–3 divided doses; IV (maximum, 600 mg/d) Reduce dose by 50% or more in renal failure Reduce 6-mercaptopurine or azathioprine doses by 65%–75% with concomitant allopurinol May need to adjust doses of dicumarol, thiazide diuretics, chlorpropamide, cyclosporine, or allopurinol when they are used concomitantly with allopurinol
Rasburicase	Contraindicated in glucose-6-phosphate dehydrogenase–deficient patients, and in patients with a known history of anaphylaxis or hypersensitivity reactions, hemolytic reactions, or methemoglobinemia reactions to rasburicase or any of the excipients Administration: 0.05–0.2 mg/kg IV over 30 min Uric acid levels should be monitored regularly and used as a guide to modulate dosing; to measure uric acid levels place blood sample immediately on ice to avoid continual pharmacologic ex vivo enzymatic degradation 10% incidence of antibody formation

year.[54] MSCC most commonly occurs when the malignancy metastasizes to the spine, with subsequent erosion into the epidural space causing compression of the spinal cord. Rarely, tumors will metastasize directly to the epidural or intradural tissue. Although all tumor types have the potential to cause MSCC, breast, prostate, and lung each account for approximately 15% to 20% of the cases, with non-Hodgkin lymphoma, renal cell carcinoma, and myeloma each causing 5% to 10% of cases.[12,54]

Pathophysiology

MSCC most commonly occurs when metastatic tumor reaches the vertebral bodies via hematogenous spread with secondary erosion into the epidural space, thus causing compression of the spinal cord. In approximately 15% of cases it occurs when a paravertebral lesion spreads into the spinal canal through an intervertebral foramen and directly compresses the spinal cord. This mechanism is most commonly seen in neuroblastomas and lymphomas.[55] Metastatic lesions can also cause MSCC via destruction of vertebral cortical bone leading to vertebral collapse with displacement of bone fragments into the epidural space. In rare cases, metastases occur directly to the spinal cord and meninges.[55–57] The damage to the spinal cord occurs via direct compression causing demyelination, axonal damage, and secondary vascular compromise. Animal models implicate vascular damage as the most prominent and destructive of the 2 mechanisms. Acute compression causes occlusion of epidural venous plexus, compromising the blood-spinal cord barrier, resulting in inflammation and vasogenic edema. At this stage, the damage can often be reversed by corticosteroids. When the arterial blood flow is impaired due to compression, spinal cord ischemia, infarction, and irreversible damage result.[58,59]

Clinical Presentation

The most common clinical presentation is back pain, which occurs in approximately 90% of cases. A prior diagnosis of malignancy is known in most cases, although in

Table 4
Treatment of metabolic abnormalities associated with TLS

Problem	Intervention	Dosages	Comments
Renal insufficiency and hypovolemia	IV fluids	Normal saline, 3 L/m^2 daily (200 mL/kg daily)	Use with caution if history of CHF
	Dialysis	—	Patients with oliguric renal failure not responding to IV fluids or patients with CHF
Hyperuricemia	Allopurinol	100 mg/m^2 per dose orally every 8 h (10 mg/kg/d divided in 3 doses) or 200–400 mg/m^2/d IV in divided doses every 8–12 h; commonly used dosages include 600 mg initially followed by 300 mg/d	Reduce dose in renal failure; multiple drug interactions (6-mercaptopurine and azathioprine); IV allopurinol should be used only in patients unable to take oral medications
	Rasburicase	0.05–0.2 mg/kg IV	Contraindicated in G6PD deficiency; transfer blood samples on ice to the laboratory; risk of sensitization and allergic reactions; expensive
Hyperphosphatemia (phosphate level> 6.5 mg/mL [>2.1 mmol/L])	Minimize phosphate intake	—	Low phosphorus diet; phosphorus-free IV fluids
	Phosphate binders (aluminum hydroxide)	50–150 mg/kg daily orally	May interfere with drug absorption
	Dialysis	—	If no response to medical therapy
Hyperkalemia	Insulin (regular)	10 units IV	—
	Dextrose (50%)	50–100 mL IV	—
	Calcium gluconate (10%)	10–20 mL (100–200 mg) IV	Do not give with bicarbonate; use if arrhythmias or ECG changes; can repeat as needed
	Sodium bicarbonate	45 mEq IV (1 ampule of 7.5% $NaHCO_3$)	Use if acidosis; can repeat in 30 min
	Sodium polystyrene sulfonate (Kayexalate)	15–30 g every 6 h orally (can be used rectally)	Can be given with sorbitol
	Albuterol	Inhaled 2.5 mg	For severe hyperkalemia
	Dialysis	—	Severe hyperkalemia not responsive to other measures; renal failure; volume overload
Hypocalcemia	Calcium gluconate (10%)	5–20 mL (50–200 mg) IV	Only if symptomatic; repeat as necessary; use with caution in patients with severe hyperphosphatemia

