ONCOLOGY

PARSA ROSTAMI.MD
HEMATOLOGIST & MEDICAL ONCOLOGIST

Oncologic Emergencies

SUPERIOR VENA CAVA SYNDROME

- Superior vena cava syndrome (SVCS) is the clinical manifestation of superior vena cava (SVC) obstruction, with severe reduction in venous return from the head, neck, and upper extremities.
- Malignant tumors, such as lung cancer, lymphoma, and metastatic tumors, are responsible for the majority of SVCS cases.
- With the expanding use of intravascular devices (e.g., permanent central venous access catheters, pacemaker/ defibrillator leads), the prevalence of benign causes of SVCS is increasing now, accounting for at least 40% of cases.

ETIOLOGY

- Lung cancer, particularly of small-cell and squamous cell histologies, accounts for ~85% of all cases of malignant origin.
- In young adults, malignant lymphoma is a leading cause of SVCS. Hodgkin's lymphoma involves the mediastinum more commonly than other lymphomas but rarely causes SVCS.
- When SVCS is noted in a young man with a mediastinal mass, the differential diagnosis is lymphoma versus primary mediastinal germ cell tumor.

- Metastatic cancers to the mediastinal lymph nodes, such as testicular and breast carcinomas, account for a small proportion of cases.
- Other causes include ***benign tumors***, aortic aneurysm, thyromegaly, thrombosis, and fibrosing mediastinitis from prior irradiation, histoplasmosis, or Behçet's syndrome.

CLINICAL MANIFESTATIONS

- Patients with SVCS usually present with neck and facial swelling (especially around the eyes), dyspnea, and cough.
- Other symptoms include hoarseness, tongue swelling, headaches, nasal congestion, epistaxis, hemoptysis, dysphagia, dizziness, syncope, and lethargy. Bending forward or lying down may aggravate the symptoms.
- The characteristic physical findings are dilated neck veins; an increased number of collateral veins covering the anterior chest wall; cyanosis; and edema of the face, arms, and chest

- Facial swelling and plethora are typically exacerbated when the patient is supine. More severe cases include proptosis and laryngeal edema, and obtundation.
- Symptoms are usually progressive, but in some cases, they may improve as collateral circulation develops.
- Signs and symptoms of cerebral and/or laryngeal edema, though rare, are associated with a poorer prognosis and require urgent evaluation.

- Seizures are more likely related to brain metastases than to cerebral edema from venous occlusion.
- Patients with small-cell lung cancer and SVCS have a higher incidence of brain metastases than those without SVCS.
- Cardiorespiratory symptoms at rest, particularly with positional changes, suggest significant airway and vascular obstruction and limited physiologic reserve.
- ***Cardiac arrest or respiratory failure can occur, particularly in patients receiving sedatives or undergoing general anesthesia***

- Rarely, esophageal varices may develop, particularly in the setting of SVC syndrome due to hemodialysis catheter.
- If the obstruction involves or is distal to the azygous vein, varices occur in the entire length of the esophagus.
- ***Variceal bleeding may be a late complication of chronic SVCS***.

DIAGNOSIS

- The diagnosis of SVCS is a clinical one.
- The most significant chest radiographic finding is widening of the superior mediastinum, most commonly on the right side.
- Pleural effusion occurs in only 25% of patients, often on the right side.
- The majority of these effusions are exudative and occasionally chylous.
- However, a normal chest radiograph is still compatible with the diagnosis if other characteristic findings are present.
- Computed tomography (CT) provides the most reliable view of the mediastinal anatomy.

