Management of Palliative Care Emergencies

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Faculty/Presenter Disclosure

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Mitigating Potential Bias

- No conflict of interest to declare

Objectives

Review the following five palliative care emergencies:

- Malignant spinal cord compression (MSCC)
- Hypercalcemia
- Superior vena cava syndrome
- Seizure
- Hemorrhage

By the end of this session, be able to:

- Identify common emergencies in palliative care and their underlying pathophysiologies
- Develop an approach to diagnosis of common palliative care emergencies
- Develop an approach to management of common palliative care emergencies and appreciate the implications for prognosis

Case 1

- 64 yo F with metastatic lung cancer
  - Back pain progressively worsening over 2 months
    - Initially pain was localized, but then began to radiate to both legs
    - Pain is worse with movement
  - Came to emergency department because of increasing leg weakness and urinary hesitancy
    - Was PPS 60%; now PPS 40%

- What are you worried about?

MSCC - Etiology

MSCC

- Occurs in 5-10% of cancer patients
- Cancer types in adults
  - Lung 15-20%
  - Breast 15-20%
  - Prostate 15-20%
  - Multiple myeloma 5-10%
  - Non-Hodgkin's lymphoma 5-10%
  - Renal cell carcinoma 5-10%
  - Colorectal cancer, sarcoma, unknown primary
- Cancer types in children
  - Sarcomas, esp. Ewing's
  - Neuroblastomas
  - Hodgkin's disease
  - Germ cell tumours

MSCC – Sites of Compression

- Dependent on relative bone mass and blood flow
- Cervical spine – 15%
- **Thoracic spine – 60%** - often breast and lung
- Lumbosacral spine – 25% - abdominal malignancies
- **Multiple sites of compression in 20-35%**

MSCC - Pathophysiology

1. Hematogenous mets to vertebral body → bone mets growing into epidural space OR pathologic # of vertebral body met
   - ~85-90% of MSCC
2. Growth of paravertebral tumour directly into spinal canal through intervertebral foramen
   - ~10-15% of MSCC; Lymphomas, neuroblastomas
3. Spinal nerve root dysfunction (esp. cauda equina) caused by direct tumor involvement from leptomeningeal disease
4. Rarely, due to epidural or cord metastases

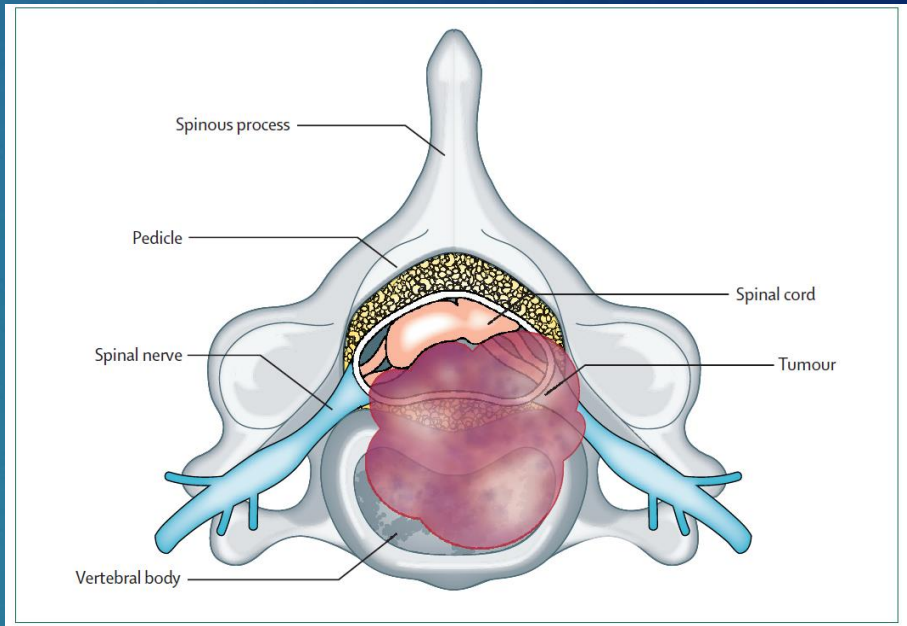


Figure 1: **Tumour in the vertebral body**
The tumour is anterior to the spinal cord and grows posteriorly to compress the spinal cord.

