

SAOC Policy Document

Oncological Emergencies

Introduction

Cancer and its therapy may lead to urgent conditions. The care of cancer patients with emergency problems presents a challenge not only to medical oncologists but also to clinicians involved in emergency medicine. There are many kinds of problems for which cancer patients may require assistance in an emergency care facility. Cancer patients may often have complex medical problems in addition to the diagnosis of cancer, such as coronary heart disease, chronic obstructive pulmonary disease or diabetes mellitus. We can define an oncological emergency as an acute condition that is caused by cancer or its treatment, requiring rapid intervention to avoid death or severe permanent damage.

1. STRUCTURAL AND OBSTRUCTIVE ONCOLOGICAL EMERGENCIES:

In this group we have to consider *superior vena cava syndrome, pericardial tamponade, spinal cord compression, increased intracranial pressure, urinary obstruction, haemoptysis and airway obstruction*

A. Superior vena cava syndrome

Superior vena cava syndrome (SVCS) results from the partial or complete obstruction of blood flow through the superior cava vein to the right atrium, causing severe reduction in venous return from the head, neck and upper extremities. The obstruction may be due to compression, invasion, thrombosis or fibrosis of this vessel. Although this syndrome is still considered one of the classical oncological emergencies, it rarely causes an immediate life-threatening situation. Malignant tumors, such as lung cancer, lymphoma and metastatic tumor are responsible for >90% of all SVCS cases. Lung cancer, particularly small-cell and squamous-cell, accounts for almost 85% of all cases. Malignant lymphomas, mainly of non-Hodgkin histology, are the second cause.

Clinical Features

- Oedema of the face, neck, upper thorax, breasts and upper extremities;

- Peri-orbital oedema and/or oedema of the conjunctivae, with or without protrusion of the eye;
- Horner's syndrome (sinking of eye with ptosis of eye lid);
- Plethora (fullness of the face);
- Increased pressure of the jugular veins;
- Dilation and prominence of collateral vessels in upper thorax and neck;
- Telangiectasia (capillary dilation);
- Compensatory tachycardia.

Symptoms

- Respiratory compromise (dyspnoea, shortness of breath, tachypnea, cough, orthopnea);
- Feeling of facial fullness;
- Headache visual disturbances;
- Dizziness;
- Hoarseness;
- Chest pain;
- Stoke's sign (tightness of shirt collar);
- Swelling of fingers (difficulty removing rings).

B. Spinal cord compression

Spinal cord compression is the first manifestation of cancer in ~10% of patients who present with this complication and will also occur during the disease course of 5–10% of all cancer patients. It should be considered a true oncological emergency. Delays in starting treatment may result in irreversible consequences, including paraplegia. In most cases spinal cord compression is caused by extradural metastases from tumors involving the spine. Bone metastases to thoracic, lumbar or cervical vertebrae may produce a cord injury when affecting the vertebral body or when the pedicle enlarges and compresses the underlying dura.

Clinical Features

The clinical presentation of SCC is similar in all patients regardless of the origin of the tumor.

- **Back pain** is the presenting complaint in 97% of patients. It is related to SCC and may occur weeks or months before neurologic deficits occur.

The pain is either localized or radicular usually intense, persistent and progressive, although thoracic compression is often felt as a constriction.

The pain is usually worst at night because the spine lengthens when recumbent and the abdominal contents place pressure against the spine and cord.

This pain does not improve with commonly used analgesics, and may get worse with recumbence or with manoeuvres increasing pressure in the epidural space

- **Weakness** is only a presenting complaint in 2% of cases. Varies based on the location of the tumor. Common patient complaints include stiffness and heaviness of the affected extremity.
- It may manifest itself as an **unsteady gait or ataxia** with a favouring or dragging of the affected extremity/ extremities. Patients experience difficulty walking or climbing stairs.
- Symptoms often associated with weakness include hyperreflexia, spasticity, and a positive Babinski sign.
- **Sensory loss** usually follows motor weakness but precedes actual motor loss.
- Symptoms of sensory loss includes numbness, tingling, paraesthesia and feelings of coldness in the affected area. Loss of sensation to light touch first, then loss of pain, followed by loss of thermal sensation, occur in 80% of patients.

