Common Problems are Common…

Acute Complications of Cancer

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BMT unit Beatson Oncology Centre
Common Problems

• Spinal Cord Compression
• Hypercalcaemia
• Neutropenic sepsis
• Superior Vena Cava obstruction
• Tumour Lysis Syndrome
• Metastases - protean manifestations
  – Liver e.g. jaundice/ coagulopathy /pain
  – Lung e.g. SOB, Haemoptysis
  – Brain e.g headaches, seizures
  – Bone e.g. pain
Spinal Cord Compression

- Most common in myeloma, prostate, breast and lung cancers
- The cause is important as may dictate therapy
- Usually a posterior extension of a vertebral body mass
- Although Intrathecal metastases cause similar symptoms
- Have a clear understanding of urgency - it is a medical emergency
Spinal Cord Compression - Clinical features

- **Back pain crucial** – coughing, lying flat
- Sensory disturbance below level of compression
- **Progressive weakness**
- Sphincter dysfunction

Usually upper motor neuron (UMN) signs
May be complex e.g. – Brown-Sequard
Or Conus Medullaris, Lhermitte’s sign
- LMN signs may occur if:
  1. Nerve roots are involved
  2. Early in the clinical course of compression
  3. Lumbar spine can cause cauda equina syndrome
Management

- Confirm the diagnosis - Urgent MRI

- In Glasgow, close liaison with Beatson Oncology centre – radiology team may be able to provide daily MRI service if problems at base hospital but must be referred early esp. at the weekend
Management

- Dexamethasone 10mg iv stat and 4 mg 6 hrly po
- Refer for urgent surgical decompression or radiotherapy
- Haematological cancers very radiosensitive while many solid organ metastasis do better with surgical decompression

- Radiosensitivity of tumours varies

<table>
<thead>
<tr>
<th>Sensitive</th>
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<tbody>
<tr>
<td>Lymphoma</td>
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<tr>
<td>Myeloma</td>
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<tr>
<td>Breast</td>
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<tr>
<td>Prostate</td>
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<td>Small-cell lung cancers</td>
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<table>
<thead>
<tr>
<th>Resistant</th>
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<tbody>
<tr>
<td>Melanoma</td>
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<tr>
<td>Sarcoma</td>
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<tr>
<td>Renal cell carcinoma</td>
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Prognosis

• Depends on tumour type
• Degree of neurological compromise at presentation remains the single best predictor of outcome
• 80% of ambulatory patients will remain mobile with limited longterm dysfunction
• Once established paraplegia is difficult to reverse
• Aim to decompress ASAP certainly within 24-48h of presentation
Hypercalcaemia of malignancy

Cancer types:
- Myeloma/Breast
- NSCLC
- Other bony mets
  - e.g. small cell lung, colon, prostate

Pathogenesis multifactorial

a) Humoral hypercalcemia of malignancy
   - Squamous (head and neck, esophagus, cervix, lung)
   - Renal
   - Ovarian
   - Breast
   - Endometrial
   - Human T-lymphotropic virus-associated lymphoma

b) Local osteolysis from bone metastasis
   - Breast
   - Multiple myeloma
   - Lymphoma

c) Calcitriol production
   - Hodgkin lymphoma
   - Non-Hodgkin lymphoma

d) Ectopic parathyroid hormone secretion
   - Parathyroid
   - Ovary
   - Lung
   - Primitive neuroectoderm
Hypercalcaemia – Clinical Features

- Drowsiness, confusion,
- Nausea and vomiting
- Polyuria and Polydipsia
- Dehydration and constipation
- Renal impairment

- Diagnosis – think of it and test!
  - Important to correct for albumin – Adjusted $\text{Ca}^{2+}$
  - In cancer patients Alb can be low avoid underestimating true $\text{Ca}^{2+}$ level
Management

• High flow fluids – 3-4L 0.9% saline
• Intravenous bisphosphonate
  – Palmidronate 60-90mg iv or zolendronic acid 4mg iv
• Calcitonin
  – 100 U 8 hourly im/sc
• Corticosteroids
• Definitive and cancer therapy
Neutropenic sepsis