MSCC – Clinical Features

High index of suspicion with known metastatic disease, progressive **back/radicular pain**, progressive gait difficulties

- Pain - 83 to 95 % of patients at the time of diagnosis
- Weakness - 60 to 85 % of patients at the time of diagnosis
- Sensory findings - less common than motor findings, but present in majority
- Bladder and bowel dysfunction – usu. a late finding, but 50-60% of patients will have at time of diagnosis
- Gait ataxia - in the setting of back pain

Note: MSCC is 1st presentation of cancer in ~20%

MSCC – Diagnosis

Diagnosis

- High clinical suspicion for patients with malignancy
- History and physical, including neurologic exam
- Urgent MRI
  - Images of the spinal cord and intramedullary pathology + defines the adjacent bone and soft tissues
  - Scan the **whole spine**!

MSCC – Management

Management

- What is Palliative Performance Scale (PPS) and what are patient's GOC
- Goals: Maintenance of neuro function, pain control, control of tumour growth, stabilization of spine
- Loading dose of Dexamethasone (16 mg) and request urgent consult radiation oncology +/- neurosurgery/ortho
- Continue Dexamethasone until completion of XRT
- Taper and discontinue Dexamethasone over two weeks following completion of XRT

MSCC – Implications for Prognosis

- Median survival following MSCC ~ 6 months
  - Ambulatory prior to tx: median survivial 8-10 mo
  - Non-ambulatory prior to treatment: median survival 2-4 mo
    - If patient remains non-ambulatory post XRT: median survivial <1 mo
- MOST important prognostic factor for regaining ambulation after treatment:
  - ***pretreatment neurologic status***
    - !Educate patients, families, and health care providers!

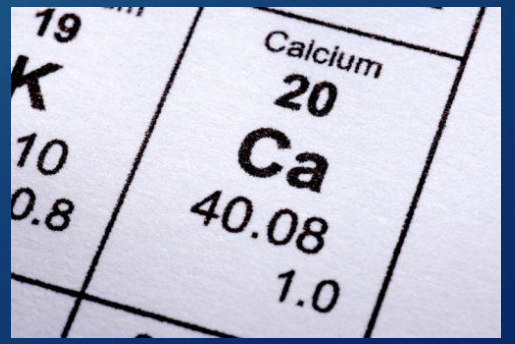
Case 2

- 69 yo female with metastatic pancreatic cancer presents to the emergency department with a 2-week history of gradually increasing:
  - Pain
  - Constipation
  - Confusion

What might be going on?