Abbreviation: CHF, congestive heart failure.

5% to 15% of cases MSCC is the initial presentation of malignancy.[60] The nature of the pain can vary with local, radicular, or referred pain. Referred pain is common with cervical compression, often presenting as subscapular pain; thoracic compression as lumbrosacral or hip pain; and lumbrosacral compression presenting as thoracic pain.[61] The most common location for MSCC is in the thoracic spine, followed by the lumbrosacral region and, lastly, cervical spine. Multiple levels are involved in almost half of all patients. Breast and lung cancer tend to metastasize more frequently to the thoracic spine, whereas colon and pelvic carcinomas tend to develop metastatic lesions in the lumbosacral spine.[54] Other presenting symptoms include motor weakness, sensory impairment, and autonomic dysfunction. In cauda equina syndrome, patients will present with decreased sensation over the buttocks, posterior-superior thighs, and perineal region. Cauda equina syndrome may present as urinary retention, and overflow incontinence (90% sensitivity, 95% specificity).[54,61]

The severity of MSCC can be scored according to several grading systems, including the Frankel grading system, which classifies each patient into 1 of the following 5 categories: (A) complete paraplegia, (B) only sensory function, (C) nonambulation, (D) ambulation, and (E) no neurologic symptoms or signs. The Barthel index also includes assessment of bowel and bladder function.[54,62] These can be useful in assessing severity and response to therapy.

Diagnosis

The gold standard for the diagnosis of MSCC is magnetic resonance imaging (MRI) with a sensitivity of 93%, specificity of 97%, and overall accuracy of 95% (**Fig. 6**).[56,63] Plain radiographs are not adequate in making the diagnosis, and have a false-negative rate of 10% to 17% and so should not be used to rule out compression. Plain films will also not detect paraspinous masses that have entered the intervertebral foramen if there is no bone erosion.[56,60] If MRI is contraindicated or not available, computed tomography myelography can be used.[12,57] There is no clinical model to rule out MSCC in cancer patients with back pain, and, therefore, all new onset back pain should prompt an immediate assessment and consideration for an MRI in this patient population. Lack of neurologic deficits is ideal and should not inhibit further investigation, but may alter the urgency of the evaluation. For those patients with back pain only, and a normal neurologic examination, emergent imaging of the spinal axis is not mandatory, but should be completed in the next 48 to 72 hours. Those with neurologic deficits need emergent evaluation before nerve damage becomes permanent. Finding unsuspected lesions is not uncommon, and up to one-third of patients have more than 1 site of compression, therefore imaging of the entire spine is required.[56]

Treatment

Corticosteroids are first-line treatment of most patients with MSCC. Steroids reduce the vasogenic edema and inflammation, and seem to have a tumoricidal effect on leukemias, lymphomas, and, occasionally, breast cancer.[56] Because the most important prognostic indicator for ambulatory outcome is the pretreatment motor function, immediate initiation of therapy is of utmost importance. Although the use of high-dose dexamethasone to promote posttreatment ambulation is a grade A recommendation from an evidence-based guideline, the optimal dose of dexamethasone is still unclear and debated because of the significant side effects of high-dose steroids. Several studies have been conducted to determine the optimal dose of dexamethasone to balance outcome with adverse effects. Two studies revealed an 11% to 14% frequency of serious side effects including a fatal ulcer, rectal bleeding and bowel

