Introduction

In 2006, cancer was the second leading cause of death in the United States and nearly million cases were diagnosed with almost 560,000 deaths. Most cancer patients will experience at least one emergency during the course of their disease and emergency and ICU physicians are increasingly tasked with managing complications related to cancer ***(Barbera et al., 2010).***

Hypercalcemia will be experienced by up to one third of cancer patients at some point in their disease course. Among patients hospitalized for hypercalcemia, malignancy is the most common cause, although primary hyperparathyroidism is much more prevalent in the generalpopulation. Breast, lung, and renal cell carcinomas; multiple myeloma; and adult T-cell leukemia/lymphoma are the prevailing causes of hypercalcemia***(Sargent and Smith, 2010).***

Airway obstruction can be caused by virtually any malignancy, but the most common culprits include tumors of the tongue, oropharynx, thyroid, trachea bronchi, and lungs. Mediastinal tumors such as lymphomas and germ cell tumors can also cause airway obstruction, more commonly in the pediatric population***(Behl et al., 2010).***

Elevated intracranial pressure (ICP) secondary to malignancy in the brain can cause devastating neurologic

injury. Successful management requires prompt recognition and therapy,The vast majority of all intracranial neoplasms are metastatic, with lung cancer, breast cancer, melanoma, renal cancer, colorectal cancer being the most commontumors of origin***(Wen et al., 2001).***

Tumor lysis syndrome occurs when cancer cells release their contents into the bloodstream, either spontaneously or following antineoplastic therapy, leading toan influx of electrolytes and nucleic acids into thecirculation. The sudden development of hyperkalemia,hyperuricemia, and hyperphosphatemia can have life threatening end organ effects on the myocardium, kidneys, and central nervous system***(Gemici, 2006).***

Aim of the Work

To discuss pathophysiology, presentation, diagnosis and treatment of oncologic emergencies in intensive care unit.

Oncologic Emergencies

An oncologic emergency is defined as any acute, potentially life-threatening event, either directly or indirectly related to a patient's cancer or its treatment. This event, if not anticipated, quickly recognized, and effectively treated, may rapidly result in permanent morbidity or the death of the patient. Furthermore, a cancer patient is not protected from any medical emergency that may befall an individual without the diagnosis of cancer. Other non-neoplastic conditions must always enter into the differential diagnosis of every oncologic emergency. This fact emphasizes the importance of a firm medical background for the clinical practice of oncology.

While some oncologic complications are insidious and may take weeks or even months to develop, others can manifest in a few hours, and quickly lead to severe negative outcomes, including paralysis, coma, and death. Despite the increasing incidence rate of cancer in the general population, cancer mortality rates are dropping due to rapid advances in treatment strategies. The overall improvement in long-term survival of patients with cancer combined with the increasing use of more efficient outpatient treatment strategies are both contributing factors to the high likelihood that primary health care providers will encounter oncologic emergencies in their practices on a more regular basis***(Halfdanarson, et al., 2006).***

Oncologic emergencies arise from the ability of cancers to spread by contiguous invasion of adjacent structures or by metastases to distant sites, resulting in thrombosis or hemorrhage; the obstruction of vessels, ducts, or hollow viscera; the replacement of normal organ parenchyma; the infiltration of serous membranes with effusion; or the abnormal production of hormones or cellular products, which results in metabolic derangements and organ failure. Additionally, the emergency may arise from the effects of the antineoplastic treatment administered to the patient.

Once an oncologic emergency has been recognized, the aggressiveness of management should be influenced by the reversibility of the immediate event, the probability of long-term survival and cure, or the ability to offer effective palliative treatment to the patient. An apparent oncologic emergency may arise in an individual not previously diagnosed with cancer. Because of the variety of its manifestations, cancer must enter into the differential diagnosis of every complex medical event***(Halfdanarson, et al., 2006).***

In a previously undiagnosed patient, every effort must be made to successfully treat the emergency, since the patient otherwise might not have even a single therapeutic attempt at the management of his cancer. During an acute emergency, the assessment of prognosis is far more complex than usual. Even the most desperately ill patient can have remarkable improvement after being stabilized and definitively treated***(Walji, et al., 2008).***

Systemic Cancer Emergencies

1- Cardiovascular Emergencies

A- Pericardial Effusion and Cardiac Tamponade

Pathophysiology:

The pericardial sac is distensible up to a volume of 2L, if stretching ccurs over a slow time period, rising intrapericardial pressure affects all 4 cardiac chambers, but the right ventricular wall is much thinner and more susceptible to extrinsic compression. Diastolic pressures throughout the chambers begin to equalize and adversely affect cardiac output by compromising filling. At this point, tamponade physiology emerges***(Spodick, 2003).***

Malignant pericardial effusions develop through direct or metastatic involvement of the pericardial sac. Direct extension is most common in those tumors with sites of origin adjacent to the heart: lung cancer, breast cancer, and mediastinal lymphoma ***(Maisch et al., 2010).***

Metastases to the epicardium are seen in noncontiguous breast and lung cancer, as well as in melanoma**.** Primary neoplasms of the pericardium are exceedingly rare, but include mesothelioma. Cancer treatment, especially thoracic irradiation, can cause transudative effusions. Immunosuppression can also allow suppurative infections to develop in the pericardial space ***(Patel and Sheppard, 2011).***

Presentation

Pericardial effusions can be asymptomatic, although their presence portends a poor prognosis, especially if larger than 350 mL. Pericarditis symptoms may precede the emergence of tamponade. Tamponade classically presents with the Beck triad: hypotension, elevated jugular venous pressure, and a muffled precordium. However, only a minority of patients actually demonstrate all 3 signs. Most patients complain of dyspnea and chest discomfort, which may begin abruptly***(Colombo et al., 2007).***

Tamponade physiology can arise from volumes of as little as 100 mL if they accumulate rapidly. Even if the effusion forms over a longer period of time, the ‘‘last drop’’ phenomenon describes the critical point of physiologic collapse at which intrapericardial pressure finally overcomes the compensatory mechanisms of the heart and causes cardiac output to drop precipitouslyIn this manner, a chronic effusion can cause hyperacute symptomatology ***(Jacob et al., 2009).***

Diagnosis

The diagnostic utility of the physical examination should not be discounted but should be coupled with appropriate studies. Tachycardia is nearly universal, and pulsus paradoxus is an ominous finding, with avalue greater than 10 mm Hg having been arbitrarily defined as abnormal**.**Chest x-rays may show cardiomegaly and the classic ‘‘water bottle’’ cardiac silhouette. Electrocardiography can show low voltage and

electrical alternans from the shifting axis of the heart as it moves like a pendulum within the fluid filled sac**(figure1)**. Echocardiography is the definitive test, demonstrating right ventricular collapse during early diastole (***Mark et al., 2011).***

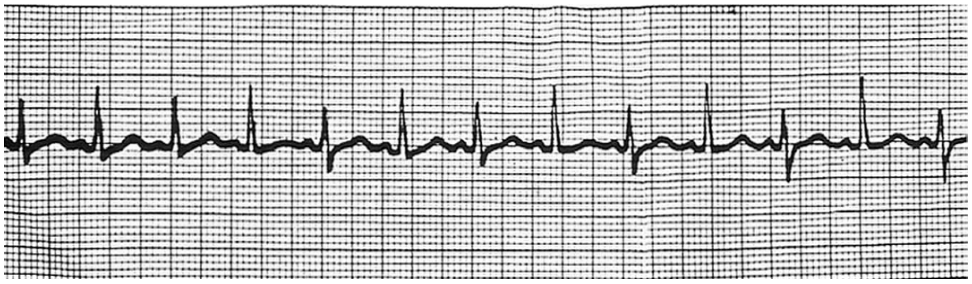

Figure (1): Electrical Alternans in the Setting of Pericardial Effusion ***(Mark et al., 2011).***

Treatment

Sonographically guided pericardiocentesis has decreased complication rates 4 fold over blind subxiphoid pericardiocentesis, which should be reserved for patients in extremis ***(Tsang et al., 2002).***

A catheter can be placed into the sac to drain residual or reaccumulating fluid. Adenocarcinoma provoked pericardial effusions are more likely to recur and these patients may be more appropriate for a pericardial window or pericardiectomy, whereas virtually all other histologies can be managed with pericardiocentesis and insertion of a drainage catheter ***(Kim et al., 2010).***

Patients often report immediate symptomatic improvement from pericardiocentesis but still require close

monitoring. Decompression can produce paradoxical hemodynamic instability requiring admission to the intensive care unit and pressor support. The risk of such decompensation increases with hematologic malignancies and also rises in direct proportion to pericardial fluid volume ***(Wagner et al., 2011).***