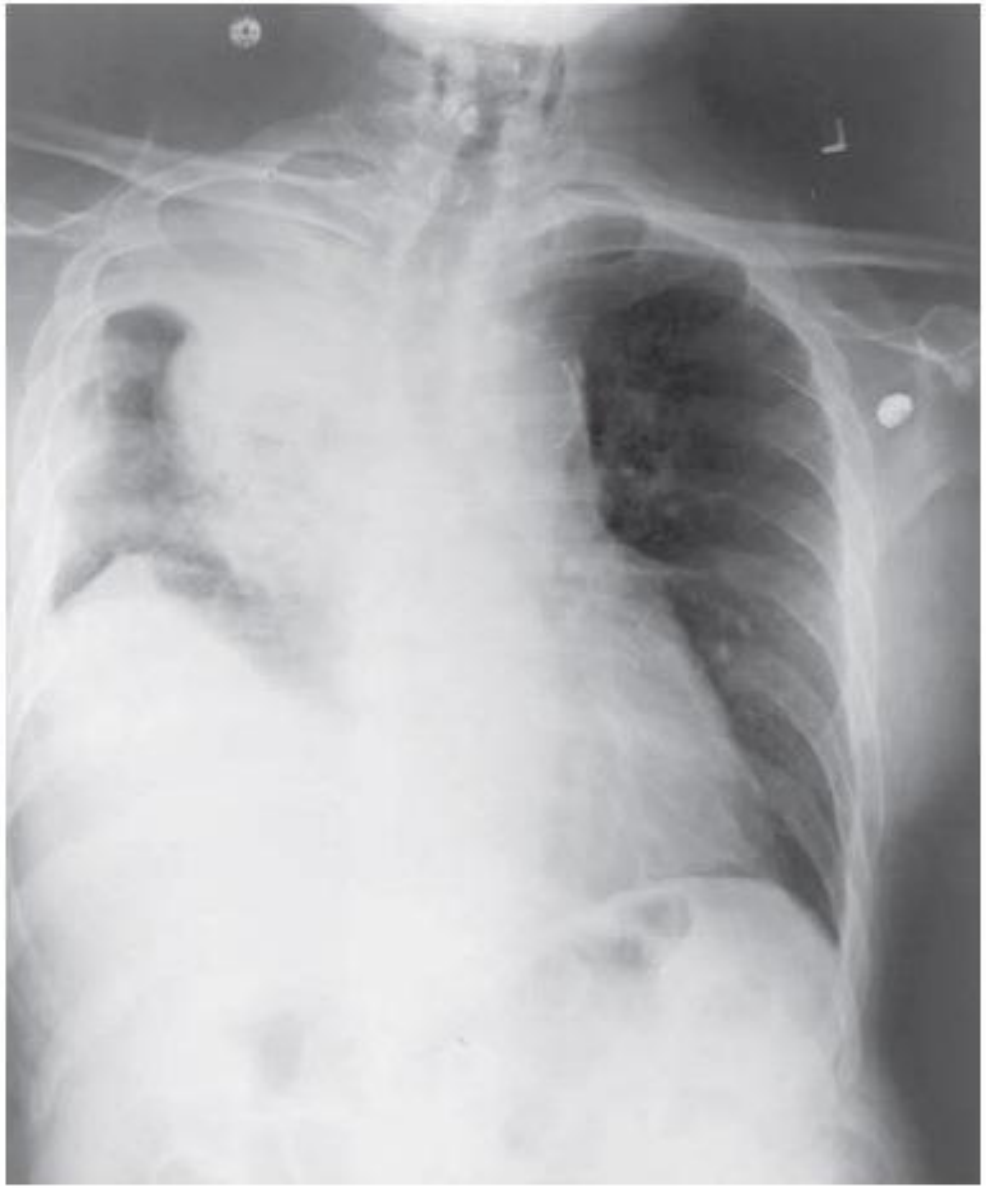
- The diagnosis of SVCS requires diminished or absent opacification of central venous structures with prominent collateral venous circulation.
- Magnetic resonance imaging (MRI) is increasingly being used to diagnose SVC obstruction with a 100% sensitivity and specificity, but dyspneic SVCS patients may have difficulty remaining supine for the entire imaging process.
- Invasive procedures, including bronchoscopy, percutaneous needle biopsy, mediastinoscopy, and even thoracotomy, can be performed by a skilled clinician without any major risk of bleeding.

- For patients with a known cancer, a detailed workup usually is not necessary, and appropriate treatment may be started after obtaining a CT scan of the thorax.
- For those with no history of malignancy, a detailed evaluation is essential to rule out benign causes and determine a specific diagnosis to direct the appropriate therapy.

