Medical Emergencies in Oncology: II

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I. INTRODUCTION

Space-occupying lesions (from local tumor growth or metastatic spread) are a major cause of morbidity and mortality from malignancies. Depending on the location of these lesions, symptoms may be limited to local swelling and discomfort; however, if vital structures are affected, this constitutes a medical emergency. Spinal cord compression, superior vena cava syndrome, and brain masses often present with characteristic symptoms; these conditions require specific diagnostic and therapeutic measures, which are described in this manual.

This is the second part of a 2-part review on oncologic emergencies. The first part discussed the management of metabolic emergencies and neutropenic fever. The second part discusses the management of space-occupying lesions and also provides sample board review questions and answers for self assessment.

II. EMERGENCIES RELATED TO SPACE-OCCUPYING LESIONS

A. Epidural spinal cord compression
   1. Definition. It is caused by compression of the thecal sac by tumor in the epidural space at the level of the spinal cord or the cauda equina. This is one of the most common neurologic emergencies, occurring in about 5% of all cancer patients.1–5
   2. Etiology
      a. Cord compression most commonly occurs because of metastases from the prostate, lung, or breast; each account for 15% to 20% of all cases.4 It occurs less frequently in renal cell carcinoma, non-Hodgkin’s lymphoma (NHL), multiple myeloma, and gastrointestinal cancers.
      b. The location often depends on the underlying malignancy. Lung and breast cancers predominantly affect the thoracic spine where approximately 60% of all cases occur. Colorectal and pelvic tumors predominantly affect the lumbar-sacral spine, accounting for 30% of cases. The remaining cases affect the cervical spine. Multifocal involvement is present in 33% of all cases.
      c. Most complications occur because of growth of metastases from the vertebral bodies (Figure 1).
         1) However, paraspinal tumors,
generally from lymph node involvement, may grow through the intervertebral foramina to compress the thecal sac; this complication is especially common in malignant lymphoma. The enlarging tumor mass may initially obstruct the epidural venous plexus leading to vasogenic edema.

2) Spinal cord compression may also be caused by direct metastatic involvement of the spinal cord or by leptomeningeal carcinomatosis.

3. Clinical presentation. In up to 20% of patients, spinal cord compression may be the initial presentation of malignancy.
   a. Pain is the initial symptom in up to 96% of all patients and may precede the onset of other symptoms by weeks to several months. Although often nonspecific in nature, the pain typically worsens with coughing, sneezing, or lying in the recumbent position and improves when standing in the upright position. Therefore, patients may have pain occurring predominantly at night, in contrast to patients with degenerative disc disease whose pain typically occurs during the day.
   b. Of all patients with spinal cord compression, 75% present with lower extremity weakness at the time of diagnosis, which is typically symmetric.
   c. Sensory deficits are less frequent but still common; they may present as ascending bilateral or unilateral numbness and as paresthesias.
   d. Autonomic dysfunctions generally appear late and almost never as the sole initial symptom. Patients generally have a worse prognosis because this dysfunction implies bilateral cord or root damage.
   e. Ambulatory function at presentation is the best predictor of post-treatment outcome and length of survival. In general, 80% of patients who are ambulatory at the time of presentation will be ambulatory after treatment.

4. Diagnosis. Rapid diagnosis with appropriate referral for treatment is the most effective way to prevent substantial loss of function.

   a. Plain radiographs of the spine may be helpful if positive but are falsely negative in approximately 15% to 30% of patients because 30% to 50% of the bone substance must be involved before lesions are detectable on plain films.
   b. Bone scans can be used in conjunction with plain radiographs to effectively rule out spinal cord compression in patients with spinal symptoms. If both studies are negative, there is only an approximately 2% likelihood of spinal cord compression.
   c. MRI has become the diagnostic method of choice.
of choice because it permits rapid diagnosis and best anatomical resolution for radiation treatment planning.

d. CT myelography may be used if MRI is not available or the patient is not able to undergo MRI examination.

e. The entire spinal cord should be imaged before initiating radiation therapy because asymptomatic metastases may be detected.

f. It is important to differentiate spinal cord compression from other processes that can occur in cancer patients (Table 1).

