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Oncologic Emergencies

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Summary

Oncologic emergencies are complications resulting from cancer itself or from treatment of cancer requiring immediate attention & reversal. It is an acute life threatening event, may be the first sign of disease or may indicate disease progression. Cancer patients presenting with oncologic emergencies should be approached in a similar way to those without cancer. The care of cancer patients with oncologic emergencies is a challenge not only to oncologists but also to clinicians involved in emergency medicine. It requires rapid intervention to avoid death or severe permanent damage. The overall goal is to prevent, reverse or minimize life threatening complications through prophylaxis, early detection and specific management.

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Introduction:

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 that produces characteristic symptoms and signs. Oncologic emergencies can occur at any time during the course of malignancy, from presenting symptom to end stage of the disease[1]. Additionally the emergency may arise from the effect of anticancer treatment administered to the patient. Once an oncologic emergency has been recognized, the aggressiveness of management should be influenced by the reversibility of immediate event and the probability of long term survival and cure. Because of the critical nature of theses complications oncologists, oncology nurses and all the oncology health professionals must be prepared to recognize the signs and symptoms of these disorders promptly so that appropriate therapy can be instituted without delay[2].

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Common Oncologic Emergencies:

- Spinal cord compression
- Superior vena cava obstruction syndrome (SVCS)
- Cerebral edema
- Hypercalcemia
- Bone metastasis
- Tumor lysis syndrome (TLS)
- Sudden death (SD)

Spinal cord compression

Causes:

- Breast cancer
- Lung cancer
- Prostate cancer
- Renal cell carcinoma
- Sarcoma
- Multiple myeloma
- Lymphoma

70% of bone lesions are osteolytic, 10% are osteoblastic, 20% are mixed.

Symptoms & signs:

- Localized vertebral or radicular pain
- Localized tenderness on palpation
- Muscle weakness
- Paraplegia

If muscle weakness is present it is incumbent on the physician to act urgently to obtain consultation with the neurosurgeon and radiation oncologist; not to wait even until next morning!

Dianosis:

- MRI is diagnostic modality of choice
- High resolution CT scan
- Plain radiograph
- Bone scan

Treatment:

- Corticosteroid: Dexamethasone should be started immediately to reduce spinal cord edema with a dose of 10-20mg i.v as loading dose, followed by 4-6 mg by mouth or iv four times a day through the initial weeks of radiation therapy, thereafter tapered on completion of radiation[3].
- Radiotherapy: Radiation is given most commonly at a dose of 30 Gy in 10 fractions (300 cGy/day). Alternatively, 400 cGy can be given for first three days, then decrease to standard dose level 200 cGy per day for a total dose of 40-45 Gy. A common technique is to apply a posterior field with 4-6 megavoltage photon. The best chance of neurological recovery depends on urgent radiation within 24 hours of developing symptoms[4].
- Surgery: It plays a crucial role. Decompressive laminectomy for posterior lesion and anterior approach for anterior lesion are used. Newer techniques are minimally invasive vertebroplasty and kyphoplasty.

Indications of surgery:

- Worsening of neurologic signs & symptoms or appearance of new lesion during the course of radiotherapy.
- Vertebral collapse at presentation.
- Spinal instability.
- Tumors refractory to radiation.
- Recurrent lesion in previously irradiated site.

Superior vena cava obstruction syndrome (SVCS):

Superior vena cava is a thin-walled vessel located in front of right main bronchus. Superior vena cava obstruction syndrome results from lymph node involvement or mediastinal tumors that compress the vena cava. Thrombus is another non-malignant cause of SVCS.

Symptoms and signs:

- Dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Facial, neck and upper extremity swelling
- Cough, hoarseness of voice
- Chest pain, neck pain
- Headache, altered consciousness.

Physical findings: It includes spectrum of findings ranging from facial edema to respiratory distress. Important other signs are neck vein distension, cyanosis, presence of prominent collateral vessels on thorax, paralysis of vocal cord and mental changes.

Radiologic evaluation:

- Chest x-ray PA view
- CT scan of chest

Tissue diagnosis: Through

- Bronchoscopy
- Mediastinoscopy/mediastinostomy
- Thoracoscopy

Treatment:

- Symptomatic treatment:
  - O2 inhalation
  - Furosemide 20-40 mg iv
  - Dexamethasone 16 mg orally
- Specific treatment for neoplas s followed by reversion to standard dose, with palliation observed after only two to four fractions. Dexamethasone should be continued for 7 days after starting of radiation. Total dose of radiation depends on tumor histology. Dose equivalent to 3500-4500 cGy delivered at standard fractionation should be used for lymphoma, while lung cancers require dose equivalent to 6000cGy or more[5].
- Specific treatment for thrombus: All patients need anticoagulant therapy with heparin initially followed by warfarin. Percutaneuous stent placement is highly effective for rapid relief of symptoms.