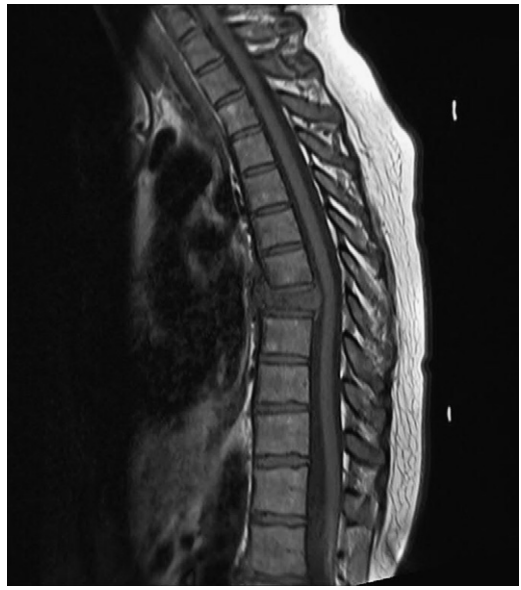

Fig. 6. Breast cancer presenting as spinal cord compression in 48-year-old woman with a strong family history of breast cancer. This case is unusual as the initial manifestation of breast cancer and in that only one level of spinal axis is involved.

perforations when doses as high as 96 mg intravenous (IV) were given. When the dose was decreased to 16 mg/d there were no serious side effects, and no detectable difference in ambulatory rates, between the groups.[64,65] Another study by Vecht and colleagues compared an initial IV dose of 10 mg to the high dose of 100 mg. There was no difference in treatment arms in terms of pain reduction, ambulation, or bowel function, although the sample size was small and not adequately powered to determine equivalence.[64–66] There is no current consensus on the best dose, but dexamethasone is typically given at 10 to 16 mg IV bolus followed by 4 to 6 mg every 4 hours, with a taper during, or immediately after, completion of radiation.[12,54,56] Due to the severity of loss of ambulation, one option that is still used is giving higher doses in patients who present with paraplegia or rapidly progressive symptoms.[56]

Radiation therapy plays a critical role in the treatment of MSCC. Although there is no consensus in dosing schedules, the therapy port usually extends 1 or 2 vertebral bodies above and below the site of compression, and is often given at 30 Gy in 10 fractions. Radiation given at greater than 30 Gy has not been shown to improve outcomes, but treatment regimens can range in duration, thus changing the dose per fraction.[54,58,67,68] In the past, radiation therapy and steroids have been the standard of care for MSCC; however, the role of surgery is becoming increasingly evident. In 2005, Patchell and colleagues[69] reported the first phase III randomized clinical trial comparing the role of decompressive surgery and radiation to that of radiation alone. Patients were given 100 mg of dexamethasone followed by 24 mg every 6 hours, and then treated with radiation therapy (30 Gy in 10 fractions) alone or surgery (generally within 24 hours) followed by the same course of radiation within 2 weeks of surgery. The study was discontinued after enrollment of 100 of the 200 planned patients because predetermined stopping criteria were met. The percentage of ambulatory patients was significantly higher in the group treated with surgery plus radiation

(84% vs 57%), as was their duration of ambulation (median 122 days vs 13 days) and median survival (126 days vs 100 days). It is difficult to extrapolate these data to all MSCC patients, as there were strict inclusion criteria. However, in patients who fulfill the criteria as outlined by Patchell and noted in **Box 2**, decompressive surgery for maximal tumor resection and stabilization followed by radiotherapy should be considered.[57,69]

BRAIN METASTASES AND INCREASED INTRACRANIAL PRESSURE

Brain metastases represent the most common type of intracranial tumor and are a common complication in cancer patients. The incidence of metastases varies by tumor type, with lung cancer being the most common, followed by breast and melanoma. Lung and melanoma tend to present as multiple brain lesions, whereas breast, colon, and renal tumors more commonly produce solitary lesions.[70,71] These lesions in the brain can lead to neurologic deficits, seizures, and increased intracranial pressure (ICP). Untreated patients have an average median survival of about 4 weeks. Prognosis is dependent on Karnofsky performance status, presence of systemic disease, and primary tumor.[70]

