Management of Palliative Care Emergencies

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Faculty/Presenter Disclosure

- Presenter: Andrea Weiss
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    - none
- Presenter: Grace Ma
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Objectives

- Malignant Spinal Cord Compression
- Hypercalcemia of Malignancy
- 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

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Before Proceeding

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Before proceeding

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Case 1

- 64 yo F with metastatic lung cancer
  - Home care patient; has chronic constipation
  - Back pain progressively worsening over 2 months
    - Initially pain was localized, but then began to radiate to both legs
    - Pain is worse with movement
    - Known bone mets in spine
    - Pain has been treated with opioids
  - Over the last week, has increasing leg weakness and urinary hesitancy
    - Was PPS 60%; now PPS 40%
- What are you worried about?

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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

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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%**

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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

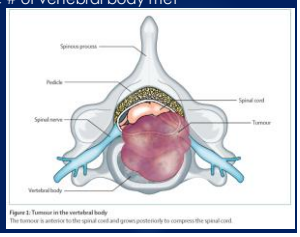

Figure 1: Tumour in the vertebral body
The tumour is anterior to the spinal cord and grows posteriorly to compress the spinal cord.

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MSCC - Pathophysiology

3. Spinal nerve root dysfunction (esp. cauda equina) caused by direct tumor involvement from leptomeningeal disease
4. Rarely, due to epidural or cord metastases

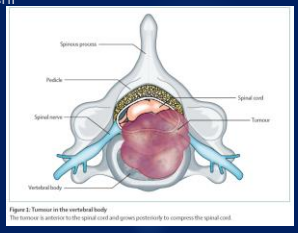

Figure 1: Tumour in the vertebral body
The tumour is anterior to the spinal cord and grows posteriorly to compress the spinal cord.

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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
- Bladder and bowel dysfunction – usually a late finding; 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%

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MSCC – approach

Diagnosis

- High clinical suspicion for patients with malignancy
- History and physical, including neurologic exam

Management

- What is PPS and what are patient's GOC?
- Goals: Maintenance of neuro function, pain control, control of tumour growth, stabilization of spine

Our patient is at home, wishes to maintain mobility, willing to go to hospital for investigations and treatment

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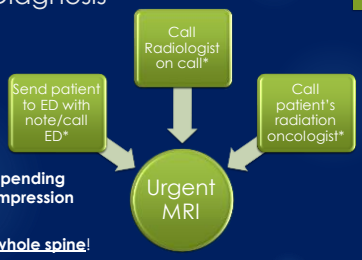
MSCC – Diagnosis



*Emphasize **impending spinal cord compression**

- Scan the **whole spine**!

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MSCC – Management

- Depending on place of practice, consider starting dexamethasone at home/before ER
- Loading dose of dexamethasone (10 mg); continue dexamethasone total daily dose 16 mg
- Request urgent consult radiation oncology +/- neurosurgery/orthopedic surgery, as available
- Continue dexamethasone until completion of XRT
- Taper and discontinue dexamethasone over two weeks following completion of XRT

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MSCC – Implications for Prognosis

- Median survival following MSCC ~ 6 months
  - Ambulatory prior to treatment: 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!

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Case 2

- 70 yo M with metastatic pancreatic cancer
  - presents to your clinic
  - 2-week history of gradually increasing:
    - Pain
    - Constipation
  - Pt is accompanied by his wife, who states that he has been confused lately
  - PPS 60%

What might be going on?

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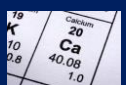
Hypercalcemia

- **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)



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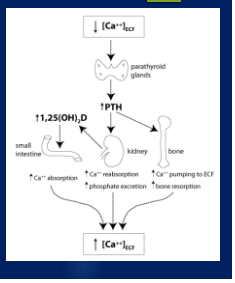
Calcium homeostasis

- **PTH** stimulates
  - **Bone resorption** and increased **renal calcium reabsorption** (phosphate excretion)
  - Converts calcidiol to calcitriol (1,25-dihydroxy**vitamin D_3**)
- Calcitriol (active form of vitamin D3)
  - Promotes GI calcium absorption
  - Promotes bone resorption



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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; IL6, 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].