5. Treatment. Spinal cord compression is often caused by advanced disease; therefore, the goal is palliation by trying to preserve mobility and relieve pain. In general, multimodality evaluation is recommended because treatment options consist of steroids, radiation therapy, and surgery.

a. Corticosteroids should be given immediately when spinal cord compression is suspected. These agents have been shown (ie, dexamethasone at 96 mg/day) to improve outcome in combination with radiation therapy when compared with radiation alone.9 No randomized controlled trial has defined the optimal dose and timing of corticosteroids, but initial doses of 10 and 100 mg did not show any difference in outcome. Daily doses of dexamethasone (ranging between 16 and 96 mg) are generally used, but some authors recommend the lower dose (4 mg, 4 times a day) in the absence of myelopathy to avoid the side effects of high-dose dexamethasone.10

b. External beam radiation is the treatment of choice for spinal cord compression. Radiation is directed only to symptomatic sites or asymptomatic areas with substantial epidural disease using a margin of 1 to 2 vertebral bodies. It is generally given at a dose of 2500 to 4000 cGy in 10 to 20 sessions over 2 to 4 weeks.3,10

c. Before the use of very focused radiation therapy, aggressive surgery with laminectomy and vertebrectomy was the treatment of choice for spinal cord compression. Although beneficial for a select group of patients—especially those with spinal instability, those who have not responded to radiation therapy, or those without a known primary tumor—it carries a mortality rate of 6% to 10%.

d. Chemotherapy may be useful in chemo-sensitive tumors such as Hodgkin’s lymphoma, NHL, germ cell tumors, and metastatic breast cancer.

e. The prognosis is poor for patients presenting with paralysis; they have a minimal chance for recovery, especially if symptoms have been present for more than 24 to 48 hours.

B. Superior vena cava syndrome

1. Definition. Superior vena cava (SVC) syndrome results from the obstruction of blood flow through the SVC, which can occur at several anatomical sites (Figure 2).

2. Etiology

a. Although previously SVC syndrome was caused predominantly by tuberculosis and syphilis, malignancy is now the most common cause of this syndrome (up to 97% of all cases).11 The SVC is 1.5 cm to 2.0 cm in diameter, has thin walls, and is easily compressible. It is surrounded by lymph nodes draining the right thorax and the inferior part of the left thorax. Therefore, the SVC can be compressed or invaded by metastases in mediastinal lymph nodes or directly by a malignancy.

b. Primary tumors are the most common cause of SVC obstruction, accounting for
80% of all cases. Breast cancer is the most common origin of metastases that cause SVC.12

c. The most common malignancies are lung cancer (up to 85% of all cases) followed by lymphoma.13 SVC syndrome develops in 2% to 4% of patients with lung cancer, more often when the primary tumor is on the right side. Small-cell lung cancer and squamous cell carcinoma are the most common histologic subtypes, accounting for up to 66% of the cases in lung cancer. Lymphoma causes approximately 9% of SVC syndrome in several series,14,15

d. Benign causes include cysts, goiter, thymoma, mediastinal inflammatory processes, and central venous catheters.

3. Clinical presentation

a. SVC syndrome may develop slowly or more rapidly, with the latter more likely to cause acute symptoms because sufficient collaterals have not developed. Symptoms may begin several weeks before presentation and may include the following (the percentage of all patients having these symptoms is shown).

1) Dyspnea, 63%
2) Cough, 55%
3) Pain, 20%
4) Dysphagia, 12%
5) Syncope, 7%

Figure 2. Anatomical locations of SVC obstruction, leading to the SVC syndrome. IVC = inferior vena cava; SVC = superior vena cava. Reprinted from Skarin AT, editor. Atlas of diagnostic oncology. 2nd ed. Mosby, 1996:88, by permission of the publisher, Mosby.
b. Jugular or thoracic venous distention, facial edema or plethora, and cyanosis are commonly found on physical examination (Figure 3). Patients may have had recent nightmares, presumably caused by central nervous system irritation caused by the venous obstruction.