Cerebral edema

Intracranial metastasis can produce variety of neurologic symptoms and signs. The history and physical examination provide first clue to the presence of metastatic lesion or associated cerebral edema. In general, gradual progression of neurologic symptoms before the development of significant deficit is more consistent with metastatic lesion.

Investigations:

- MRI is the modality of choice
- CT scan

If a patient with cancer has focal neurologic sign or symptom, headache or altered consciousness, lumbar puncture should not be done until CT/MRI shows no

evidence of mass, midline shift or increased intracranial pressure to avoid brainstem herniation.

Treatment:

- Dexamethasone 10-20 mg i.v loading dose followed by 4-6 mg four times daily.
- Mannitol 50-100 mg i.v over 30 minutes. It may be repeated six hourly.
- Specific treatment for intracerebral tumor: Radiation or surgery combined with radiation[6].

Hypercalcemia:

Relatively uncommon.

Causes:

- Bone metastasis (86%)
- Breast cancer
- Lung cancer
- Renal cell carcinoma
- Hematological malignancies (15%)

Humoral mediators:

The pathogenesis of hypercalcemia appears to be secondary to humoral mediators like parathyroid hormone-related protein, osteoclast-activating factors, cytokines like IL-6, RANKL (Receptor Activator for Nuclear factor K-B Legand), TNF-á.

Signs & Symptoms:

- Polyuria
- Nocturia
- Anorexia, nausea, constipation
- Muscle weakness, fatigue.
- If progresses-
  - ❒ Azotemia
  - ❒ Severe dehydration
  - ❒ Mental obtundation, coma
  - ❒ Cardiovascular collapse

Laboratoy findings:

- K^+ "!
- BUN '!
- Creatinine '!
- Arterial blood gas analysis: Hypochloremic metabolic alkalosis
- Bone scan: to see bony involvement.

Treatment:

Treatment of hypercalcemia has two objectives:

I. To reduce the level of serum calcium.
II. To treat the underlying cause[7].

Treatment of hypercalcemia includes:

- Rehydration with 0.9% normal saline.
- Bisphosphonate therapy.
- Continuing saline diuresis.
- Calcitonin.
- Steroids.

Bone metastasis:

Metastasis to bone occurs from many types of tumor causing constant pain, patient morbidity and limiting Quality Of Life (QOL).

Clinical features:

- Constant aching pain
- Bony tenderness.

Radiologic evaluation:

- X-ray
- MRI
- Whole body bone scan.

Treatment:

- Surgery: Surgical stabilization is most often the initial treatment. Pathological fracture of non-weight bearing bone can be managed by splinting or sling immobilization.
- External Beam Radiotherapy: Radiation dose of 15-20 Gy in 3-4 fractions leads to complete pain relief in 50% of patients.80-90% patients show significant improvement at 30-40 Gy. Radiation produces some healing and reossification in 65-85% of lytic lesions in unfractured bone[8].
- Strontium 89: Radioisotope Strontium 89 can be given i.v. It has 2-25 times greater affinity to metastatic bone than normal bone. It emits â-radiation. Response lasts for 3-6 months. Patients may receive multiple doses at 3 months interval if there is adequate hematologic recovery.
- Bisphosphonates: Pamidronate and Zoledronic acid are specific inhibitors of osteoclastic activity. These reduce bone pain and fractures.

Tumor lysis syndrome (TLS):

This syndrome occurs in patient with any tumor undergoing rapid cell turnover like acute leukemia, lymphoma (high and intermediate grade), and less commonly in solid tumors like Small Cell Lung Cancer and germ cell tumor. TLS is characterized by the metabolic abnormalities like hyperuricemia,

hyperkalemia, hyperphosphatemia and hypercalcemia. It is more common in patients with renal insufficiency[9].

Prevention:

- If patients having tumors that predispose to the complication, it is useful to start allopurinol 600-1200 mg/day by mouth in divided doses for 1-2 days at least 24 hours before initiating chemotherapy and to continue with dose 300 mg twice a day for 2-3 days[10].
- Urine should be kept alkaline (P^H 7). Sodi-bi-carb and acetazolamide may help.
- Intravenous hydration should be started to make brisk diuresis to maintain urine output 100-150 ml/hr. Furosemide may be added.