Pathophysiology

Most brain metastases are secondary to hematogenous spread from the primary tumor. Accordingly, as 90% of cerebral blood flow occurs in the supratentorial region, most metastatic lesions occur in the supratentorial region. Within the brain, the lesions tend to occur at the borders of the territories of the major arteries (watershed areas) and at the gray-white matter junction. The most common cause of increased ICP is cerebral edema. Vasogenic edema occurs when the blood-brain barrier is disrupted by the tumor. Tumors can also induce increased ICP from hydrocephalus due to

Box 2
Patchell criteria for decompressive surgery

Inclusion criteria
At least 18 years of age
Tissue-proven diagnosis of cancer (not of CNS or spinal column origin)
MRI evidence of MSCC (displacement of the spinal cord by an epidural mass)
At least 1 neurologic sign or symptom (including pain)
Not paraplegic for more than 48 hours
MSCC restricted to 1 area (can include several contiguous spinal or vertebral segments)
Expected survival of at least 3 months
General medical status acceptable for surgery
Exclusion criteria
Multiple discrete lesions
Radiosensitive tumors (lymphomas, leukemia, multiple myeloma, and germ cell tumors)
Mass with compression of only the cauda equina or spinal roots
Preexisting neurologic problems not directly related to MSCC
Prior radiotherapy that would exclude them from receiving study dose

increased cerebrospinal fluid (CSF) volume in the ventricular space, because normal flow or absorption is obstructed by the tumor itself.[72]

Clinical Presentation

Approximately 75% of patients with brain metastases have neurologic symptoms at the time these lesions are detected. Symptoms vary significantly and depend on the location of the lesions or lesions. The most common presenting feature is subacute onset of headache, which occurs in roughly 50% of cases, but can also present with focal neurologic deficits, seizures including status epilepticus, neurocognitive changes or any combination of these features. Generally, these symptoms arise over days to weeks, but can appear acutely if there is hemorrhage into the lesion, which occurs more frequently with melanoma, choriocarcinoma, and renal and thyroid carcinoma.[70,73] Metastatic lesions become an oncologic emergency in cases of increased ICP and status epilepticus. Patients with increased ICP classically present with headache, nausea, and vomiting. The headaches tend to be more severe in the mornings and when supine. Other symptoms include weakness, ataxia, seizures, and mental status changes. If papilledema is detected on physical examination, this almost always indicates ICP. The triad of signs referred to as the Cushing response (hypertension with wide pulse pressure, bradycardia, and an irregular respiratory rate) is a late effect and needs to be addressed immediately.

Diagnosis

Contrast-enhanced MRI is the most sensitive and specific diagnostic tool available. Computerized tomography (CT) can be used if MRI is not available or contraindicated, but it is less sensitive, especially if the tumor is small or located in the posterior fossa. However, CT is the preferred scanning technique in an acute situation when hemorrhage or hydrocephalus is suspected.[12,70,72]

Treatment

The first line treatment of patients with increased ICP is dexamethasone. Corticosteroids seem to restore leaky capillary permeability, reduce peritumoral edema, and reduce local brain compression, which can relieve the symptoms. The effect of steroids is usually seen within 24 hours, but the full effect is not seen for several days, and changes on imaging may not appear for a week. There is no consensus on dose, but this usually ranges from 10 to 24 mg IV bolus, followed by 4 mg every 6 hours.[12,70] In severe cases, mannitol and hyperventilation are used. Mannitol can be administered as IV boluses or as continuous infusion to decrease cerebral edema. Intubation and controlled hyperventilation lead to a rapid decrease in cerebral edema. The effect of mannitol and hyperventilation are transient and not definitive therapy. These should be reserved for critical cases in patients with rapidly declining clinical states.[71] More definitive treatment modalities include whole-brain radiation therapy (WBRT), surgery, or stereotactic radiosurgery. Whole-brain radiation is the classic treatment of patients with multiple brain metastases or with a tumor too large for surgery or stereotactic radiosurgery. WBRT generally improves median survival to 3 to 6 months, compared with 1 to 2 months with supportive care alone.[70,71] Surgical debulking can also be performed, depending on tumor location, and is the most rapid way to alleviate increased ICP. Stereotactic radiosurgery can be used in selected cases. Chemotherapy can be used in highly chemosensitive tumors such as germ cell, lymphoma, or small cell carcinomas, or in cases in which radiation therapy is not an option.