4. Diagnosis
   a. The clinical presentation is often very typical, strongly suggesting the diagnosis.
   b. Only 16% of patients present with a normal chest film. Chest radiographs often show the following (the percentage of all patients having these abnormalities is given).\(^\text{14}\)
      1) Mediastinal widening, 64%
      2) Pleural effusions, 26%
      3) Right hilar mass, 12%
   c. Chest CT or MRI gives further information about anatomical relations and whether the obstruction is caused by an extrinsic or intrinsic process; this imaging often obviates the need for superior venacavography or nuclear imaging.
   d. Magnetic resonance angiography is useful in evaluating clot formation in the SVC.
   e. Bronchoscopy with sputum cytology is positive in 33% to 68% of all patients.\(^\text{13,16}\)
   f. Thoracentesis may yield the diagnosis if pleural effusion is present.
   g. Previously, radiation therapy was often applied emergently to the obstructing lesion often before establishing a histologic diagnosis. However, more recently, mediastinoscopy performed by experienced thoracic surgeons has been carried out to obtain a tissue diagnosis with a success rate of 80% to 100% in order to target therapy appropriately.\(^\text{17}\) The procedure can be safely carried out in most patients. Excess bleeding or infection is rarely encountered.
   h. Supraclavicular lymph node biopsy can be diagnostic in up to 87% of patients but is rarely performed without palpable adenopathy.
   i. Thoracotomy is rarely indicated to establish the diagnosis.

5. Treatment options depend on the underlying pathology and whether the disease is amenable to a curative approach at presentation. Appropriate staging can often be delayed until the acute symptoms are controlled.\(^\text{18}\)
   a. In patients with small-cell lung cancer, multiagent chemotherapy results in rapid improvement. In a recent study, the response to chemotherapy or radiation was the same for patients with small-cell lung cancer.\(^\text{19}\) In patients with malignant lymphoma or non-Hodgkin’s disease, initial chemotherapy may be followed by radiotherapy depending on the stage of
disease. For patients with non–small-cell lung cancer or other metastatic malignancies, radiotherapy is generally used first for relief of the SVC syndrome and local disease control. In randomized studies, corticosteroids have not shown any major improvement in the response.

b. Patients who do not respond to these treatments or those who have recurrent SVC syndrome after previous treatment can be treated with endovascular stents. These stents are placed by interventional radiologists and have become more popular for the treatment of SVC syndrome in recent years. The stents are inserted in the SVC and normally relieve symptoms within 48 hours of the procedure.20

1) Anticoagulation may be useful until full stent expansion has occurred.
2) Complications of stent placement include migration, stent fracture, stent thrombosis (approximately 20%), infection, and pulmonary edema secondary to cardiac decompensation with rapidly increased venous return.

c. Rarely, patients develop persistent thrombi with chronic SVC syndrome, which may respond to endovascular stents or bypass procedures.

C. **Brain mass**

1. Definition. Brain metastases are a common and potentially devastating complication of systemic cancer.

2. Etiology

a. Metastases develop in 10% to 30% of all patients and present as a single metastasis in 25% to 50% of patients. Although any primary tumor can result in brain metastases, they are most commonly seen in patients with the following cancers (percentages of metastases are given):10,21

   1) Lung, 50%
   2) Breast, 15% to 20%
   3) Melanoma, 10%
   4) Unknown primary, 8% to 10%

b. Most often, metastases occur via hematogenous spread and localize according to the cerebral blood flow: 80% to 90% involve the hemispheres, 10% to 15% involve the cerebellum, and 5% involve the brain stem. Pelvic tumors metastasize more frequently to the posterior fossa.

