Paediatric Oncologic Emergencies

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Why Focus on Oncologic Emergencies?

- May delay/interrupt definitive therapy
- Avoid end-organ injury
- Avoid long-term sequelae and compromise of quality of life
- Avoid mortality
Case 1

9 year old boy with a two month history of left sided facial swelling, drenching night sweats significant weight loss, rapidly expanding abdominal mass over last three weeks and bony pains. On examination left-sided maxillary swelling and tenderness, left-sided cervical lymphadenopathy, abdominal distension, bilateral testicular enlargement.

Anticipate? Recognize? Manage?
Case 2

4pm: 6 year old, unwell for last 2 months, sick looking, febrile, pale, has a large spleen. WBC 235,000x10⁹/L Hb 6.5g/dl platelets 21x10⁹/L. Admitted to children’s ward, anti-malarial, broad spectrum antibiotic cover and GXM for pRBCs & platelets

Anticipate? Recognize? Manage?

12:45am Mother concerned about reduced urine output and increasing agitation, no seizures. Has developed tachypnoea RR 52breaths/min, SpO₂ 82% and bilateral crepitations

Anything else to anticipate?
Case 3

4 year old boy with 3-months history of intermittent low-grade fever progressively increasing abdominal swelling, bruising around his eyes for last two weeks, worsening lethargy. Now presents with a four-day history of refusal to walk and incontinence of stool and urine

Case 3
Objectives

• Discuss pathophysiology diagnosis and approach to common paediatric oncologic emergencies
  • Tumor Lysis Syndrome
  • Hyperleukocytosis/Leukostasis
  • Spinal Cord Compression
  • Fever/Neutropenia
  • Superior Mediastinal Syndrome
  • Disseminated Intravascular Coagulation
  • Increased intracranial pressure
  • Posterior Reversible Encephalopathy Syndrome
  • Neutropenic colitis
Approach to Management

Reactive

Proactive
Approach to Management

Anticipate
Recognize
Manage appropriately
Understand the Timing of Oncologic Emergencies

Remain vigilant!

• Initial presentation
• Progression of disease
• Therapy related
Tumor Lysis Syndrome
Tumor Lysis Syndrome

• Occurs when tumor cells release their contents into the bloodstream
  • Spontaneously (primary)
  • In response to therapy (secondary)
• Characteristic findings of
  • Hyperuricemia
  • Hyperkalemia
  • Hyperphosphatemia
  • Hypocalcemia
C
Lysis of cancer cells
Release of cellular contents

DNA
DNAase breaks down DNA, releasing purines

Adenosine

Guanosine

Phosphate

Potassium

Cytokines

Hypoxanthine

Inosine

Hypotension

Inflammation

Acute kidney injury

Xanthine oxidase

Xanthine oxidase

Rasburicase

Allopurinol

No tumor lysis syndrome

Uric acid

Phosphate

Potassium

Tumor lysis syndrome

Urine excretion

Accumulation

Howard et al., NEJM, 2011
Risk Factors

- Cancer Mass
- Cell lysis potential
- Patient factors
- Supportive care errors of commission/omission (iatrogenic)
<table>
<thead>
<tr>
<th>Metabolic Abnormality</th>
<th>Criteria for Classification of Laboratory Tumor Lysis Syndrome</th>
<th>Criteria for Classification of Clinical Tumor Lysis Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperuricemia</td>
<td>Uric acid &gt;8.0 mg/dl (475.8 μmol/liter) in adults or above the upper limit of the normal range for age in children</td>
<td>Cardiac dysrhythmia or sudden death probably or definitely caused by hyperkalemia</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>Phosphorus &gt;4.5 mg/dl (1.5 mmol/liter) in adults or &gt;6.5 mg/dl (2.1 mmol/liter) in children</td>
<td>Cardiac dysrhythmia, sudden death, seizure, neuromuscular irritability (tetany, paresthesias, muscle twitching, carpopedal spasm, Trouseau’s sign, Chvostek’s sign, laryngospasm, or bronchospasm), hypotension, or heart failure probably or definitely caused by hypocalcemia</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Potassium &gt;6.0 mmol/liter</td>
<td>Increase in the serum creatinine level of 0.3 mg/dl (26.5 μmol/liter) (or a single value &gt;1.5 times the upper limit of the age-appropriate normal range if no baseline creatinine measurement is available) or the presence of oliguria, defined as an average urine output of &lt;0.5 ml/kg/hr for 6 hr</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>Corrected calcium &lt;7.0 mg/dl (1.75 mmol/liter) or ionized calcium &lt;4.5 mg/dl (1.12 mmol/liter)</td>
<td></td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>Not applicable</td>
<td></td>
</tr>
</tbody>
</table>

Howard et al., NEJM, 2011
Management

• Hydration
  • Aim for 2ml/kg urine output
  • Improves renal perfusion/uric acid excretion
  • Loop diuretics in patients with low urine output