Prognosis

The degree of neurologic dysfunction at the time of diagnosis is the greatest predictor of outcome. 80% of patients with little or no ambulatory dysfunction will remain ambulatory.

C. Pericardial tamponade

Pericardial tamponade occurs when pericardial fluid accumulates causing hemodynamic instability. In cancer patients, two mechanisms may lead to accumulation of excess fluid in the pericardial space: obstruction of lymphatic drainage or excess fluid secretion from tumor nodules on pericardial surfaces. In almost half of cancer patients presenting with pericardial effusion, non-malignant causes, such as drug or radiation induced pericarditis, hypothyroidism, uraemia, infection or autoimmune disease, should also be considered.

Etiology and risk factors

Malignant causes include the following:

- Neoplastic pericarditis with effusion: primary tumors of the pericardium (mesotheliomas and sarcomas);
- Metastatic tumors of the pericardium (lung, breast, leukaemia, lymphoma, melanoma, sarcomas);
- Radiation pericarditis (exposure of the heart to 400 Gy or more).

Signs and symptoms

- Dyspnoea.
- Abdominal pain.
- Retrosternal chest pain.
- Tachycardia.
- Low systolic blood pressure.
- Dizziness
- Thready diminished pulse pressure or pulsus paradoxus

D. Urinary obstruction

Urinary obstruction may occur in patients with gynaecological or urological tumors particularly cervical or prostatic carcinoma. Sometimes metastatic disease to the pelvis may produce urinary obstruction, leading to bilateral

hydro nephrosis and renal failure. A patient with flank pain with sudden anuria, sometimes alternating with polyuria and a progressive rise in serum creatinine should be suspected of having urinary obstruction. Renal ultrasound is the easiest way of detecting bilateral hydro nephrosis. CT is often helpful in detecting the exact location of the obstruction, particularly if there is a retroperitoneal or pelvic mass.

E. Increased intracranial pressure

Increased intracranial pressure may be caused by brain metastases. Around a quarter of cancer patients will die with intracranial metastases. Lung, breast and melanoma are the most common tumors that metastasize to the brain. Clinical manifestations of brain metastasis are headache, nausea, vomiting, seizures, behavioural changes and sometimes focal neurological changes. This picture may not be different from intratumoral bleeding. Patients with melanoma, chorio carcinoma and clear cell carcinoma of renal origin frequently present with bleeding. The tumor mass together with its surrounding oedema may produce hydrocephalus and as the mass enlarges various herniation syndromes may occur depending on the location of the tumors within the cranium.

Etiology and risk factors

- Most common etiology is brain metastases. Metastatic brain tumors are four to five times more common than primary lesions.
- Lung and breast cancers are the solid tumors that most frequently metastasize to the brain in adults.
- Other causes that may occur in oncology patients are hematomas, haemorrhage, cerebral irritation, or infection with exudate.
- Patients with thrombocytopenia or platelet dysfunction are at risk for cerebral bleeding.

Clinical features

General symptoms include:

- Headaches
- Nausea

- Vomiting
- Change in level of consciousness
- Impaired cognitive function
- Changes in personality
- Hemiparesis
- Language difficulty
- Dysphagia
- Ataxia
- Seizures

Headaches are commonly most severe on walking. This may be due to carbon dioxide retention during sleep that causes cerebral vessel dilation and enhances cerebral oedema.