c. Metastases are more commonly found at the junction of the gray and white matter because cerebral blood vessels get smaller and tumor cells may become trapped in this area.

d. Although most brain metastases (80%) are the complication of a known primary malignancy, occasionally they may be the initial presentation or may occur synchronously with the primary tumor.

e. Complications mainly arise by different mechanisms:

   1) A growing tumor mass with associated vasogenic brain edema leads to progressive focal neurologic dysfunction.
   2) Seizures occur as the presenting symptom in 10% to 20% of patients.
   3) Thromboembolic events, blockage of vessels by tumor cells, or hemorrhage into a metastasis will cause classic features of stroke.
   4) Meningeal metastases occur infrequently but develop particularly in patients with lung, breast, and bladder cancers, as well as high-grade lymphomas.

3. Clinical presentation. Symptoms are related to the location of the metastasis in the brain and the underlying mechanism of injury, occurring in more than 66% of all patients (Table 2).10,22,23

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headaches</td>
<td>40–50</td>
</tr>
<tr>
<td>Focal neurologic deficits</td>
<td>20–40</td>
</tr>
<tr>
<td>Seizures</td>
<td>15–20</td>
</tr>
<tr>
<td>Cognitive deficits</td>
<td>15–75</td>
</tr>
</tbody>
</table>

a. Headaches occur normally on the same side as the tumor, are usually dull; non-throbbing; and may be associated with nausea, vomiting, or blurry vision.

b. Focal deficits may present in a rapid, stroke-like fashion or more insidiously.

c. Unusual behavior, forgetfulness, and sudden fatigue may herald meningeal carcinomatosis.
4. Diagnosis. CT or MRI are the diagnostic modalities of choice in cancer patients with neurologic symptoms.
   a. Although MRI is more sensitive and allows differentiation of metastases from other lesions and readily defines meningeal metastasis, CT is more readily available.
   b. Tumors are typically ring enhancing with marked edema, occurring at the junction of the gray and white matter. Apparent solitary metastases are present in approximately 50% of all cases.

5. Treatment strategies include those aimed to provide symptomatic relief and those to remove metastases.
   a. Corticosteroids are indicated as immediate therapy in any patient with symptomatic edema. They act by decreasing capillary membrane permeability. Dosing schedules are largely empirical; however, 10 mg of dexamethasone as loading dose, followed by 16 mg daily (given in 4 doses) is frequently used. If the patient does not respond, the dose may be increased up to 100 mg/day.10,24
   b. Patients with increased intracranial pressure who are at risk for herniation should receive high-dose steroids, osmotic therapy with IV mannitol (0.5 to 2.0 mg/kg), and hyperventilation to lower the pCO₂ (partial pressure of arterial CO₂) to 25 to 30 mm Hg.
   c. Anticonvulsants should be given to every patient presenting with metastasis-related seizures, preferably as single agent therapy using carbamazepine, phenobarbital, or phenytoin. Although commonly given prophylactically to patients with brain metastases, recent studies have not shown the efficacy of this treatment.25 Therefore, prophylactic therapy is not recommended because of the substantial side effects related to anticonvulsant therapy (ie, Stevens-Johnson syndrome, bone marrow depression).
   d. Anticoagulants have now been shown to be safe in patients with systemic thromboembolic complications, although previously they were generally felt to be contraindicated in patients with brain metastases because of the high risk of intracranial bleeding. Anticoagulation may be used—unless contraindicated because of recent craniotomy, thrombocytopenia, risk of falling down, or poor compliance—where inferior vena cava filters are indicated.26
   e. For patients with an unknown primary malignancy or single brain metastasis, neurosurgery followed by radiation therapy to the whole brain has been shown to be superior to radiation alone with regard to symptom relief and survival.27,28 Patients with stable extracranial disease can especially benefit from this treatment. Modern techniques involving stereotactic radiosurgery have been widely used with minimal side effects and a high rate of local control.
   f. In multiple brain metastases, surgery is only indicated to provide relief from a large, life-threatening tumor mass or to obtain tissue for diagnosis of an unknown primary cancer. Total cranial radiation (30 to 50 Gy in 10 to 20 fractions) is the treatment of choice to palliate neurologic symptoms. Survival is generally determined by the extent of extracranial disease.
   g. With the exception of leukemia or lymphoma, meningeal tumor involvement carries a poor prognosis with survival limited to several weeks. New treatment strategies with depot forms of cytosine arabinoside may relieve symptoms and prolong survival in some patients.