- Definitions vary – not helpful to be too rigid
- Fever > 38°C in an unwell cancer patient with low neutrophils: but *hypothermia* may occur in severe neutropenic sepsis so review all these patients who report feeling ill
- Level of neutropenia is crucial
  - < 0.5 x 10⁹/L is severe neutropenia and effective phagocytic function is severely compromised
- Expected length/depth of neutropenia
  - Adjuvant chemo versus leukaemia induction
Guidelines

• NICE 2012
  – In the view of many Haematologists these are deeply flawed in treatment recommendations
  – Written by oncologists
  – The nature of adjuvant chemo versus aggressive therapy causing prolonged or profound neutropenia (often when BM is major organ involved e.g. leukaemia post transplant) is NOT properly addressed
  – Role of Tazocin as monotherapy and guidance on line removal most contentious

• ESMO 2010
## Multinational Association for Supportive Care (MASCC) index

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>Burden of illness: no or mild symptoms</td>
<td>5</td>
</tr>
<tr>
<td>Burden of illness: moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Burden of illness: severe symptoms</td>
<td>0</td>
</tr>
<tr>
<td>No hypotension (systolic BP &gt;90 mmHg)</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumor/lymphoma with no previous fungal infection</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status (at onset of fever)</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt;60 years</td>
<td>2</td>
</tr>
</tbody>
</table>

- Scores $\geq 21$ are at low risk.
- Points attributed to the variable ‘burden of illness’ are not cumulative.
- The maximum theoretical score is 26.
- Can be used to assess severity before Neutrophil count is known
Neutropenic sepsis – clinical features

- Often not an obvious source of sepsis
  - Always consider a hickman/PICC line if in situ
  - Look for femoral lines
- Neutropenic sepsis is a medical emergency
- High risk ‘disease’ can be rapidly progressive / fatal within 4-6 hours
  - Septic shock is usual cause of fatalities
  - Often gram negative sepsis / toxin producing MRSA
Initial management of febrile neutropenia.

Temperature >38.5°C and ANC <0.5x10^9/l
Prompt assessment and vigorous resuscitation if needed

Calculate MASCCE score

High risk

Inpatient broad spectrum intravenous antibacterial therapy

Low risk

Inpatient oral antibacterial therapy for some cases

Management - high risk (default)

- Culture all bodily secretions - peripheral/central bc
- Discuss patients with on call haem/oncology teams if unsure
- Supportive care
  - IV fluids
  - If systolic BP < 80 mmHg in my experience likelihood of requiring HDU/ITU support is high

**Empirical HIGH DOSE IV antibiotic therapy**

- Either single agent meropenem
  - Or/
- Broad spectrum penicillin and an aminoglycoside e.g. Tazocin/ gentamicin
Management - 2

• If there is a central line or skin sepsis or known history of MRSA – add Vancomycin/Teicoplanin

• Remove ‘presenting’ central lines if severe sepsis

• If persistent hypotension unresponsive to aggressive fluid resuscitation 2-3 L ASAP
  – Contact ITU/HDU team – inotropes, catheterise
  – Consider hydrocortisone – hypoadrenalism
  – Use Meropenem and Amikacin to cover ESBL
Superior vena cava obstruction

- Extrinsic compression
  - Lymphoma, Germ cell tumour, Lung cancer
- Intravascular occlusion
  - Thrombosis – secondary to central line or thrombophilia
**Clinical features:** inversely proportional to speed of occlusion

![Bar chart showing signs and symptoms of SVC Syndrome](image)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial edema</td>
<td>82%</td>
</tr>
<tr>
<td>Distended neck veins</td>
<td>83%</td>
</tr>
<tr>
<td>Distended chest veins</td>
<td>53%</td>
</tr>
<tr>
<td>Arm edema</td>
<td>46%</td>
</tr>
<tr>
<td>Facial plethora</td>
<td>20%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>54%</td>
</tr>
<tr>
<td>Cough</td>
<td>54%</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>17%</td>
</tr>
<tr>
<td>Syncope</td>
<td>10%</td>
</tr>
<tr>
<td>Headaches</td>
<td>0%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6%</td>
</tr>
<tr>
<td>Stridor</td>
<td>4%</td>
</tr>
<tr>
<td>Confusion</td>
<td>4%</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>2%</td>
</tr>
<tr>
<td>Obtundation</td>
<td>2%</td>
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</table>
Management