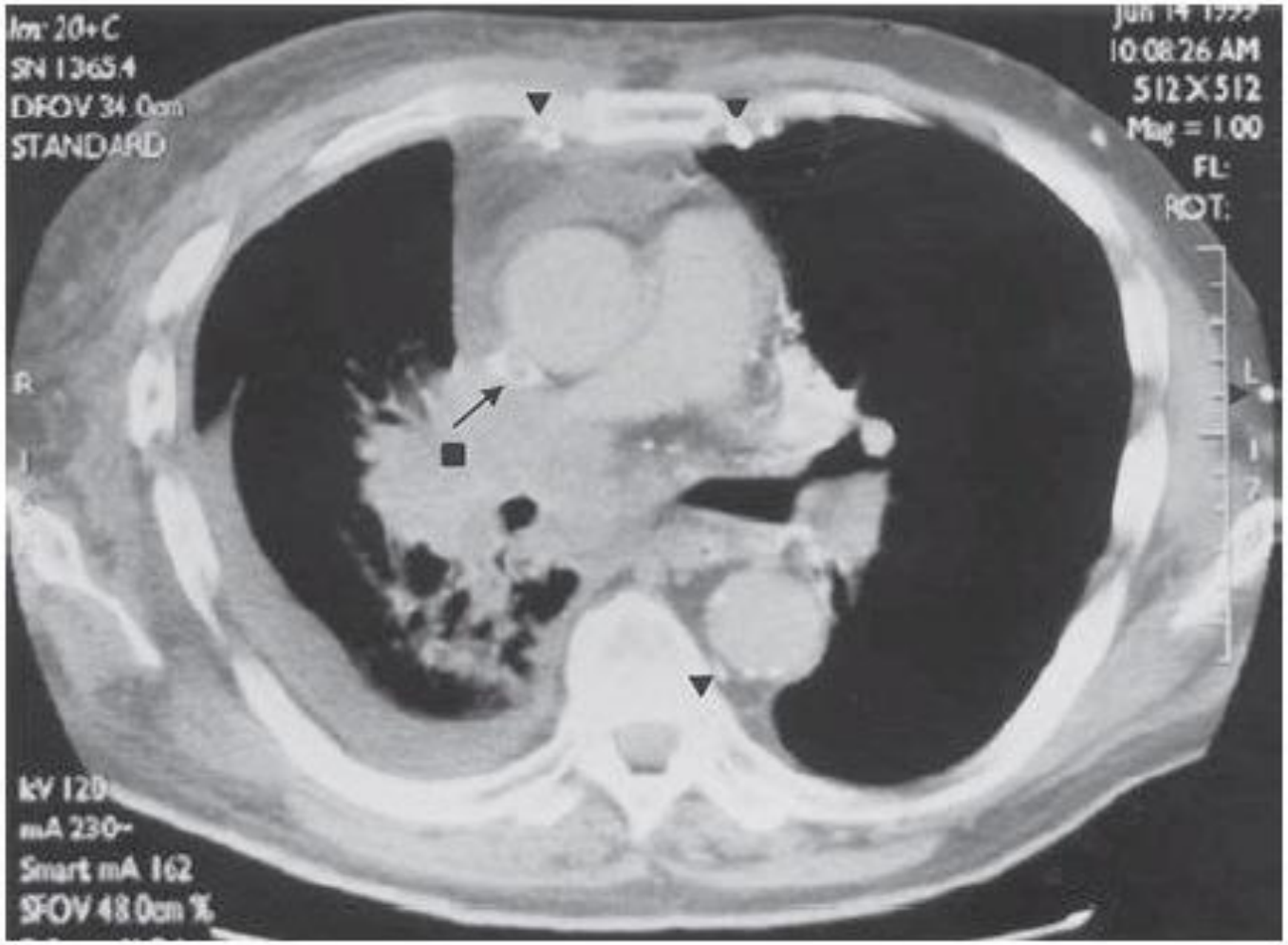
TREATMENT
Superior Vena Cava Syndrome

- The one potentially life-threatening complication of a superior mediastinal mass is tracheal obstruction.
- Upper airway obstruction demands emergent therapy. Diuretics with a low-salt diet, head elevation, and oxygen may produce temporary symptomatic relief.
- Glucocorticoids have a limited role except in the setting of mediastinal lymphoma masses.