III. SUMMARY

A. Space-occupying lesions represent true oncologic emergencies if they affect vital structures.
B. Epidural spinal cord compression is the most common neurologic complication of cancer, typically caused by metastases from prostate, lung, or breast cancer. Pain is the initial symptom in almost all patients, and ambulatory function at presentation is the best predictor of outcome. Magnetic resonance imaging has become the primary diagnostic method, and treatment consists of corticosteroids given immediately and radiation treatment.
C. Superior vena cava (SVC) syndrome is most
commonly caused by direct obstruction of the 
SVC by lung cancer or lymphoma. The typical 
presentation includes dyspnea, cough, jugular 
venous distention, and facial swelling. Mediastinoscopy has the highest diagnostic yield in 
patients presenting without known malignancy. 
Treatment is disease specific but also depends 
on whether curative or palliative treatment is 
required.

D. Brain metastases develop in 10% to 30% of all 
cancer patients and occur via hematogenous 
spread. Most of these metastases are caused by 
lung and breast cancer, but they can also be 
caused by melanoma. Headaches are present in 
50% of the patients, and computed tomography 
or magnetic resonance imaging are the diagnostic 
modalities of choice. Treatment options include 
corticosteroids as well as osmotic therapy and 
hyperventilation if herniation is a concern. 
Depending on location and number of metas-
tases, surgery and radiation are indicated.

BOARD REVIEW QUESTIONS

More than one answer may be correct for the following 
questions. Note that some of these questions pertain to 
material in the first part of this manual (Hospital Physician 
Oncology Board Review Manual, Volume 5, Part 4, "Medical 
Emergencies in Oncology: I").

1. Patient 1 is a 31-year-old woman who receives in-
duction chemotherapy for acute myelogenous 
leukemia. She has the following laboratory values 
12 hours after her first chemotherapy dose: potas-
sium, 8.2 mmol/L; uric acid, 12 mg/dL; phospho-
rus, 6.8 mg/dL; and creatinine, 1.5 mg/dL. Her 
electrocardiogram shows absent P-waves and QRS 
prolongation. What is the appropriate order of 
treatments in patient 1?
A) Sodium polystyrene sulfonate and lactulose 
B) Intravenous glucose and subcutaneous insulin 
C) Intravenous calcium gluconate 
D) Intravenous loop diuretics

2. After patient 1 receives successful induction che-
motherapy, she undergoes consolidation che-
motherapy. Twelve days after her first dose, when the 
patient is at home, she reports chills and a tempera-
ture of 39.2 °C. Patient 1 is not receiving prophyl-
lactic antibiotics or growth factors. Which is the appropriate step?
A) Admit the patient for empiric therapy with 
ceftazidime, amphotericin, and vancomycin 
B) Call in a prescription for granulocyte–colony-
stimulating factor and advise her to take 
aspirin 
C) Admit the patient for observation 
D) Admit the patient for empiric therapy with 
ceftazidime

3. Patient 2 is a 57-year-old woman with metastatic 
breast cancer who presents to the office with in-
creasing lethargy, thirst, polyuria, and consti-
pation. Her serum calcium level is 15.7 mg/dL. 
What is the appropriate order of initial treatment 
in patient 2?
A) Dexamethasone (10 mg) 
B) Pamidronate (90 mg) 
C) Aggressive hydration with normal saline 
D) Furosemide (80 mg)