Seizures occur in about one-quarter of patients with intracranial metastases, and these patients require anticonvulsant therapy. In cases of status epilepticus, treatment usually consists of lorazepam, phenytoin, or fosphenytoin.[12,70] In the past, patients with brain metastases were treated prophylactically with antiepileptic medications, but this is no longer recommended as a meta-analysis. Sirven and colleagues[74] revealed that prophylactic treatment does not reduce the frequency of first seizures in this patient population. These medications also have significant side effects, including bone marrow suppression, and interactions with chemotherapeutic and targeted agents, as many are metabolized via P450, and most of these antiepileptic medications induce the cytochrome P450 system.[70]

HYPERVISCOSITY SYNDROME DUE TO DYSPROTEINEMIA (MONOCLONAL GAMMOPATHY)

Hyperviscosity syndrome (HVS) refers to the clinical consequences of increased blood viscosity. These can occur secondary to a variety of malignancies including monoclonal gammopathies, such as Waldenstrom macroglobulinemia (WM), multiple myeloma, and acute leukemias. This section of the review focuses on hyperviscosity secondary to dysproteinemia. The most common cause of HVS due to dysproteinemia is WM, which occurs in up to 30% of these patients.[75]

Pathophysiology

HVS occurs as a result of increased viscosity of the blood, and leads to adverse effects on tissue perfusion. In normal blood, the most important determinant of blood viscosity is the hematocrit, with serum protein concentration playing a lesser role. In normal physiologic conditions, fibrinogen is the key component in protein concentration in blood because of its large molecular size, shape, and charge. In cases of HVS, excessive amounts of circulating immunoglobulins (Igs) are produced. IgM is the most likely culprit, as it is the largest Ig (molecular weight [MW] 1,000,000). These proteins are mainly intravascular and, as the concentration increases, they form aggregates and bind water via their carbohydrate contents. This process increases the osmotic pressure and increases the resistance to blood flow. Igs are also cationic and lower the repellant forces between anionic red blood cells, which can lead to rouleaux formation and reduction in the malleability they need to travel through the microvasculature. Eventually, this leads to impaired transit of blood cells, microvascular congestion, decreased tissue perfusion, and tissue damage. Although this is predominately via IgM, it can occur with IgA molecules, as they tend to polymerize and aggregate. It can also occur with the IgG3 subclass, as these undergo a concentration-dependent aggregation.[75,76]

There is no concise relationship between serum viscosity (SV) and clinical symptoms. The normal range for SV is 1.2 to 2.8 centipoise (cP). In general, patients will not become symptomatic with a SV less than 3, although more recent studies have shown retinal changes in levels as low as 2.1 cP.[77] In WM patients, about one-third of those with an SV greater than 4 will not have symptoms. High-risk patients have a serum IgM level greater than 4 g/L, although IgM levels of 3 g/L can produce symptoms in some patients.[12,75]

Clinical Presentation

The signs and symptoms of HVS vary and are nonspecific in nature. The classic triad of symptoms includes neurologic abnormalities, visual changes, and bleeding, although all 3 need not be present to make the diagnosis.[75] Neurologic manifestations include headache, altered mental status, vertigo, ataxia, or paresthesias.

Hyponatremia and hypercalcemia are often present. The hyponatremia seen on laboratory studies is pseudohyponatremia due to an artifact from the hyperproteinemia.[78] Visual changes are secondary to vascular changes, which play a major role in HVS. These vascular changes can be detected early on at lower SV in the periphery of the retina, which then progresses to central retinal hemorrhages and vascular dilatation as the viscosity increases.[78,79] The classic fundoscopic examination, which should be performed in all patients with suspected HVS, reveals dilated, engorged veins that look like sausage links; a condition known as fundus paraproteinaemicus. If untreated, this will progress to complete retinal vein occlusion, and flame-shaped hemorrhages. The retinal vein changes can lead to blurry vision, decreased visual acuity, and eventually blindness if not treated.[75,80] Mucosal bleeding is another common clinical manifestation of HVS. The proteins coat the platelets and hinder their clot formation ability. Bleeding can be seen in the gastrointestinal tract, gingival, uterus, or cause epistaxis. Purpura can also be seen on physical examination.[75]