- Radiation therapy is the primary treatment for SVCS caused by non-small-cell lung cancer and other metastatic solid tumors.
- Chemotherapy is effective when the underlying cancer is small-cell carcinoma of the lung, lymphoma, or germ cell tumor.
- SVCS recurs in 10–30% of patients; it may be palliated with the use of intravascular self-expanding stents .



A


Im: 20+C
SN 13654
DFOV 34.0cm
STANDARD
10:08:26 AM
512X512
Mag = 1.00
FL:
ROT:
R
L
kV 120
mA 230~
Smart mA 162
SFOV 48.0cm %

B

- Early stenting may be necessary in patients with severe symptoms; however, the prompt increase in venous return after stenting may precipitate heart failure and pulmonary edema.
- Other complications of stent placement include hematoma at the insertion site, SVC perforation, stent migration in the right ventricle, stent fracture, and pulmonary embolism.

SPINAL CORD COMPRESSION

- Malignant spinal cord compression (MSCC) is defined as compression of the spinal cord and/or cauda equina by an extradural tumor mass.
- Spinal cord compression occurs in 5–10% of patients with cancer.
- The underlying cancer is usually identified during the initial evaluation; **lung cancer is the most common cause of MSCC.**

ETIOLOGY

- **Metastatic tumor** involves the vertebral column more often than any other part of the bony skeleton.
- Lung, breast, and prostate cancers are the most frequent offenders.
- Multiple myeloma also has a high incidence of spine involvement.
- Lymphomas, melanoma, renal cell cancer, and genitourinary cancers also cause cord compression.
- The thoracic spine is the most common site (70%), followed by the lumbosacral spine (20%) and the cervical spine (10%).

- Involvement of multiple sites is most frequent in patients with breast and prostate carcinoma.

- Another cause of cord compression is direct extension of a paravertebral lesion through the intervertebral foramen.
- These cases usually involve a lymphoma, myeloma, or pediatric neoplasm. Parenchymal spinal cord metastasis due to hematogenous spread is rare.

- Intramedullary metastases can be seen in lung cancer, breast cancer, renal cancer, melanoma, and lymphoma, and are frequently associated with brain metastases and leptomeningeal disease.
- Expanding extradural tumors induce injury through several mechanisms.
- Expanding extradural tumors induce mechanical injury to axons and myelin. Compression compromises blood flow, leading to ischemia and/or infarction.

CLINICAL MANIFESTATIONS

- The most common initial symptom in patients with spinal cord compression is localized back pain and tenderness due to involvement of vertebrae by tumor.
- Pain is usually present for days or months before other neurologic findings appear. It is exacerbated by movement and by coughing or sneezing.
- It can be differentiated from the pain of disk disease by the fact that it worsens when the patient is supine. Radicular pain is less common than localized back pain and usually develops later.

- Typical cervical radicular pain radiates down the arm;
- in the lumbar region, the radiation is down the legs.
- **Lhermitte's sign**, a tingling or electric sensation down the back and upper and lower limbs upon flexing or extending the neck, may be an early sign of cord compression.
- Loss of bowel or bladder control may be the presenting symptom but usually occurs late in the course.
- Occasionally patients present with ataxia of gait without motor and sensory involvement due to involvement of the **spinocerebellar tract.**

- On physical examination, pain induced by straight leg raising, neck flexion, or vertebral percussion may help to determine the level of cord compression.
- Patients develop numbness and paresthesias in the extremities or trunk.
- *Loss of sensibility* to pinprick is as common as loss of sensibility to vibration or position.
- *Motor findings* include weakness, spasticity, and abnormal muscle stretching. An extensor plantar reflex reflects significant compression.