F. Massive haemoptysis

Massive haemoptysis is defined as the expectoration of volumes ranging from one single episode of 100 ml to >600 ml of blood during 24–48 h. When respiratory difficulty occurs, haemoptysis should be treated urgently. Airway bleeding leading to life-threatening airway obstruction, aspiration, and anaemia or hypovolemic shock is also considered massive haemoptysis. In fact, fatal haemorrhage may present in one-third of patients with massive haemoptysis and the risk of death is directly associated with the amount of blood expectorated. The rate of haemoptysis, the amount of blood retained in the lungs and the underlying pulmonary reserve are also well-recognized risk factors

G. Acute airway obstruction

Acute airway obstruction involves the upper airways and may be caused by malignant or non-malignant conditions. This term refers to a blockage at the level of the main stem bronchi or above. It may result from intraluminal tumor growth or from extrinsic compression of the airway. Tumors that obstruct the upper airway by direct extension are primary tumors of the head and neck and lung. Non-malignant causes of airway obstruction are food or foreign body aspiration, airway oedema or haemorrhage, tracheal stenosis and infections. Angioedema may also cause severe and life-threatening airway obstruction. Primary tumors of the lung are the most common cause of lower airway obstruction

2. METABOLIC EMERGENCIES

The most common metabolic emergencies in cancer patients are related to hypercalcemia, and inappropriate secretion of the antidiuretic hormone.

A. Hypercalcemia

Hypercalcemia is the most frequent paraneoplastic syndrome and a serious emergency leading to morbidity and mortality in cancer patients. Around 10% of advanced solid tumors, most often lung, breast, head and neck and renal cancer, as well as malignant lymphoma and myeloma may produce hypercalcemia.

The main mechanisms by which cancer-related hypercalcemia may be produced are bone metastases, increased parathyroid hormone-related protein production and calcitriol secretion. But cancer patients may also develop hyperparathyroidism and other conditions that induce hypercalcemia in the general population of patients. In primary hyperparathyroidism, the intact parathyroid hormone (i-PTH) serum levels will be abnormally high.

Clinical features

Clinical manifestations vary tremendously, depending on the level of the serum calcium, the rate of onset, the underlying cause, and the patient's general condition.

Clinical Signs

- Lethargy
- Change in mental status (restlessness, confusion, stupor, coma)
- Vomiting
- Dysrhythmias
- Polyuria
- ECG changes
- Renal calculi
- Renal failure

Symptoms

- Anxiety
- Fatigue and weakness
- Anorexia and Nausea
- Polydipsia
- Constipation

Prognosis

Hypercalcemia is reversible in 80% of episodes if it is recognized and prompt aggressive therapy initiated. It has been shown that the more severe the Hypercalcemia, the poorer the prognosis, and vice versa. Without prompt treatment it is associated with a 50% mortality rate

B. Inappropriate secretion of antidiuretic hormone

The inappropriate secretion of the antidiuretic hormone (SIADH) should always be considered when a patient presents with hyponatremia. SIADH is due to the production of arginine vasopressin by the tumor cells. Hyponatremia is associated with plasma hyposmolarity and inappropriately high urinary osmolarity, together with a high level of excretion of urinary sodium without plasma volume depletion. Other causes of hyponatremia, such as renal failure, hypothyroidism or adrenal insufficiency, have to be excluded.

3 TREATMENT RELATED EMERGENCIES

Cancer treatment may be responsible for some related problems, requiring urgent intervention. This is the case for tumor lysis syndrome, anaphylactic reactions related to chemotherapeutic agents and haemorrhagic cystitis.

A. Tumour lysis syndrome

Tumor lysis syndrome is caused by the destruction of a large number of actively proliferating tumor cells as a consequence of cancer chemotherapy. It is a well-recognized clinical entity in which a combination of several electrolyte disorders such as hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and lactic acidosis, can lead to acute renal failure. This syndrome was first described in patients with Burkitt's lymphoma who died a few days after receiving treatment with chemotherapy. The main cause of death in these patients was arrhythmia related to electrolyte disturbances, particularly hyperkalemia and renal failure.