Other clinical consequences of HVS include congestive heart failure, ischemic acute tubular necrosis, pulmonary edema, with multiorgan system failure and death if treatment is not promptly initiated.[12,75]

Diagnosis

There is no single diagnostic test to assess for HVS. Physical examination and history are important, as are laboratory studies, including electrolyte panel, SV, peripheral blood smear, and quantitative Ig levels. The diagnostic workup will need to rule out other causes of the presenting symptoms, and will vary depending on presentation.

Treatment

The mainstay of therapy is plasmapheresis. Plasmapheresis is the fastest, most effective method to reduce plasma viscosity. It is especially rapid in IgM-related cases, as most IgM is intravascular. In cases of IgA- or IgG-related HVS, it may take several sessions to achieve the same result as seen in 1 treatment with IgM-related HVS. If plasmapheresis is not readily available, phlebotomy of 100 to 200 mL of whole blood has been used to reduce acute symptoms. Normal saline, given until repletion of intravascular volume, followed by loop diuretics, is another means to reduce hypercalcemia and SV.[81] Ultimately, the underlying dysproteinemia needs to be addressed as these therapies do not control the underlying disease. The definitive treatment varies according to diagnosis, but often involves chemotherapeutic agents such as alkylating agents or nucleoside analogs.[12,78] Until SV is reduced and capillary perfusion improved, red-cell transfusions should be avoided unless critical, as this can increase SV, thus worsening HVS.

HYPERLEUKOCYTOSIS AND LEUKOSTASIS

Although most leukemias present with more subtle features, up to 30% of adult acute myelogenous leukemias can present with hyperleukocytosis, putting patients at risk for leukostasis. Hyperleukocytosis has been conventionally defined as an initial white blood cell (WBC) count greater than 100,000/μL. Hyperleukocytosis is more common in acute leukemias, especially in acute lymphoblastic leukemia (ALL) with 11q23 rearrangement, and acute monocytic leukemia (AML) subtypes M3v, M4, and M5. Hyperleukocytosis portends a poor prognosis, with higher risk of early mortality, especially in ALL. The WBC count is the most important prognostic factor in ALL; patients who present with a WBC greater than 50,000/μL have a particularly poor prognosis, and few children with hyperleukocytosis become long-term survivors.[82–84]

Pathophysiology

Initial studies suggested that the increase in circulating leukocytes caused sludging of the leukemic blasts on the microvasculature secondary to increased whole blood viscosity. There is increasing evidence that interactions between the vascular endothelial cells and leukemic blasts enhance the aggregation of blasts. There is also differential expression of adhesion molecules on the lymphoblast cells and myeloblast, which has been implicated in the higher incidence of leukostasis in AML versus ALL.[84,85]

Clinical Presentation

The presentation of leukostasis due to leukemias is similar to the HVS seen with dysproteinemia. In general, the presenting symptoms are related to the respiratory system and CNS. Pulmonary symptoms can range from exertional dyspnea to severe respiratory distress. Arterial blood gases should be interpreted with caution, as pseudohypoxia, as detected with low arterial oxygen tension, may be secondary to rapid consumption of plasma oxygen from the increased leukocytes. Chest radiograph findings can vary from normal to diffuse infiltrates. Neurologic manifestations span the spectrum from mild confusion to somnolence. Intracranial hemorrhage also occurs and can present with focal neurologic deficits. Other symptoms include retinal hemorrhage, retinal vein thrombosis, myocardial infarction, limb ischemia, renal vein thrombosis, and disseminated intravascular coagulation. Fever is also common and high. Although infection is found in only a few cases, it does need to be ruled out, as this syndrome can mimic sepsis syndromes.[12,83,84]

Diagnosis

As with HVS, there is no specific diagnostic test. Laboratory evaluation should include evaluation for thrombocytopenia, coagulopathy, and TLS.