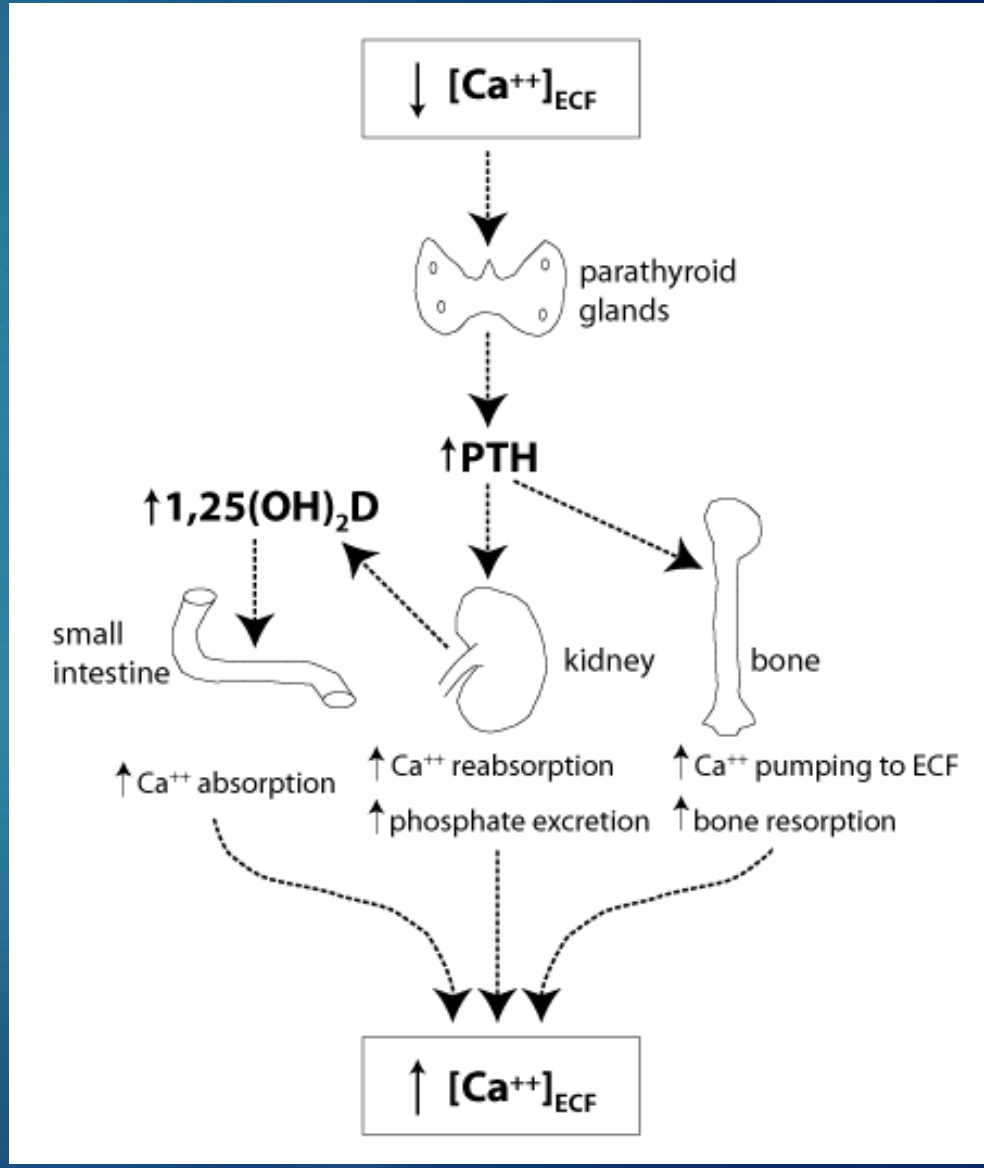
Hypercalcemia

- Most common paraneoplastic syndrome: 10-30% with advanced cancer
- Can be caused by many types of cancer, solid tumors and leukemia
  - renal, **breast**, **myeloma**, squamous cell (especially **lung**), lymphoma, leukemia
- May be the first presentation of cancer
- Up to 30% of cancer patients with hypercalcemia, especially those in remission, will have another cause for it (e.g., primary hyperparathyroidism)



Calcium homeostasis

- **PTH** stimulates
  - **bone resorption** and increased **renal calcium reabsorption** (phosphate excretion)
  - Converts calcidiol to calcitriol (1,25-dihydroxy**vitamin D_3)**
- Calcitriol
  - Promotes GI calcium absorption
  - Promotes bone resorption



Hypercalcemia - Pathophysiology

Table 1. Mechanisms of hypercalcaemia in malignant disease

Mechanism of hypercalcaemia	Associated types of tumours	Main mediator	Frequency
Humoral hypercalcaemia of malignancy	Squamous cell cancers (lung, cervical, oesophageal, head and neck), breast, ovarian and renal carcinomas.	PTHrP	~80%
Local osteolytic invasion	Multiple myeloma, breast carcinoma, lymphomas	RANKL, IL-6, TNF-α, PTHrP	~20%
Active vitamin D secretion by tumour cells	Lymphomas	$1,25(OH)_2D$	<1% (Rare)
PTH secretion	Primary parathyroid carcinoma	PTH	<1% (Rare)
	MEN syndromes and other tumours (variable)		

$1,25(OH)_2D$, 1,25-dihydroxyvitamin D; IL-6, interleukin-6; MEN, multiple endocrine neoplasia; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related protein; RANKL, receptor activator of nuclear factor κB ligand; TNF-α, tumour necrosis factor alpha. Adapted from reference [3].