- Motor and sensory loss usually precedes sphincter disturbance.
- Patients with ***autonomic dysfunction*** may present with decreased anal tonus, decreased perineal sensibility, and a distended bladder.
- The absence of the anal wink reflex or the bulbocavernosus reflex confirms cord involvement.
- In doubtful cases, evaluation of postvoiding urinary residual volume can be helpful.

- Other illnesses that may mimic cord compression include osteoporotic vertebral collapse, disk disease, pyogenic abscess or vertebral tuberculosis, radiation myelopathy, neoplastic leptomeningitis, benign tumors, epidural hematoma, and spinal lipomatosis.

- Cauda equina syndrome is characterized by low back pain; diminished sensation over the buttocks, posterior-superior thighs, and perineal area in a saddle distribution; rectal and bladder dysfunction; sexual impotence; absent bulbocavernous, patellar, and Achilles' reflexes; and variable amount of lower-extremity weakness.
- This reflects compression of nerve roots as they form the cauda equina after leaving the spinal cord.
- The majority of cauda equine tumors are primary tumors of glial or nerve sheath origin; metastases are very rare.

TREATMENT

- Patients with cancer who develop back pain should be evaluated for spinal cord compression as quickly as possible
- Treatment is more often successful in patients who are ambulatory and still have sphincter control at the time treatment is initiated.
- Patients should have a neurologic examination and plain films of the spine.
- Those whose physical examination suggests cord compression should receive dexamethasone starting immediately.