Etiology and risk factors

Tumor lysis syndrome may occur spontaneously in patients with inordinately high tumor burdens. However, it is most commonly caused as a result of treatment related malignant cell death.

TLS has been reported to occur with surgery, biotherapy, hyperthermia, hormonal therapy, radiation therapy, but most frequently associated with chemotherapy.

It may occur anywhere from 24 hours to 7 days after anti-neoplastic is initiated.

Patients most at risk are those who have large tumor cell burdens, with high proliferative fractions, marked elevated WBC counts, elevated LDH or uric acid levels, pre-existing renal dysfunction, splenomegaly or lymphadenopathy.

Clinical features

Patients exhibit the signs and symptoms associated with each metabolic abnormality:

	GI	RENAL	CARDIAC	NEUROMUSCULAR
Hyperkalemia	Nausea		BP changes	Twitching
			ECG changes	Cramping
			Arrhythmias	Weakness
			Heart block	Parasthesis
			Asystole	Ascending flaccid paralysis
Hyperuriceamia	Nausea	Oedema		Lethargy
	Vomiting	Flank pain		Gout- like symptoms
	Diarrhoea	Haematuria		
	Anorexia	Oliguria		

		Cloudy, sediment in urine		
		Anuria		
		Azotemia		
		Crystalluria		
Hyperphosphatemia		Oliguria		
		Anuria		
		Azotemia		
		Renal insufficiency		
Hypocalcemia			Hypotension	Twitching
			Heart block	Cramping
			Cardiac arrest	Tetany
				Chvostek`s sign
				Trousseau`s sign
				Laryngospasm
				Paresthesias
				Seizures
				Confusion

B. Anaphylactic reactions related to chemotherapeutic agents

Anaphylactic reactions related to chemotherapeutic agents may sometimes create medical emergencies. Angioedema and urticaria are the most common manifestations of anaphylaxis and make up >90% of allergic reactions to drugs. Other frequent manifestations are abdominal pain, chest tightness, upper airway obstruction, bronchospasm and hypotension.

Laryngeal oedema followed by hypotension is the most frequent cause of death related to allergic reactions.

The three main issues in treating anaphylactic reactions are early recognition, airway maintenance and hemodynamic support. The acute management of anaphylaxis in adults should start by removing the drug considered to be responsible. Immediate assessment of the airway and administration of epinephrine subcutaneously, depending on the severity, should follow. Intravenous fluids should be given, particularly in case of hypotension. Glucocorticoids and antihistamines may also be added. If resistant hypotension develops intensive care unit management will be required.

C. Haemorrhagic cystitis

Hemorrhagic cystitis can be observed in patients receiving high doses or prolonged treatment with ifosfamide or cyclophosphamide.

Both alkylating agents are metabolized to acrolein, a chemical agent with strong irritant properties that is excreted in the urine. Common symptoms may include dysuria, burning, frequency, gross haematuria, urgency and incontinence.

The best way of managing this problem is prevention.

Oral or intravenous hydration increases urinary flow and reduces the contact of acrolein with the bladder mucosa.

Mesna should always be administered with ifosfamide or with high-dose cyclophosphamide to detoxify acrolein and its metabolites in urine and it is very effective in preventing haemorrhagic cystitis.

4. OTHER EMERGENCIES TO CONSIDER

A. Sepsis

Septic shock comprises a group of diverse life-threatening syndromes that result from different pathophysiologic circumstances: decreased cardiac function, haemorrhage, trauma, antigen or anti-body reaction, and sepsis. The three major classifications of shock are Hypovolemic, cardiogenic and distributive or vasogenic. Hypovolemic shock is a result of decreased intravascular volume. Cardiogenic shock results from the heart's impaired ability to pump blood adequately. Distributive shock or vasogenic shock is the result of an abnormality in the vascular system.

Septic shock can be caused by bacterial, fungal, viral and protozoal organisms. Gram negative bacteria have historically been the primary

organisms associated with septic shock. More recently there has been an increase in septic shock induced by gram positive organisms. This may be attributed to the increased use of long-term central venous access.