Instillation of chemotherapy into the pericardial space has been explored as a means of lowering recurrence rates of malignant pericardial effusions**.** Before undertaking elective invasive pericardial procedures, their risks should be carefully weighed alongside expectations for overall treatment efficacy and life expectancy ***(Oida et al., 2010).***

B- Superior Vena Cava Syndrome

Pathophysiology

The thin walled superior vena cava (SVC) returns all blood from the cranial, neck, and upper extremity vasculature to the right side of the heart. Primary or metastatic tumors can cause compression. Nononcologic etiologies include syphilitic aortic aneurysms (vanishingly rare since the advent of penicillin), fibrosing mediastinitis (classically associated with histoplasmosis), substernal hypertrophy of the thyroid, granulomatous disease (such as tuberculosis and sarcoidosis), and thrombosis, particularly that due to an underlying hypercoagulable state or endothelial damage from an indwelling vascular device***(Mark et al., 2011).***

Presentation

The extent of SVC obstruction and acuity of development dictate the patient's presentation. Blockage is better tolerated when there has been time for collateral veins to develop in adjacent venous systems like the azygos and internal mammary, a process that usually takes weeks. The veins on the patient's chest wall may be visibly distended **(Fig.2)**. Edema in the arms, facial plethora (not necessarily unilateral), chemosis, and periorbital edema may also occur. Stridor is an alarming sign that edema is narrowing the luminal diameter of the pharynx and larynx. Hoarseness and dysphagia can result from edema around the aerodigestive tracts. Presyncope or syncope is more common early on, when cardiac output declines without compensation. Headaches stem from distention of cerebral vessels against the dura, but confusion may indicate cerebral edema. All of these symptoms may be more noticeable when the patient is supine. Cancers classically associated with SVC syndrome include lung cancer (particularly right-sided), breast cancer, primary mediastinal lymphoma, lymphoblastic lymphoma, thymoma, and germ cell tumors (either primary or metastatic to the mediastinum) ***(Mark et al., 2011).***

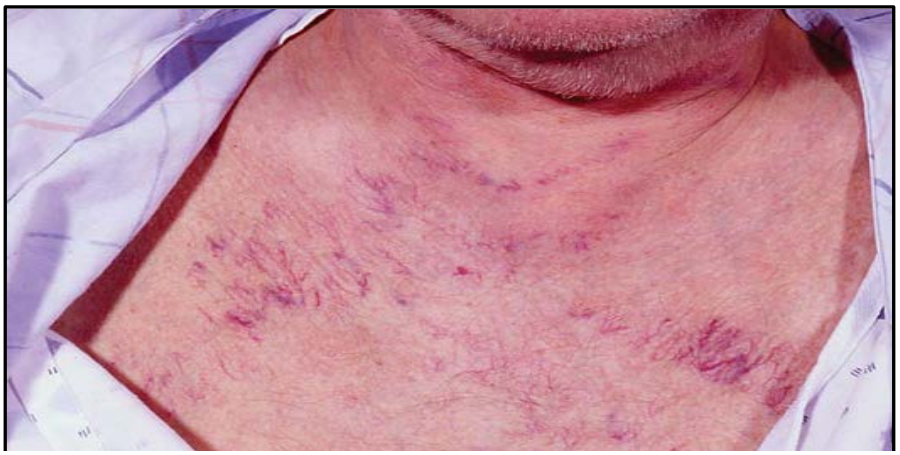

Figure (2): Dilated Chest Wall Veins in Superior Vena Cava Syndrome ***(Mark et al., 2011).***

Diagnosis

Radiographic imaging is crucial to diagnosis and treatment planning, especially if radiation and endovascular stents are potential interventions. While the gold standard for localizing obstruction remains selective venography, multidetector computed tomography (CT) or magnetic resonance imaging (MRI) are usually preferable for their noninvasiveness, easier availability, and decreased contrast load ***(Ganeshan et al., 2009).***

Treatment

SVC syndrome requires prompt recognition and treatment, but the clinical course typically permits completion of appropriate diagnostic studies before definitive therapy begins**.** Thus, when SVC syndrome heralds malignancy, the practitioner usually still has time to perform biopsies or other

diagnostic procedures without endangering the patient, although therapy should not be delayed unnecessarily**.** Patients who have neurologic symptoms or airway compromise merit immediate treatment; endovascular stenting can provide prompt palliation that should not interfere with further diagnostic maneuvers and generally relieves symptoms more quickly than chemo radiation***(Ganeshan et al., 2009).***