Treatment

Leukoreduction can be achieved quickly with leukapheresis. Although there are no evidence-based guidelines for initiation of leukapheresis, it is usually initiated at a blast count greater than 100,000/μL, or the presence of symptoms regardless of blast count. In ALL, leukapheresis is usually not done unless symptoms develop or the white count becomes greater than 200,000/μL. Supportive measures that should be initiated include hydration with IV fluids with careful monitoring of fluid balance, as these patients are at risk for cardiopulmonary complications. TLS should be prevented with the use of allopurinol or recombinant urate oxidase. Transfusions should be avoided unless absolutely necessary, as this may increase blood viscosity and can exacerbate the syndrome. Induction chemotherapy should be initiated immediately.[83,84] Single-fraction radiation to the cranium for cerebral leukostasis, or to the lungs for pulmonary leukostasis causing hypoxia, have been used as temporizing measures in select patients, although this is controversial and there are no controlled studies that confirm benefit.[12]

AIRWAY OBSTRUCTION

Malignant airway obstruction can arise from locally advanced tumors that arise from the region of the tracheobronchial tree or from lesions metastatic to the mediastinum or major airways. Primary bronchogenic carcinomas are estimated to be the most common cause of malignant airway obstructions, and it is estimated that up to 30% of patients with primary lung tumors will, at some point in their course, develop airway

obstruction.[86] In patients with primary bronchogenic cancers, airway obstruction does not seem to adversely effect overall survival, with median survival of 8.2 versus 8.4 months respectively for patients with and without airway obstruction.[87] However, prompt recognition and treatment can lead to a markedly improved quality of life, with up to 95% of patients reporting a decrease in dyspnea with prompt treatment.[88]

Causes

Primary lung cancers are the most common cause of malignant airway obstruction, but other local tumors, such as thyroid, esophageal, primary mediastinal (including thymic, lymphoma, and germ cell), and rare tumors such as pulmonary carcinoid or adenocystic, can also cause obstruction. Metastatic lesion directly to the bronchial tree, lymph nodes, or mediastinal structures include lung, breast, thyroid, colon, sarcoma, and melanoma, although virtually any cancer can cause obstruction.

Presentation

Symptoms at presentation include stridor, dyspnea, hemoptysis, and cough. These symptoms are nonspecific and are often mistaken for more common conditions, such as an exacerbation of chronic obstructive pulmonary disease (COPD), asthma, infections, bronchitis, or heart disease. The rate of development of symptoms is often dependent on the tumor and its aggressiveness. Patients with slow-growing tumors may have a prolonged course of symptoms, with a sudden exacerbation due to local accumulation of secretions or bleeding.

Physical Examination Findings

Physical examination findings may include similarly nonspecific findings such as stridor, wheezing, or loss of breath sounds. Regional lymphadenopathy may help to point to the cause and identify tissue for diagnostic evaluation.

Evaluation

Chest radiographs are nonsensitive and nonspecific, but may show tracheal narrowing. CT scanning is more sensitive and more likely to show bronchial narrowing (**Fig. 7**). Axial and coronal views can often delineate the anatomy, and may provide significant help for the pulmonologist in evaluation and bronchoscopy. CT can also define the mediastinal anatomy and help guide evaluation for primary and metastatic lesions.

Bronchoscopy offers the advantage of allowing the anatomy to be directly visualized, allowing treatment of an obstruction, and obtaining tissue for diagnosis. Care must be taken in evaluating what type of procedure to perform, as bronchoscopy can increase the risk for completion of obstruction, and anesthesia may further limit gas exchange. The choice between rigid versus flexible bronchoscopy will depend on the anatomy, the experience of the physician, and the treatment options locally available.

Spirometry can demonstrate presence of central airway obstruction, but, in the emergent setting, is less likely to be useful compared with bronchoscopy and CT scanning. Flow-volume loops may demonstrate a classic pattern suggestive of major airway obstruction.

