Oncological emergencies

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Presentation to Internal Medicine GME resident physicians:
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Presentation goals

- Briefly review clinical presentation, diagnosis, and management of common oncological emergencies
- Discuss evidence based management options
- Provide opportunity for answering questions
- Encourage and motivate resident physicians for further reading and self learning
Oncologic emergencies: Examples

- Not possible to cover all emergencies in 1 hour
- Please find a nice text book or review some of the articles listed
Oncologic emergencies: Examples

- **Metabolic**
  - Hypercalcemia
  - SIADH
  - Tumor lysis syndrome

- **Structural**
  - SVC syndrome
  - Spinal cord compression
  - Pericardial effusion – Cardiac tamponade

- **Others:**
HYPERCALCEMIA OF MALIGNANCY
Hypercalcemia: Recent case

- Calcium – 13.7
- Creatinine – 1.2
- Albumin – 3.9
- Intact PTH - less than 1 pg

- Diagnosis: Myeloma
Hypercalcemia

• Up to 20% cancer patients may experience hypercalcemia
Hypercalcemia: pathophysiology

- Humoral: 80%
- Osteolytic: 20%
Hypercalcemia: pathophysiology

- **Humoral (about 80%)**:  
  - Cytokine mediated increase in osteoclast activity +  
  - Reduced calcium clearance (increased renal tubular re-absorption)

- **Osteolytic bone metastases (about 20%)**:  
  - Direct effect
Hypercalcemia: Causes

- **Malignancy** (most common in patient cause)
- **Hyper-parathyroidism** (most common outpatient cause)
- **Others:**
  - Drugs (diuretics etc),
  - Granulomatous disease (TB, Sarcoidosis, etc), infections,
  - Milk Alkali syndrome,
  - Immobilization,
  - Thyrotoxicosis, adrenal insufficiency
Hypercalcemia of Malignancy: Causes

- Lung cancer
- Breast cancer
- Multiple myeloma
- Others: Head and neck, Kidney, Bladder, Cervix...

- Prostate cancer causes osteoblastic lesions and rarely causes hypercalcemia
Hypercalcemia: Symptoms

- Careful history is very important
- Symptoms depend on level of calcium and rapidity of calcium rise
- Severity
  - Mild: 10-11.5 – no symptoms
  - Moderate: 11.5-13.5
  - Severe: more than 14.5
  - Life threatening: 14-15
- Acute: Cancer
- Chronic: HyperPTH
Hypercalcemia: Symptoms

- Lethargy, altered mentation, stupor, coma
- Fatigue
- Constipation
- Nausea and vomiting
- Polydipsia, polyuria
- Cardiac arrhythmias
- (Stones, moans and groans – HyperPTH)
PTH mediated Hypercalcemia:

- High PTH or inappropriately normal PTH in the setting of high calcium
  - Primary: from parathyroid glands
  - Secondary: Low calcium triggering high PTH – renal failure
  - Tertiary: relative autonomous PTH production by parathyroid hyperplasia after years of renal failure
Benign familial hypercalcemia

- Benign familial hypocalciuric hypercalcemia
- Inactivating mutation in calcium sensing receptor
- Urinary calcium / creatinine clearance ratio less than 0.01
- First degree relatives involved
- Autosomal dominant
- Asymptomatic – mild-lifelong
- No parathyroid surgery needed
Hypercalcemia of Malignancy: Non PTH mediated

- High calcium and Low intact PTH
- Humoral factors
  - PTH related protein: Squamous cell, ovarian, breast, renal cell
  - 1, 25 dihydroxy vitamin D3: B cell NHL
- Osteolysis: Myeloma, breast cancer
Hypercalcemia of Malignancy: Non PTH mediated

High calcium

Low iPTH
Evaluation of hypercalcemia

Hypercalcemia

- PTH low
  - Cancer
  - Granulomatous disease
  - Drug induced
  - Thyroid or adrenal disease
  - PTHrP, Vitamin D

- PTH high or normal
  - 24 hour urine calcium high
    - HyperPTH
  - 24 hour urine calcium low
    - Benign familial

- Benign familial

- Cancer
  - Granulomatous disease
  - Drug induced
  - Thyroid or adrenal disease
  - PTHrP, Vitamin D
Hypercalcemia: Management

- Mainstay is IV hydration with normal saline 200-400 ml/hour

- Diuresis and calciuresis—after volume replacement

- Use loop diuretic: inhibits calcium reabsorption
Hypercalcemia: Management

- Bis-phosphonates:
  - Inhibit osteoclastic bone resorption
  - Very effective - for 1-8 weeks
  - Pamidronate and Zoledronate
  - Zoledronate is better (faster, higher CR and longer lasting)

- Calcitonin:
  - Rapid action but rapid tachyphylaxis - inhibits osteoclasts
Hypercalcemia: Management