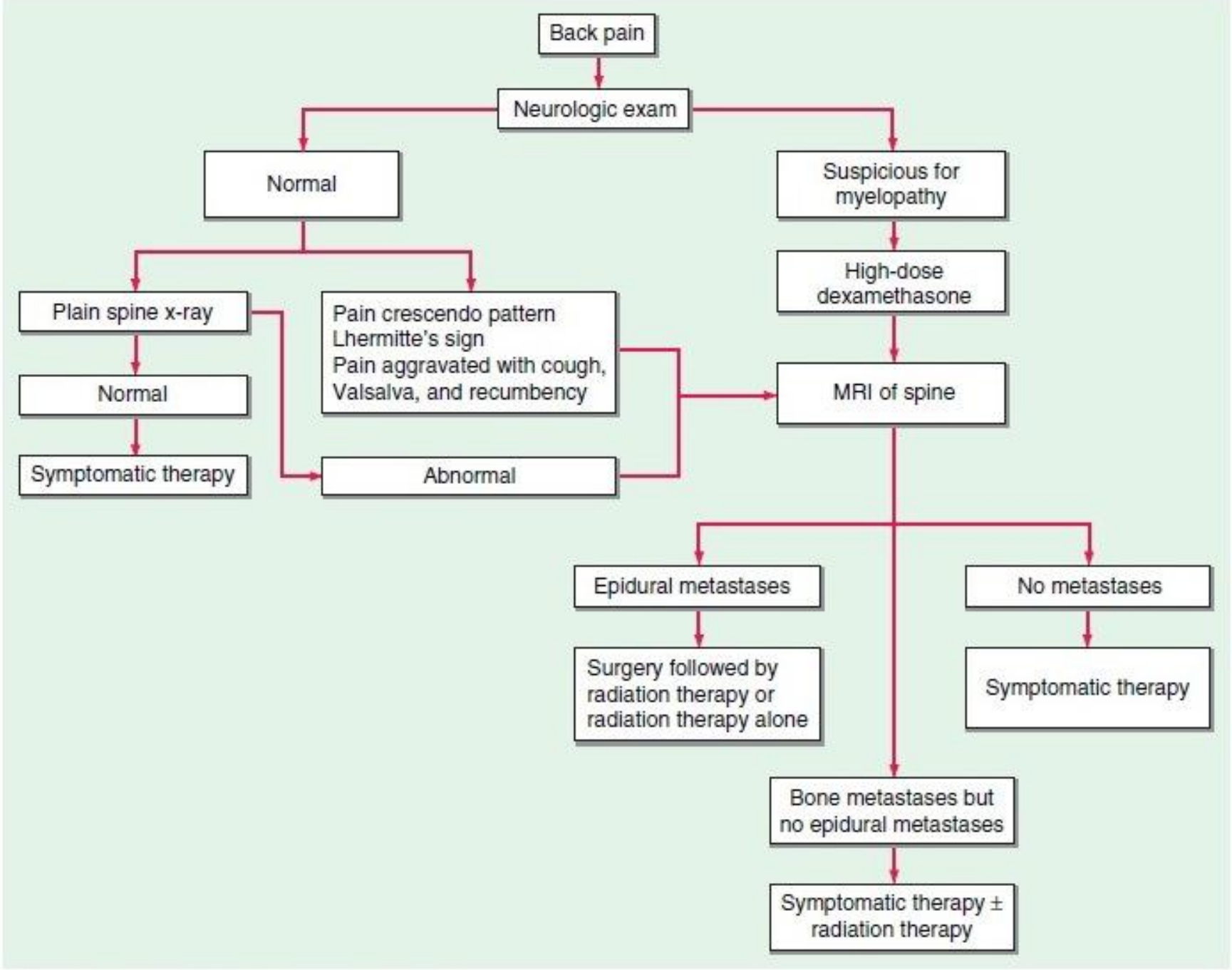


FIGURE 71-2 Management of cancer patients with back pain.

- In patients with cord compression and an unknown primary tumor, a simple workup including chest radiography, mammography, measurement of prostate-specific antigen, and abdominal CT usually reveals the underlying malignancy.

TREATMENT

Spinal Cord Compression

- The treatment of patients with spinal cord compression is aimed at relief of pain and restoration/preservation of neurologic function
- Management of MSCC requires a multidisciplinary approach.
- Radiation therapy plus glucocorticoids is generally the initial treatment of choice for most patients with spinal cord compression

TREATMENT-RELATED EMERGENCIES TUMOR LYSIS SYNDROME

- Tumor lysis syndrome (TLS) is characterized by hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, and is caused by the destruction of a large number of rapidly proliferating neoplastic cells.
- Acidosis may also develop. Acute renal failure occurs frequently.

ETIOLOGY

- TLS is most often associated with the treatment of Burkitt's lymphoma, acute lymphoblastic leukemia, and other rapidly proliferating lymphomas, but it also may be seen with chronic leukemias and, rarely, with solid tumors.
- TLS has been observed with administration of glucocorticoids, hormonal agents such as letrozole and tamoxifen, and monoclonal antibodies such as rituximab and gemtuzumab.

- TLS usually occurs during or shortly (1–5 days) after chemotherapy. Rarely, spontaneous necrosis of malignancies causes TLS.

- Effective treatment kills malignant cells and leads to increased serum uric acid levels from the turnover of nucleic acids.
- Owing to the acidic local environment, uric acid can precipitate in the tubules, medulla, and collecting ducts of the kidney, leading to renal failure.
- Lactic acidosis and dehydration may contribute to the precipitation of uric acid in the renal tubules.

- The finding of uric acid crystals in the urine is strong evidence for uric acid nephropathy. The ratio of urinary uric acid to urinary creatinine is >1 in patients with acute hyperuricemic nephropathy and <1 in patients with renal failure due to other causes.
- Hyperphosphatemia, which can be caused by the release of intracellular phosphate pools by tumor lysis, produces a reciprocal depression in serum calcium, which causes severe neuromuscular irritability and tetany.

- Deposition of calcium phosphate in the kidney and hyperphosphatemia may cause renal failure.
- Potassium is the principal intracellular cation, and massive destruction of malignant cells may lead to hyperkalemia.
- **Hyperkalemia** in patients with renal failure may rapidly become life threatening by causing ventricular arrhythmias and sudden death.

- Hyperuricemia and high serum levels of lactate dehydrogenase (LDH >1500 U/L), both of which correlate with total tumor burden, also correlate with the risk of TLS.
- In patients at risk for TLS, pretreatment evaluations should include a complete blood count, serum chemistry evaluation, and urine analysis.
- High leukocyte and platelet counts ***may artificially*** elevate potassium levels ("pseudohyperkalemia") due to lysis of these cells after the blood is drawn.