4. Patient 2 is successfully treated for the hypercal-
cemia. She calls 3 months later, stating she has just 
developed pain in her lower back that is radiating 
down her legs. She denies incontinence and is able 
to walk up 2 flights of stairs to her apartment. 
Which is the most appropriate step?
A) Referral to radiation therapist for immediate 
lumbar spine radiation therapy 
B) Prescription of stronger analgesic over the 
phone 
C) Immediate referral to emergency department 
for clinical evaluation and urgent CT or MRI 
D) Appointment for office visit the following 
Monday 
E) Prescription of 3-day course of dexametha-
sone (20 mg/day) over the phone

5. Patient 3 is a 71-year-old smoker with extensive dis-
case caused by small-cell lung cancer that is now 
refractory after multiple chemotherapy regimens. 
He has a history of superior vena cava (SVC) syn-
drome. He now presents with shortness of breath 
and facial swelling. Chest CT suggests recurrent 
obstruction of the SVC. What is the most appropri-
ate step?
A) High-dose steroids 
B) Single-agent chemotherapy 
C) Referral to thoracic surgery for local debulk-
ing 
D) Referral to interventional radiology for 
endovascular stenting 
E) Initiation of anticoagulation
DETAILED ANSWERS

1. (C, B, D, A) Intravenous (IV) calcium gluconate; IV glucose and subcutaneous insulin; IV loop diuretics; then sodium polystyrene sulfonate [Kayexalate] and lactulose. Patient 1’s laboratory studies are typical of the acute tumor lysis syndrome, typically associated with high tumor burden in leukemias or lymphomas. She also shows evidence of severe hyperkalemia with substantial electrocardiogram changes and may develop life-threatening arrhythmias at any time. Rapid administration of calcium gluconate (10 mL of a 10% solution) is indicated to decrease membrane excitability, followed by administration of insulin and glucose to shift K+ intracellularly, which will temporarily lower the extracellular K+ concentration. Loop diuretics increase renal K+ excretion if renal function is adequate, and cation exchange resins (sodium polystyrene sulfonate given with lactulose to prevent constipation) promote Na+/K+ exchange in the gastrointestinal tract.

2. (D) Admit the patient for empiric therapy with cefazidine. Febrile neutropenia is a common complication of high-dose consolidation chemotherapy for acute myelogenous leukemia. Even if the patient has no other comorbidities or risk factors, rapid administration of broad-spectrum antibiotics (ie, third-generation cephalosporin or carbapenem) and hospitalization are indicated. Vancomycin is only used if gram-positive cocci are suspected (eg, obvious line infection). Antifungal therapy is not recommended as initial treatment, and aspirin is not advisable in a patient who is likely pancytopenic.

3. (C, B) Aggressive hydration with normal saline; pamidronate (90 mg). Patient 2 has hypercalcemia related to her bone metastases. Her symptoms also suggest substantial dehydration. Aggressive hydration will initially lower serum calcium levels, and administration of bisphosphonates is most effective in lowering calcium levels. Calcitonin may also be used because it acts more rapidly than pamidronate; however, pamidronate is much more effective. Steroids are more helpful in the cytokine-mediated hypercalcemia in lymphoma. Once the patient is rehydrated, furosemide can be used to enhance renal calcium excretion.

4. (C) Immediate referral to emergency department for clinical evaluation and urgent CT or MRI. Patient 2 describes typical symptoms suggestive of early spinal cord compression. Because her prognosis is dependent on rapid diagnosis and treatment, she should be evaluated immediately to initiate treatment if necessary.

5. (D) Referral to interventional radiology for endovascular stenting. Patient 3 presents with recurrent SVC syndrome from small-cell lung cancer. Given the previous treatment, palliation to relieve his symptoms is the primary treatment goal. This palliation is best achieved by endovascular stenting. Single-agent chemotherapy is unlikely to have an effect because the disease has become refractory to treatment; surgery will likely result in substantial morbidity without long-term benefit. Steroids are useful in the treatment of SVC syndrome caused by lymphoma.

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