Decreased diagnostic yield with prebiopsy use of steroids is not well documented, even in cases of hematologic malignancy, but the overall efficacy of steroids is questionable. Randomized trials weighing management options in malignancy related SVC syndrome have been understandably difficult,but determining the histology of the responsible malignancy can often guide therapy***(Wilson et al., 2007).***

Chemotherapy may be the only necessary treatment in patients presenting in non emergent fashion with small cell lung cancer, lymphoma, or germ cell tumors. Changes in the SVC lumen following mediastinal radiation may be disproportionately small relative to the magnitude of symptom improvement, and some of the benefits previously attributed to radiation may actually result from the additional time during therapy for collateral veins to form. Cases of catheter related thrombosis have been successfully treated with instillation of thrombolytics into the device,but fibrinolytic therapy should be administered carefully in cases in which brain metastases have been diagnosed or not excluded***(Guijarro et al., 2007).***

2- Neurologic Emergencies

A- Malignant Spinal Cord Compression

Malignant spinal cord compression (MSCC) was first described in 1925 by Spiller and remains a common oncologic emergency that requires prompt treatment to relieve pain and preserve neurological function**.** Although all tumor types have the potential to cause MSCC, breast, prostate, and lung cancer 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***(Abrahm et al., 2008).***

Although most cases of MSCC occur in patients with a known diagnosis of malignancy, 5% to 25% of MSCC cases occur as the initial presentation of malignancy ***(Schiffe, 2003).***

Pathophysiology:

MSCC is defined as the compressive indentation, displacement, or encasement of the thecal sac that surrounds the spinal cord or caudaequina by cancer. Compression can occur by posterior extension of a vertebral body mass, by anterior extension of a mass arising from the dorsal elements, or by growth of a mass invading the vertebral foramen***(Prasad and schiff, 2005).***

The majority of the cases occur when metastatic tumor reaches the vertebral bodies via hematogenous spread, with secondary erosion into the epidural space. Approximately 15% of the cases occur when a paravertebral lesion spreads into the

spinal canal through an inter vertebral foramen and directly compresses the spinal cord. This is more commonly seen in neuroblastomas and lymphomas**.** Metastases to vertebral bone can lead to weakening of the bone and vertebral collapse with displacement of bone fragments into the epidural space as well. In rare cases, metastases occur directly to the spinal cord and meninges ***(Kwok et al., 2006).***

The most common location for MSCC is in the thoracic spine (60%) followed by the lumbosacral region (30%) and, lastly, the cervical spine (10%)It is also important to recognize that metastatic lesions are seen at multiple levels of the spinal cord in almost half of all patients ***(Cole and Patchell, 2008).***

Presentation:

Early detection is critical because the single most important prognostic factor for regaining ambulation after treatment of MSCC is pretreatment neurologic status**.** The clinical presentation of MSCC can vary significantly depending on severity, location, and duration of the compression. The most common initial symptom is back pain, which occurs in approximately 90%of the cases ***(Prasad and Schiff, 2005).***

The back pain associated with MSCC may gradually worsen over time and usually precedes neurologic symptoms by weeks to months. Referred pain is common and varies according to the location of the offending lesion. Cervical compression can present as subscapular pain, thoracic

compression as lumbosacral or hip pain, and lumbosacral compression as thoracic pain ***(Mark et al., 2011).***

Once symptoms other than pain are present, the progression can be quite rapid. These symptoms include motor weakness, sensory impairment, and autonomic dysfunction. Caudaequina syndrome may present as urinary retention and over flow incontinence (90% sensitivity and 95% specificity). Other symptoms include decreased sensation over the buttocks, posterior superior thighs, and perineal region ***(Abrahm et al., 2008).***

Physical examination findings depend on the location of the lesion as well as the degree and duration of impingement. Most patients have tenderness to percussion over the affected spinal region. The Valsalva maneuver may worsen their back pain. Hyperreflexia, spasticity, and loss of sensation (position, temperature, pinprick, and vibratory) can occur early. Deep tendon reflexes may then become hypoactive or absent. Late signs include weakness, Babinski sign, and decreased anal sphincter tone ***(Mark et al.,2011).***

Diagnosis:

Because there is no clinical model to rule out MSCC in cancer patients with back pain, all reports of new onset back pain should prompt an immediate assessment. For those patients with only back pain and a normal neurologic examination, imaging of the spinal axis should be completed within the next 48 to 72 hours***(Cole and Patchell,2008).***