- In pseudohyperkalemia, no electrocardiographic abnormalities are present.
- Urine output should be watched closely.

TREATMENT
Tumor Lysis Syndrome

- Recognition of risk and prevention are the most important steps in the management of this syndrome .

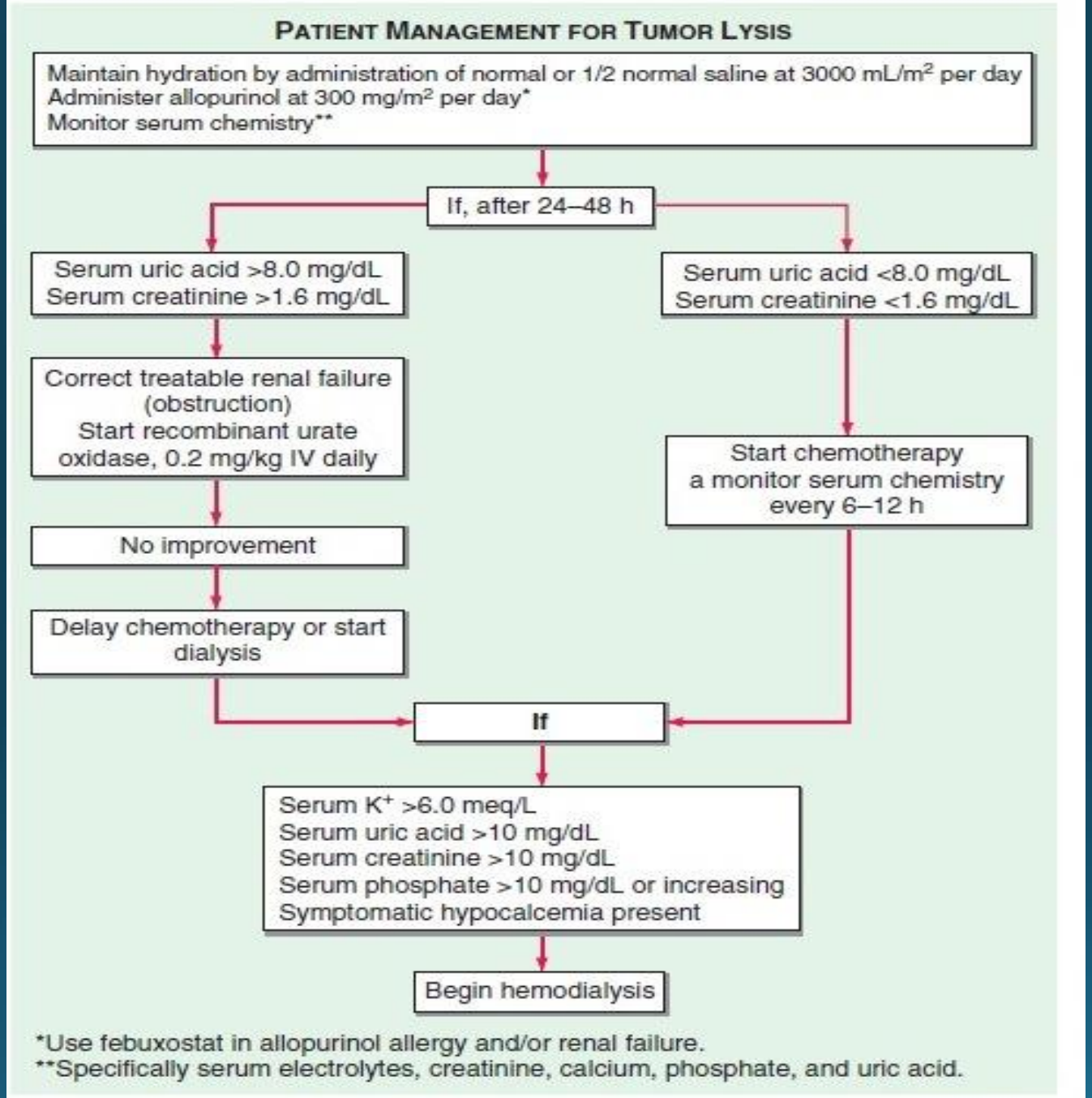


FIGURE 71-4 Management of patients at high risk for the tumor lysis syndrome.