Hypercalcemia - Symptoms

"stones, groans, moans, psychiatric overtones"

- **GI** (nausea, vomiting, constipation)
- Muscle weakness, **bone pain**
- **Neuropsychiatric** (lethargy, confusion, delirium, coma)
- Hypercalcemia can lead to nephrogenic diabetes (polyuria, polydipsia, dehydration)
- Palpitations
- Chest pain
- Cardiac arrhythmia

Hypercalcemia – Diagnosis

- Suspect in any cancer patient presenting with altered mental status
- Investigations:
  - Measure serum calcium – ionized or correct for albumin
    - Corrected Ca = (40 – Serum Albumin)(0.02) + (measured Serum Ca)
      - This is for SI units
  - Normal serum Ca (2.2-2.6 mmol/L)
  - Hypercalcemia
    - Mild <3, mod 3-3.5, severe >3.5, or with symptoms
  - Measure serum PTH to confirm malignant etiology
    - If inappropriately normal or high, consider primary or concomitant hyperparathyroidism

Hypercalcemia - Treatment

Day 1

1. Stop medications that increase calcium; e.g., Ca/vitD/thiazide diuretics
2. Promote renal Ca excretion
   - Hydration
3. Reduce bone resorption
   - bisphosphonate +/- Calcitonin if severe symptoms

Day 2: continue fluids +/- calcitonin

Day 3: if calcium is normal, decrease fluids by 50%, stop calcitonin

Day 4: stop fluids

* Median relapse after bisphosphonates 17-40 days (likely zoledronate longer but more expensive)

Hypercalcemia - Refractory

- Denosumab - mAb directed against RANKL that modulates osteoclast and osteoblast activity
- Consider steroids in hematological malignancy
  - inhibit conversion of 25(OH)D to active 1,25 (OH)2D in the activated mononuclear cells in the lung and lymph nodes→ reduce GI absorption of Ca
- Dialysis - severe malignancy-associated hypercalcemia and renal insufficiency (e.g., Cr > 400 and/or heart failure, for whom hydration is unsafe)
- Cinecalcet – calcimimetic for parathyroid carcinoma or 1° or 2° hyperparathyroidism

Hypercalcemia - Prognosis

- Implications
  - Median survival 30-60 days following diagnosis of hypercalcemia
  - No evidence that treatment improves survival in absence of cancer treatment
  - Good evidence for improvement in symptoms
  - Hypercalcemia will recur, large role for education on prognosis and planning
  - Severe refractory hypercalcemia is poor prognostic factor

Case 3

- 47 y.o M with lymphoma, presents to clinic complaining of
  - Dyspnea
  - Facial flushing
  - Fatigue
  - Purple rash across chest
  - Neck fullness