Treatment

The primary and most urgent goal of treatment is to establish a patent airway to allow for proper gas exchange. Bronchoscopy done with a rigid scope allows for rapid opening of the airway and can often simultaneously obtain tissue diagnosis for those

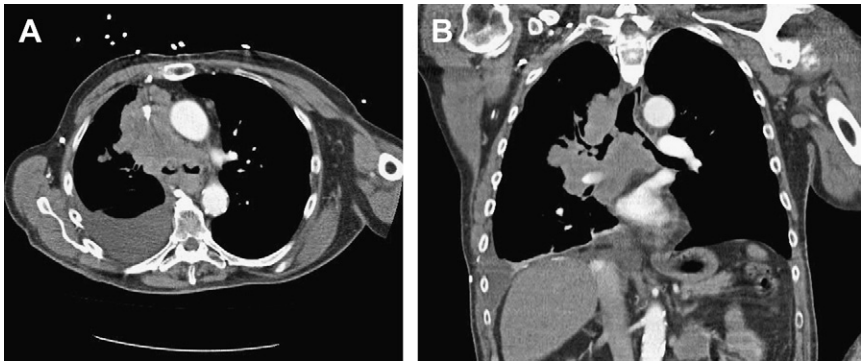

Fig. 7. Axial (*A*) and coronal (*B*) views of bilateral mainstem bronchi with intrinsic tumor masses causing obstruction from NSCLC.

cases that present de novo. Rigid bronchoscopy also allows for placement of metallic, self-expanding stents that are particularly useful for cases of extrinsic airway compression or control of bleeding. Flexible bronchoscopy can also be used to place certain stents, remove secretions or tumor, and obtaining tissue for diagnosis. Airway dilatation (bronchoplasty) can be completed, but the effect of this on malignant airway compression tends to be transient, and some other form of more definitive tumor control should follow, such as radiation or chemotherapy.

Stents

Several different types of stents are available for use in airway obstruction.[89] The most common stents are those made from silicone, metal, or a hybrid of the two. Stents are the treatment of choice to relieve acute airway obstruction in patients with extrinsic tumor compression[90] or with tracheoesophageal fistulas.[91] Although there is no evidence of a survival advantage for patients treated with stenting, 95% of patients do report relief of symptoms[88] after stent placement. Complications from stenting occur in up to 15% of patients, and include tumor ingrowth, stent migration (less common with metallic stents[92]), retained secretions, development of excessive granulation tissue, and, rarely, perforations.[93,94]

Laser

Neodymium-doped yttrium aluminum garnet (Nd:YAG) or CO_2 lasers can be used to open the airway in patients with malignant intrinsic airway obstruction.[95] A recent review[96] of the effectiveness of laser therapy showed a 76% decrease in dyspnea and 94% rate of hemoptysis control, with no procedure-related mortality. Similar to bronchoplasty, the effects are temporary and need to be combined with other antitumor therapies to maintain patent airways. Complications include perforation of the bronchial wall, combustion of the endotracheal tube or fiber-optic bronchoscope, hypoxemia, and respiratory failure.

Photodynamic Therapy

Photodynamic therapy is available at a limited number of centers. It uses the IV injection of light-sensitive molecules, then local activation of the material by exposure to light of a certain wavelength. Patients must avoid all sunlight exposure for up to 6 weeks following the procedure, as all tissues are exposed to the light-sensitizing

porphyrin. This technique is of limited value in acute airway obstruction because of its slow therapeutic effect.

Radiation Therapy

For tumors that are sensitive, whether airway obstruction is due to intrinsic tumor or extrinsic compression, radiation therapy can be an effective treatment. When airway obstruction is severe and acute, some more rapid intervention to establish airway and gas exchange is warranted, which may be then be supplemented by addition of radiation. External beam therapy is the most commonly applied modality, but, in regions that have previously undergone radiation therapy, local brachytherapy may be applicable.[97,98]

Chemotherapy

Tumors that are sensitive to chemotherapy, such as lymphomas, SCLCs, and germ cell tumors, may also respond rapidly to systemic chemotherapy. If gas exchange is sufficient to maintain the patient while administering chemotherapy, this is a reasonable treatment. For patients with critical airway compression, a more immediate form of therapy to alleviate the obstruction is called for, which can then be supplemented by subsequent chemotherapy.

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