- Steroids:
  - works well in lymphoma and sarcoidosis

- Dialysis – rarely needed

- Oral Etidronate – rarely used now

- Gallium – CI over 5 days - rarely used

- Mithramycin – toxic – rarely used
Hypercalcemia: Management

- Treat underlying malignancy
- Hypercalcemia is usually an end stage manifestation of malignancy
TUMOR LYSIS SYNDROME (TLS)
Tumor lysis syndrome

- As a result rapid breakdown of tumor cells
- Seen in cancers with rapid cell turnover
- Seen in Burkitt’s type high grade lymphoma, ALL, with bulky disease, high WBCs, sometimes with small cell cancer, highly chemo-sensitive cancers
- Auto-tumor lysis or treatment induced
Tumor lysis syndrome: Lab

- **Increase** in uric acid, potassium and phosphate
- Hypocalcemia
- Renal failure
- DIC can occur

- Pre existing renal failure and ureteric obstruction increase risk
Tumor lysis syndrome: Management

- **Prophylaxis** in high risk situations – Hydration, Allopurinol, Rasburicase
- **Treatment** with IV hydration, urine alkalinization, IV **Rasburicase** – for rapid lowering of uric acid
- Hemo-dialysis
- Emergency management in ICU might be needed in life-threatening situations
- Monitor electrolytes closely
MALIGNANT SPINAL CORD COMPRESSION (MSCC)
Spinal cord compression

- Medical emergency
- When spinal cord is compressed by tumor or abscess or others
- Vasogenic edema plays a major role

- 5-10% cancer patients develops cord compression
- T spine: 70%, L spine 20%, C spine 10%, multiple 10%
MSCC - presentation

• Symptoms: Pain in 90%, weakness in 75%, sensory problems in 50%, autonomic problems in 50%

• Signs: Focal deficits, hyper reflexia, tenderness over spine

• Radiology:
  ◦ Plain x-rays – can rarely find level
  ◦ CT – better
  ◦ MRI: Best – screen entire spine
  ◦ Myelography is rarely done
Primary malignancy in MSCC

- Lung, breast, prostate cancers – most common
- Others: renal cell, colo-rectal etc.
- Myeloma, NHL etc

- 80% occur in patients with known cancer
- 20% cord compression arise as initial manifestation of cancer
MSCC - prognosis

- Rapid diagnosis and treatment is necessary to avoid permanent damage and irreversible injury to spinal cord
- Recovery prospects depend on neurologic function at time of diagnosis and start of treatment
- Rapid onset and progression are bad signs
- Paralysis over 48 hours – poor chances of recovery
Spinal cord compression treatment: Steroids

- Dexamethasone 10 mg IV stat, then 16 mg daily
- Higher doses up to 100 mg might be more toxic but not definitely better
- Taper over 2 weeks after improvement or irreversibility.
- Provides
  - Pain relief
  - Reduces edema
  - Direct oncolytic for some.
Spinal cord compression treatment

- Radiation:
  - For known primary
  - With spinal stability
  - Radio-sensitive tumors

- Chemotherapy
  - For chemotherapy sensitive tumors
Spinal cord compression treatment

- Surgery - decompression
  - If primary tumor is not known
  - If neurology deficit is less than 48 hours old, single level, survival 3-6 months
  - With spinal instability
  - After RT failure
  - In radio-insensitive tumors
  - Progressive symptoms during RT
SUPERIOR VENA CAVA SYNDROME (SVC SYNDROME)
SVC syndrome

- Acute obstruction of blood flow to right atrium
- Common causes: Lung cancer (over 60%), lymphoma, germ cell tumors, benign causes –catheter related
- Symptoms: Dyspnea, face and extremity swelling, chest pain, dysphagia
- Signs: Distension of veins, ext edema, face edema, cyanosis
- Over half SVC syndrome present as initial manifestation of cancer
SVC syndrome - diagnosis

- Diagnosis is clinical
- Radiology:
  - Mediastinal widening, effusion, sometimes normal chest x-ray
  - CT is very helpful
- Diagnosis:
  - CT guided needle biopsy
  - Mediastinoscopy
SVC syndrome: Treatment

- Treat cancer with RT, chemotherapy: results in rapid resolution of SVC syndrome
- Anti-coagulation is generally used for acute thrombosis (less than 10 days) – generally catheter related
- Supportive care
  - Stents or surgical bypass or angioplasty
  - Oxygen
  - Elevate head end of bed
  - Steroids, Diuretics – reserved for cerebral or airway edema – questionable efficacy
SYNDROME OF INAPPROPRIATE SECRETION OF ANTI-DIURETIC HORMONE (SIADH)
SIADH: Clinical case

- 70 year old female
- Lethargy, weakness
- CT Chest (11-17-03):
  - 1.5 cm left lung mass
  - 5.5 x 3 cm mediastinal mass
- Biopsy: Small cell lung cancer
SIADH: Clinical case