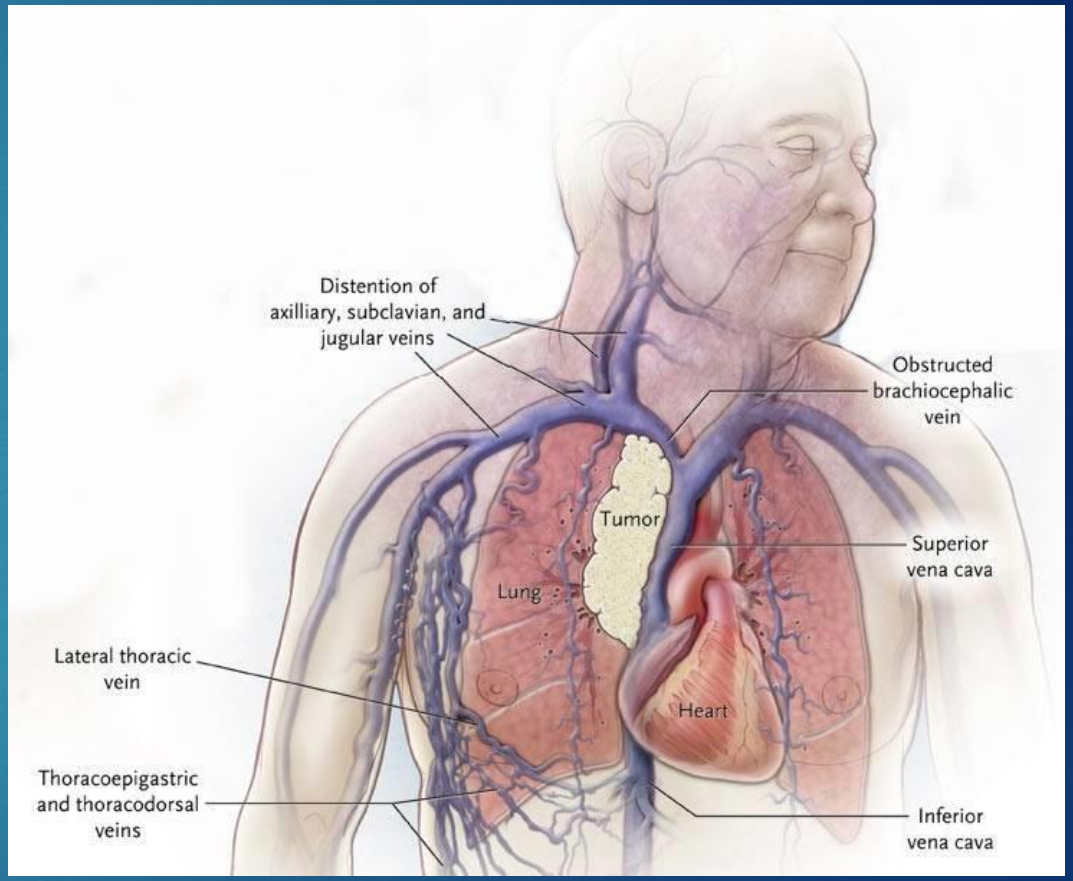
SVC Syndrome

- Superior vena cava obstruction
- Not (always) an emergency
- First described in 1757, resulting from SVC obstruction due to syphilis
- Since mid-20th century, malignancy causes ~60-85% of SVCO
  - Cancer types
    - Lung small cell > non-small cell (2-4%)
    - Lymphoma (2-4%)
    - Metastatic breast, esophagus, colorectal
  - Non-malignant etiologies
    - Indwelling intravascular devices, postradiation fibrosis, fibrosing mediastinitis, infection with nocardiosis

SVCO – Anatomy & Pathophysiology

SVC

- Extends from confluence of brachiocephalic veins and ends in the superior right atrium
- Encircled by chains of lymph nodes
- Drains venous blood from head, neck, upper extremities, upper thorax
- Tight space: surrounded by sternum, trachea, right bronchus, aorta, pulmonary artery, perihilar and paratracheal lymph nodes
- SVC is thin-walled, easily compressible



SVCO – Clinical Presentation

- Usually insidious onset
- Common symptoms
  - Dyspnea (at rest)
  - Cough
  - Facial/neck edema and head fullness
  - Arm edema
  - Chest pain
  - Dysphagia
  - Headache
- Common signs
  - Venous distension of neck
  - Venous distension of chest wall
  - Cyanosis
  - Plethora of face
  - Stridor
  - Hoarseness
  - Cerebral edema: ALOC
  - Pleural effusions
  - Hemodynamic compromise (if severe)

SVCO – Assessment/Diagnosis

- History and physical
- Confirmation requires imaging
  - CXR, ultrasound, CT, or MRI
- If no previous diagnosis of malignancy, consider:
  - Sputum cytology
  - Bronchoscopy with transbronchial needle aspiration for cytology
  - Thoracentesis if pleural effusion
  - Biopsy of supraclavicular node