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Hypercalcemia - Symptoms

"stones, groans, moans, psychiatric overtones"

- **GI** - Nausea, vomiting, constipation, abdominal pain
- **MSK -** Muscle weakness, bone pain
- **Neurologic** - Lethargy, confusion, delirium, coma
- **Renal** - nephrogenic diabetes (polyuria, polydipsia, dehydration), nephrolithiasis
- ❤️ - cardiac arrhythmia, short QT, hypertension

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Before proceeding

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Hypercalcemia – Diagnosis

- Vigilance
- Severity of symptoms → Urgency

Non-Urgent	Send to lab for bloodwork OR Arrange for labs at home ($+Time)	
Urgent	Send to ED via EMS	Hospital admission

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Hypercalcemia - Diagnosis

- Investigations: Measure serum calcium, albumin, renal function
  - Serum calcium – ionized or corrected
    - 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
    - moderate 3-3.5
    - severe >3.5 or with symptoms

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Hypercalcemia - Treatment

- Depending on goals of care and practice setting:
  - No treatment, comfort care only
  - IV fluids or hypodermoclysis
  - IV fluids + bisphosphonate
    (if patient has not previously received IV bisphosphonate, patient may need to receive first dose in hospital setting)
  - Involvement of home care team (nursing, coordinator…)

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Hypercalcemia – Treatment hospital

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 (may not be available/covered) if severe symptoms

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Hypercalcemia – Treatment hospital

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)

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Hypercalcemia - Refractory

- Denosumab – monoclonal Ab directed against RANKL that inhibits osteoclasts
- 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 – inhibits PTH secretion, used for parathyroid carcinoma or 1° or 2° hyperparathyroidism

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Hypercalcemia - Prognosis

- Implications
  - Median survival short months 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

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Case 3

- 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

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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)

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Seizures

- Focal or general
- Usually short duration (i.e., < 2 minutes)
- Status epilepticus:
  - ≥5 minutes of continuous seizures, or
  - ≥2 discrete seizures between which there is incomplete recovery of consciousness
- Initiate treatment if:
  - Three partial seizures occur within 24 hours
  - Partial or generalized seizure lasts longer than 5 min

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Seizures – Investigations (?)

Depending on goals of care and setting of care

- Blood glucose 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

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Seizures - 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

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Seizures - Treatment

2. **Palliative Care Unit/Hospice/Hospital + GOC are for comfort focus**

- **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

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Seizures - Treatment

- 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

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Seizures - 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 min prn x 4 doses in 12 hours
  - Midazolam 10 mg SC; q15min up to a total of 3 times
  - Phenobarbital 120 mg SC q15 min until settled

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Seizures - Refractory

- For refractory seizures, **phenytoin** or **phenobarbital**

Hospital
- Phenytoin 15-20 mg/kg IV, no more than 50 mg/min (non-sedating)
- 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

Hospital/PCU/Hospice/Home – Goal: comfort only
- Phenobarbital 120 mg SC/IV q15 min until settled, then 120-240 mg SC/IV q 4-6h

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Prognosis - Seizures

- Highly dependent on etiology

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Case 4

49 yo M with head and neck cancer; previously treated with radical radiotherapy & surgery

- Hospice patient
- Now with recurrence eroding into vasculature
- Before transfer to hospice, was seen by ENT – they were unable to ablate
- Continues to ooze despite packing
- ENT stated that it will likely progress from oozing to catastrophic bleed

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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

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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

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Management of Bleeding

Treatment depends on goals of care, 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)

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Management of Bleeding

- Consider specialist therapy:
  - Radiotherapy (e.g., skin, lung, esophagus, rectum, bladder, uterus, vagina)
  - Coagulation: cryotherapy, laser
  - Embolization

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Management of Bleeding

- Can be for sedation if for comfort measures
- Make patient and family aware and be prepared:
  - Dark towels
  - Basins
  - Anxiolytics

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Management of Bleeding

- 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

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Objectives

- Malignant Spinal Cord Compression
- Hypercalcemia of Malignancy
- Seizure
- Hemorrhage

By the end of this session, be able to:

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- Develop an approach to diagnosis of common palliative care emergencies
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Thank you!

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