**Investigation**
- CT thorax – chest/abdo/pelvis may give clues to primary pathology
- Biopsy is essential – prior to steroids when at all possible.
- History may help- e.g. previous diagnosis, smoker

**Treatment**
- Corticosteroids- Dexamethasone 16-24mg/24h
- Germ cell and lymphoma exquisitely sensitive to chemotherapy
- Other tumour types will need radiotherapy
- Stenting is increasingly popular – Interventional radiotherapy
Tumour Lysis syndrome (TLS)

- Medical emergency as a result of acute metabolic disturbances caused by rapid death of tumour cells
- Renal function is key factor
  - TLS can cause AKI – usually due to urate production
    - (less commonly high phosphate)
  - TLS is made more likely if renal impairment
- Most common- Aggressive Haematological malignancies (also: germ cell, nscc, breast)
- Usually precipitated by aggressive chemotherapy
- But…TLS may occur
  - Spontaneously- part of presentation
  - With ‘gentle’ therapy – e.g. steroids, rituximab
# Tumour Lysis syndrome

<table>
<thead>
<tr>
<th>Metabolic Abnormality</th>
<th>Value or Change From Baseline&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Clinical Implications</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalemia</td>
<td>≥6.0 mmol/L or 6 mEq/dL or 25% increase</td>
<td>Muscle cramps, Paresthesias, Dysrhythmias, Ventricular fibrillation, Cardiac arrest</td>
<td>Polystyrene sulfonate 1 gm/kg, Insulin 0.1 unit/kg with dextrose 25% 2 mL/kg, Sodium bicarbonate 1–2 mEq/kg IV push, Calcium gluconate 100–200 mg/kg slow IV infusion</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>≥2.1 mmol/L for children or ≥1.45 mmol/L for adults or 25% increase</td>
<td>Nausea, Vomiting, Diarrhea, Lethargy, Seizures, Acute kidney injury</td>
<td>Volume loading, Removal of phosphate from IV fluids, Oral phosphate binders, Hemodialysis</td>
</tr>
<tr>
<td>Hypocalcaemia</td>
<td>≤1.75 mmol/L or 25% decrease</td>
<td>Muscle cramps, Tetany, Hypotension, Dysrhythmia, Acute kidney injury</td>
<td>Calcium gluconate 50–100 mg/kg slow IV infusion with electrocardiogram monitoring, give only if symptomatic.</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>≥476 μmol/L or 8 mg/dL or 25% increase</td>
<td>Acute kidney injury</td>
<td>Volume loading, Rasburicase (see text for dosing), Allopurinol by mouth or IV</td>
</tr>
</tbody>
</table>

<sup>a</sup>Cairo–Bishop definition requires two or more laboratory abnormalities within 3 days prior to or 7 days after initiation of cytotoxic therapy (124).
Hydrogen peroxide is produced when uric acid is converted to Allantoin. This can cause methaemoglobin production and haemolysis so Rasburicase is C/I in G6PD deficiency.
Management summary

• High flow fluids – twice maintenance 5-6 l/day
• Pragmatically may need diuretics
• Twice daily electrolyte and renal function
• Rasburicase in high risk/Allopurinol standard risk
• Standard management of hyperkalaemia
  – Ion exchange resins, Insulin/Dextrose, Ca gluconate
  – Possibly sodium bicarbonate – discussed with renal
• Renal Dialysis – haemofiltration if severe
  – hyperkalaemia, hyperphosphataemia, hyperuricaemia
  – NB Only replace Calcium if symptomatic as will ppt with phosphate in kidneys and worsen TKI
Short reference list

• Oncologic emergencies

• Haematological emergencies managing hypercalcaemia in adults and children with haematological disorders
  *British Journal of Haematology*, 149, 465–477

• NICE guidance 2012 – neutropenic sepsis

• ESMO guidelines

• *Davidson’s Principles and Practice of Medicine*