SVCO - Treatment

- Goals of treatment (PPS and GOC)
  - Symptom relief
  - Treat complications
  - Treat underlying condition
- True **emergency** if:
  - **Stridor** due to central airway obstruction
  - Severe **laryngeal edema**
  - **Coma** from cerebral edema airway obstruction or cerebral edema

SVCO – Treatment - Emergency

Emergency:

- Endovenous recanalization
  - mechanical thrombolysis
  - pharmacologic thrombolysis
  - balloon angioplasty
- SVC stent placement
- Surgical venous bypass
  - Thymoma, thymic carcinoma, germ cell tumor
- Radiotherapy no longer the best option **for emergency**

SVCO – General Treatment

- Elevate head of bed (no evidence)
  - To decrease hydrostatic pressure and head and neck edema
- Anticoagulation for thrombosis-related SVCO
- Steroids
  - In lymphoma* or thymoma; unclear benefit in other malignancies
- Consider diuretics
- O2
- Non-emergent
  - Medical oncology and/or radiation oncology consults

SVCO - Prognosis

- Median survival ~6 months after presentation for NSCLC
- Prognosis depends on type of cancer and if patient has had previous treatment

Table 3:

Factors with significant association with overall survival

	P-value[a]	Survival (months)	
Age	0.000	50 or below	35.1
		>50	2.8
Smoking history	0.012	Never smoker	35.7
		History of smoking	3.4
Steroid use	0.007	No steroid	51.9
		Steroid use	5.9
Primary malignancy	0.008	Bronchogenic	3.1
		Extrathoracic malignancy	3.4
		Lymphoma	80.1
		Thymic malignancy	1.8

[a]In univariate analysis.

Case 4

- 72 yo F with metastatic lung cancer
  - Receiving palliative care at home
  - Patient's daughter calls MD because she thinks her mother is having a seizure
  - The family is also calling 911

Seizures

- Occur in ~20-25% of malignancies with cerebral involvement
- Due to:
  - Brain metastases
  - Primary tumors
  - Leptomeningeal disease
  - Paraneoplastic syndromes
  - CVA
  - Infection
  - Metabolic disorders (glucose, calcium, sodium)
  - Medication withdrawal (alcohol, benzos)

Seizures

- Focal or general
- Usually short duration (i.e., < 2 minutes)
- Status epilepticus: seizure activity > 30 min, or recurrent seizures without return of consciousness within a 30-min span.
- Initiate treatment if:
  - Three partial seizures occur within 24 hours
  - Partial or generalized seizure lasts longer than 5 min

Seizures – Investigations (?)

Depending on goals of care and setting of care

- Blood sugar stat
- ABG
- CBC, electrolytes, BUN and Cr, Ca and Mg , liver function tests
- Cultures as appropriate
- Review medications/toxicology screen
- CT head
- ECG
- Lumbar puncture

Seizure - Treatment

- Treatment – initial management; depends on location and GOC

1. **Hospital – GOC are for full medical management**
   - airway management and oxygenation, (ABCs)
   - 50 mL dextrose 50% + thiamine 100 mg IV
   - **Lorazepam** 4 mg IV (or 0.1mg/kg). Infuse no faster than 2mg/min
     - Onset of activity 6-10 minutes IV
   - Diazepam 0.15 mg/kg IV, up to 10 mg per dose, may be substituted if lorazepam not available
   - If no IV access, midazolam 10 mg IM/SC, nasally or buccally, for patients with a body weight >40 kg and 5 mg for patients with a body weight of 13 to 40 kg

Seizures – Initial Treatment

2. **Palliative Care Unit/Hospice**

- **Lorazepam** (dosage recommendations vary) 2 mg SC, SL, or PR; and 2 mg q10-20 minutes prn x 4 doses in 12 hours
  - duration of effectiveness (8 to 24 hours)
- Diazepam 10 mg PR; and 10 mg q5min prn until effective; maximum total dose of 40 mg
- Midazolam 5-10 mg SC and q15min up to a total of 3 times
- Example of hospice protocol:

Seizures – Call MD if patient's first seizure

☑ Lorazepam 2mg SC x1 prn **use first line** (then wait 5 minutes); use EDB, LU 481

☑ Midazolam 5mg SC x1, may repeat q5 min prn up to 3 doses total (15mg) **use second line** use EDB, LU 495

Seizures – Initial treatment

3. Home

- Challenging setting → most families will call 911/go to emergency department, especially in the context of a first seizure
- Medications to have available in the home:
  - Lorazepam 2 mg SL or SC; 2 mg q10-20 minutes prn x 4 doses in 12 hours
  - Midazolam 10 mg SC; q15min up to a total of 3 times
  - Phenobarbital 120 mg SC q15 mins until settled

Seizures - Refractory

- For refractory seizures, **phenytoin** or **phenobarbital**
  - Phenytoin 15-20 mg/kg IV, no more than 50 mg/min (non sedating)
  - Phenobarbital 120 mg SC/IV q15 mins until settled, then 120-240 mg SC/IV q 4-6h
  - Phenobarbital 20 mg/kg IV, infuse at 60 mg/min
    - Phenobarbital can also be given by SC administration → easier to use in a hospice or home-care setting

Prognosis - Seizures

- Highly dependent on etiology

Case 5

49 y.o. M with head and neck cancer; previously treated with radical radiotherapy & surgery

- Now with recurrence eroding into vasculature
- ENT is unable to ablate
- Continues to ooze despite packing
- ENT tells you that it is likely a matter of time before he progresses from oozing to catastrophic bleed
- Inpatient

Bleeding - Etiologies

Ranges from slow minimal oozing, to major catastrophic bleeding

- Tumor invasion
  - infiltration of vessels, angiogenesis
  - Head and neck cancers
  - Lung and GI cancers
- Treatment side effects
  - mucositis from chemo/rads
- Thrombocytopenia
  - marrow invasion/suppression, DIC, splenomegaly
- Nutritional deficiencies
  - low vitamin K
- Drugs
  - COXi, anticoagulants
- Coagulopathy
  - liver disease
- Other

Major Bleeding

- Causes distress to patient, family, caregiver
- How common?
  - 30% in hematologic malignancies
  - 6-10% of cancer patients
  - 1.5% of patients receiving palliative care
- Can be anticipated sometimes
- May be visible or invisible

Management of Bleeding

Treatment depends on goals of care (local to systemic to supportive), otherwise general principles of management/resuscitation

- Stop anticoagulants and NSAIDs
- Hemostatic dressings (e.g., Kaltostat® or Gelfoam®)
- Topical tranexamic acid 5% (500 mg/10 mL)
- Systemic tranexamic acid: 10 mg/kg per dose IV at 3-4 times per day or 1.5 g IV/po and then 1 g IV/po TID (decrease dose in renal failure)
- Consider specialist therapy:
  - Radiotherapy (e.g., skin, lung, esophagus, rectum, bladder, uterus, vagina)
  - Coagulation: cryotherapy, laser
  - Embolization

Management of Bleeding

- Can be for sedation if for comfort measures
- Make patient and family aware and be prepared:
  - Dark towels
  - Basins
  - Anxiolytics
- Sedation
  - Midazolam prefilled syringes nearby; 2.5-5 mg sc stat, q5-10 min prn and 5-10 mg q2h
  - Midazolam CADD 0.5-2.5 mg/hr sc
    (CADD = (continuous ambulatory delivery device)
  - Lorazepam 1-4 mg sc q4-6h and q4-6h prn
- Aftercare – family/health care team

Objectives

Review the following five palliative care emergencies:

- Malignant spinal cord compression (MSCC)
- Hypercalcemia
- Superior vena cava syndrome
- Seizure
- Hemorrhage

By the end of this session, be able to:

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Thank you!
Questions?

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