Criteria for Sepsis

Sepsis is a systemic response to infection. This systemic response is manifested by two or more of the following conditions as a result of an infection:

- Temperature > 38 °C or < 36 °C
- Heart rate > 90 beats per minute
- Respiratory rate > 20 breaths per minute
- White Blood Cell Count > 12000 cells per mm³ or smaller than 4000 cells per mm³ or bigger than 10% immature band formed

Clinical features

The first signs of progressive sepsis may be fever, shaking chills and mild hypotension. The early phase of septic shock has been referred to as the warm or hyper-dynamic phase. It is characterised by vasodilation, decreased peripheral vascular resistance and increased cardiac output. The patient may present as warm and flushed. The respiratory rate is rapid, which leads to alkalosis. The patient may be nauseated, has diarrhoea and be mildly confused. As septic shock progresses papillary leakage causes fluid to third-space, cardiac output decreases and peripheral vascular resistance increases. The patient develops oliguria and metabolic acidosis. Peripheral vasoconstriction leads to ischemia and decreased blood flow to vital organs. Bleeding occurs in patients with DIC. Peripheral oedema becomes more severe. The patient becomes cold, clammy and cyanotic. Confusion progresses to coma. Without successful intervention symptoms progress to the cold phase, also known as late or refractory shock. At this point the condition is irreversible. Circulatory and respiratory collapse ultimately occurs.

Respiratory Features

Hyperventilation and respiratory alkalosis may occur, both with and without fever. Alveolar capillary leakage leads to pulmonary oedema and hypoxemia. ARDS occurs most frequently in patients with gram negative infection. The development of ARDS increases morbidity from 80% to

90%. Concomitant thrombocytopenia raises the morbidity rate even higher.

Cardiovascular features

Systemic vascular resistance drops dramatically due to vasodilation. Hypotension is associated with the release of complement TNF alpha and IL-1. Metabolites of nitric oxide are also related to the decrease in vascular resistance. Cardiac output increases to try and compensate. Systemic vascular resistance ultimately increases with vasoconstriction leading to ischemia and decreased organ perfusion. Elevated lactic acid levels occur with hypo perfusion of vital organs and hypoxemia. This is a poor prognostic sign.

Haematological features

Gram negative sepsis is also associated with the development of DIC. The release of bacterial toxins stimulates the clotting cascade that exhaust clotting factors and leads to simultaneous haemorrhage and thrombosis.

Other features

Septic shock due to GI pathogens may also be accompanied by jaundice, stress ulcers and bleeding. Renal symptoms of oliguria and proteinuria may progress to acute tubular necrosis and renal failure.

B. DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

- DIC is considered to be an acquired bleeding disorder.
- DIC is an alteration in the blood clotting mechanism, with abnormal acceleration of the coagulation cascade in which both thrombosis and haemorrhage may occur simultaneously.
- It is not a disease entity but rather an event that can accompany various disease processes.
- An underlying pathology, benign or malignant is responsible for DIC.

Etiology and risk factors

A variety of pathologies involve a triggering event, which can cause either endothelial tissue injury or blood vessel injury.

It is usually related to the disease process and /or the treatment of the cancer, and it often occurs concomitantly with sepsis.

Malignancies: - Acute promyelocytic myelogenous leukemia, Acute myelogenous leukemia; Melanoma; Ca Lung; colon; breast; stomach; pancreas; ovary and prostate.

Signs and symptoms

- Bleeding – ecchymosis, epistaxis, hematemesis, melaena.
- Shock – hypotension, tachycardia, cold clammy skin.
- Joint pains and stiffness.

References:

- Oncology Nursing, fourth edition; Shirley E Otto
- Annals of Oncology 15 (Supplement 4): iv 299 – iv 306, 2004

Date reviewed: 26/01/2016

Next review date: 26/01/2018

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