Infections in Patients with Cancer

INTRODUCTION

- Infections are a common cause of death and an even more common cause of morbidity in patients with a wide variety of neoplasms.
- Autopsy studies show that most deaths from acute leukemia and half of deaths from lymphoma are caused directly by infection.
- Fortunately, an evolving approach to prevention and treatment of infectious complications of cancer has decreased infection-associated mortality rates and will probably continue to do so. This accomplishment has resulted from three major steps:

- Early treatment: The practice of using "early empirical" antibiotics reduced mortality rates among patients with leukemia and bacteremia from 84% in 1965 to 44% in 1972. The mortality rate due to infection in febrile neutropenic patients dropped to <10% by 2013.
- This dramatic improvement is attributed to early intervention with appropriate antimicrobial therapy

- Empirical treatment: “Empirical” antifungal therapy has also lowered the incidence of disseminated fungal infection, with dramatic decreases in mortality rates.
- An antifungal agent is administered—on the basis of likely fungal infection—to neutropenic patients who, after 4–7 days of antibiotic therapy, remain febrile but have no positive cultures.

- Prophylaxis: Use of antibiotics for afebrile neutropenic patients as broad-spectrum prophylaxis against
- infections has decreased both mortality and morbidity even further.
- The current approach to treatment of severely neutropenic patients (e.g., those receiving high-dose chemotherapy for leukemia or high grade lymphoma) is based on initial prophylactic therapy at the onset of neutropenia, subsequent
- "empirical" antibacterial therapy targeting the organisms whose involvement is likely in light of physical
- findings (most often fever alone), and finally "empirical" antifungal therapy based on the known likelihood that fungal infection will become a serious issue after 4–7 days of broad-spectrum antibacterial therapy.

HUMAN ANTIBODY INFUSION REACTIONS

- The initial infusion of human or humanized antibodies (e.g., rituximab, gemtuzumab, trastuzumab, alemtuzumab, panitumumab, brentuximab vedotin, blinatumomab) is associated
- with fever, chills, nausea, asthenia, and headache in up to half of treated patients. Bronchospasm and hypotension occur in 1% of patients.
- Severe manifestations including pulmonary infiltrates, acute respiratory distress syndrome (ARDS), and cardiogenic shock occur rarely.
- Laboratory manifestations include elevated hepatic aminotransferase levels, thrombocytopenia, and prolongation of prothrombin time

- The pathogenesis is thought to be activation of immune effector processes (cells and complement) and release of inflammatory cytokines, such as tumor necrosis factor α, interferon gamma, interleukin 6, and interleukin 10 (cytokine release syndrome [CRS]). Although its origins are not completely understood,
- CRS is believed to be due to activation of a variety of cell types including monocytes/macrophages and T and B lymphocytes. Severe reactions from
- **rituximab** have occurred with high numbers (>50 × 109 lymphocytes) of circulating cells bearing the target antigen (CD20) and have been associated with a rapid fall in circulating tumor cells, mild electrolyte evidence of TLS, and, very rarely, death

- In addition,
- increased liver enzymes, D-dimer, and LDH and prolongation of the prothrombin time may occur.
- Diphenhydramine, hydrocortisone, and acetaminophen can often prevent or suppress the infusion-related symptoms.
- If they occur, the infusion is stopped and restarted at half the initial infusion rate after the symptoms have abated. Severe CRS may require intensive support for ARDS and resistant hypotension.

- Emerging clinical experience at several institutions has concluded that tocilizumab is an effective treatment for severe or life-threatening CRS. Tocilizumab prevents IL-6 binding to both cell-associated and soluble IL-6Rs and therefore inhibits both classical and trans-IL-6 signaling.