- Sodium, serum: 117
- Urine sodium: 52
- Serum osmolalality: 238 mmol
- Urine osmolalality: 361 mmol
- U. Osm>S. Osm
- Urine is inappropriately concentrated compared to serum
SIADH: Clinical case

Pre-treatment

Post-treatment

Small cell lung cancer - lung mass
SIADH: Clinical case

Pre-treatment

Post-treatment

Small cell lung cancer - mediastinal adenopathy
SIADH: Clinical case

Pre-treatment

Small cell lung cancer-liver metastases

Post-treatment
SIADH: Clinical case

![Graph showing Na level changes with Chemotherapy]

- CHEMOTHERAPY
SIADH

- Observed in 1-2% of cancer patients
- About 3-15% of small cell lung cancer patients have the syndrome
SIADH: Mechanism

- Inappropriate secretion of anti-diuretic hormone of central origin
  OR
- Ectopic production of anti-diuretic hormone (or ADH type substance)
SIADH: Pathophysiology

- Increased total body water
- Increase in plasma volume
- Inability to excrete maximally dilute urine in presence of low serum osmolality
- ADH secretion continues despite low plasma osmolality
Hyponatremia causes

- Hypervolemic
- Euvolemic
- Hypovolemic

SIADH
SIADH: Differential diagnosis of hyponatremia (Euvolemic)

- Hypothyroidism
- Adrenal insufficiency
- SIADH
- Drugs
- Pain
SIADH: Causes

- Malignancy
- CNS disease (CNS metastases, infections, trauma, bleeding)
- Pulmonary diseases (cancer, TB, abscess, pneumonia)
- Drugs (Cytoxan, Morphine, Vincristine, diuretics, Amitriptyline etc.)
SIADH: Common cancers

- Small cell lung cancer (about 60%)
- Carcinoid tumors
- Pancreatic, esophageal, colon cancers
- Prostate cancer
- Bladder cancer
- Adrenal carcinoma
- Hodgkin’s disease
- AML
SIADH: Symptoms

- Factors determining the symptoms:
  - Level of sodium
  - Rapidity of sodium decline
SIADH: Symptoms

- Asymptomatic
- Neurological changes: memory loss, apathy, loss of thinking, lethargy, confusion, focal findings (Na level 120-125 meq)
- Fatigue, anorexia, myalgia
- Seizures and coma and death if Na is <115 (medical emergency).
SIADH: Physical exam

- Determine volume status (fluid overload, euvolemic or volume depletion)
- Neurological findings sometimes focal
- Signs of primary cancer
SIADH: Diagnosis

- Diagnosis is suspected because of low sodium level
- Check serum and urine electrolytes and osmolality
- Diagnostic feature:
  - Less than maximally dilute urine with low serum osmolality (water intoxication)
SIADH: Laboratory features

- Low sodium and low uric acid are almost only abnormalities in electrolytes
- Suspect additional complications for any additional electrolyte abnormalities (e.g. Hypokalemia—ACTH production, Hypercalcemia—bone mets or ectopic PTH like)
SIADH: Treatment goals

- Correction of sodium
  - Slow correction at 0.5-1 meq/l/hr
  - Increase sodium to **no more than 20-25 meq/48 hours** from the baseline
  - Target sodium level **125-130 meq/L**
  - **Na needed** = (desired serum Na - measured Na) x kg body weight x 0.6

- Long term goal: Treat primary cause for long term control
SIADH: Immediate management

- Induced diuresis (N. Saline with Lasix)- replace electrolytes
- 3% Hypertonic saline-for coma or seizures
- Central Pontine Myelinolysis may occur if correction is $>$2meq/l/hr
- Therapy for CNS or other cancer
Central Pontine Myelinolysis

- Symmetrical focal myelin destruction in basal central pons
- Follows 1-3 days of hyponatremia followed by rapid correction over 20 meq/L
- Flaccid or Spastic quadriparesis
- Meticulous maintenance of electrolytes may reverse it
SIADH: Chronic management

- **Treat** the underlying tumor
- **Fluid restriction** (<0.5-1 L/day)
- **Demeclocycline PO 300-600-1200 mg/day**
  - Induces renal resistance to ADH and allows free water excretion (reversible nephrogenic diabetes insipidus)
- **Lithium salts-less reliable**
SIADH and Cancer prognosis

- Not an indicator of poor outcome
- Not an indicator of disease burden
SIADH and cancer status

- Hyponatremia correlates with the activity of cancer
- May serve as a marker
SIADH-Clinical case- (SCLC - lung, adenopathy, liver mets)
Additional review

- Review: Endocrine and metabolic emergencies: hypercalcaemia :Richard Carroll et al. Therapeutic Advances in Endocrinology and Metabolism 2010 1: 225
- The Syndrome of Inappropriate Antidiuresis: David H. Ellison, M.D et al. NEJM 356;20 may 17, 2007
Thanks