Monitoring:

- Serum electrolytes
- Serum phosphate
- Serum calcium, uric acid, creatinine.

These should be checked before and daily after starting chemotherapy. If the patient is at very high risk of developing TLS, then it should be checked at every 6 hrs for 24-48 hrs[11].

Treatment:

- Hydration with half normal saline solution.
- Oral aluminium hydroxide.
- Treatment of hyperkalemia.

Sudden death:

Nearly every oncologist eventually will deal with a cancer patient who suddenly, unexpectedly, and inexplicably dies.

Tumor-Related Sudden Cardiac Death:

The vast majority of episodes of sudden death are the result of underlying heart disease. The inciting event is usually a cardiac dysrhythmia, most often ventricular fibrillation[12] A review of the causes of death in 816 cancer patients found that 4% died of cardiac disease, and that 90% of these were due to atherosclerotic coronary artery disease.[13] Autopsy studies indicate that direct cardiac involvement by tumor is common and, more often than is generally recognized, may be the primary cause of death.[14] Primary cardiac neoplasms are rare, and the vast majority of tumors affecting the heart are metastatic to the pericardium or myocardium and fewer to the heart valves and endocardium.[15,16] In autopsy series, cardiac metastases are seen most frequently in patients with malignant melanoma (60%) and bronchogenic carcinoma (15 to 35%), followed by breast cancer, lymphoma, and leukemia.[17]

Therapy-Related Sudden Cardiac Death:

Radiotherapy

Mediastinal radiation therapy commonly affects the pericardium and may cause acute pericarditis, pericardial fibrosis, effusion, and tamponade.[18,19,20] Pericarditis may occur many months or years after completion of a course of radiation therapy.

Chemotherapy

Anthracyclines

Many chemotherapeutic agents are recognized to have cardiotoxicity. Drugs of the anthracycline family (doxorubicin, daunorubicin, idarubicin), and, to a lesser degree, mitoxantrone and mitomycin, are known to cause direct myocardial cell injury and cardiomyopathy. Dysrhythmias of all types have been noted in as many as 41% of patients treated with doxorubicin[21,22,23] like ventricular premature contractions, and supraventricular and ventricular tachycardias[24] .Use of anthracyclines has been associated with an acute pericarditis–myocarditis syndrome.[25] This syndrome, manifested as fever, acute pancarditis, and the development of congestive heart failure, may be rapidly fatal.

Cyclophosphamide

Treatment with high-dose cyclophosphamide may cause an acute cardiomyopathy, pericardial effusion, ventricular arrhythmia, and sudden death.[26] It is most commonly seen with high-dose conditioning protocols administered in the bone marrow transplantation setting in which more than 140 mg/kg of cyclophosphamide is administered.[27] The mechanism is believed to be due to endothelial cell damage with the anthracyclines.[28] Supraventricular tachycardias and ST-T wave abnormalities may also be seen with the use of ifosfamide.[29]

5-Fluorouracil (5-FU)

5-FU has been associated with coronary artery vasospasm, angina pectoris, and acute myocardial

infarction.[30,31,32,33] Calcium channel blockers appear to be effective in treating patients who exhibit vasospasm or worsening angina while receiving 5-FU.[34]

Cisplatin

An association has been reported between cisplatin treatment and increased cardiovascular death rates, including sudden death in young men treated with combination chemotherapy for germ cell tumors.[35,36]

Taxanes

Paclitaxel (Taxol) and docetaxel (Taxotere), act to stabilize microtubules. These agents have a significant incidence of severe anaphylaxis-like hypersensitivity reactions and cardiovascular events (angina, myocardial infarction, and sudden death) which occur shortly after initiating administration.[37,38]

Biologic Therapies

Hypotension, tachyarrhythmias, angina, myocardial infarction, congestive heart failure, and sudden death have been reported as complications of treatment with interleukin-2 (IL-2), various interferons, and monoclonal antibodies.[39,40,41,42,43,44] Commonly used monoclonal antibodies are Trustuzumab, Herceptin, Cetuximab etc.

Conclusion:

There are lots of oncologic emergencies; only the important and most common oncologic emergencies are described here. In the majority of cases they carry a grim prognosis, but a substantial number of patients, especially those with lymphoma, myeloma or prostate cancer have the potential for long term survival. The major determinant of outcome is the patient's functional status at the initiation of therapy; accurate diagnosis in a timely fashion is the paramount. Radiation in combination with other medical therapies is the most commonly used treatment to combat against these emergency situations. Selected patients may benefit from surgical intervention.

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