• Alkalization? 
  • no longer routinely recommended
  • Precipitation of xanthine crystals
  • Decreases Ca and P solubility
Management

- Allopurinol 10mg/kg/day
- Rasburicase 0.15mg-0.2mg/kg/day
- Correct electrolyte imbalances
Take Home

The prevention and treatment of TLS are based on **aggressive hydration**, correction electrolyte imbalance, and **reduction of uric acid** levels.
Hyperleucocytosis
Hyperleukocytosis

• Laboratory definition of WBC $>100,000 \times 10^9$/L caused by leukemic cell proliferation

• 3 main complications:
  • Disseminated intravascular coagulation (DIC)
  • Tumor lysis syndrome (TLS)
  • Leucostasis
Leucostasis

• Pathological diagnosis: clearly defined

• Clinical diagnosis (may occur with WBC<100,000)
  • rarely made with high confidence
  • empirically diagnosed in patient with acute leukemia, HL, and respiratory or neurologic symptoms
  • difficult to distinguish from those of common infections or hemorrhagic complications of acute leukemia
Risk Factors

• Younger age (11q23 rearrangements)
• AML M4/M5
• Microgranular variant of AML M3
• T-ALL
• Philadelphia positive ALL
Pathogenetic mechanisms in leukostasis.

Christoph Röllig, and Gerhard Ehninger Blood
2015;125:3246-3252
## Clinical Findings

### Symptoms of leukostasis

<table>
<thead>
<tr>
<th>Organ</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Dyspnea, hypoxemia, diffuse alveolar hemorrhage, respiratory failure</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Confusion, somnolence, dizziness, headache, delirium, coma, focal neurologic deficits</td>
</tr>
<tr>
<td>Eye</td>
<td>Impaired vision, retinal hemorrhage</td>
</tr>
<tr>
<td>Ear</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Heart</td>
<td>Myocardial ischemia/infarction</td>
</tr>
<tr>
<td>Vascular system</td>
<td>Limb ischemia, renal vein thrombosis, priapism</td>
</tr>
</tbody>
</table>

Christoph Röllig et al.  
Blood 2015 125:3246-3252
Clinical case.
Management

- IV Hyperhydration, allopurinol or rasburicase
- If possible, **avoid** colloidal transfusion products
  - albumin, pRBCs and FFP
- Maintain Platelet count >50,000
- Leucoreduction with hydroxyurea ± steroids justifiable
- Leukopheresis or exchange transfusion
  - (availability/?/risk of bleeding)
- Chemotherapy as soon as possible
Hydroxyurea

• Hydroxyurea used before a proper induction regimen is implemented in order to lower the tumor burden and reduce the risk of tumor lysis
• Dose of 50-100 mg/kg reduces the white blood cell count by 50% to 80% within 24–48 h
Hydroxyurea

- No data indicating that this approach is superior to immediate induction or that tumor lysis can be prevented by a low-dose cytoreduction strategy
- Side effects are usually minimal and are typically limited to patients who are exposed to hydroxyurea for a prolonged period
Pearls

• Leucostasis is a clinical diagnosis
  • You may be the first to suspect it, communicate suspicion to your team!
  • Consider address other differentials

• Treatment may be life-saving
  • Initiate cytoreduction as soon as possible!

• Leucostasis makes transfusion risky!
  • Increases hyperviscosity (transfuse if necessary/avoid if possible)
DIC

- Caused by high cell turnover and associated high levels of released tissue factor, which then triggers the extrinsic pathway via factor VII
- Occurs in 30% to 40% of Hyperleucocytosis in AML

**Diagnosis:**
- decrease in platelet count and fibrinogen
- elevation of D-dimers, FDPs
- prolongation of PT & aPTT

**Management:**
- Platelet transfusions, (maintain platelet count 20-30x10⁹/L
- Fresh frozen plasma should be initiated immediately in these for abnormal coagulation and associated endothelial damage
Spinal Cord Compression

• Occurs in ~2-5% of children with cancer at diagnosis, progression, or recurrence of disease

• Tumor invasion of vertebrae, collapsing the spinal cord or causing increased pressure in the spinal canal.

• Compression of the vertebral venous plexus causes cord edema, venous hemorrhage, and ischemia
Spinal Cord Compression
Differential diagnosis

• Neuroblastoma
• Soft tissue sarcoma
• Ewing sarcoma
• Lymphoma
• Germ cell tumors
• Metastatic CNS tumors
Clinical Presentation

• Neck, back pain (80%)

• Refusal to walk

• Acute weakness in lower extremities

• Sensory deficits, radicular pain

• Bowel and bladder dysfunction
Approach

• Detailed neurological examination
• Complete laboratory studies
• Tumor markers
• MRI / CT of spine
• Other metastatic work up as indicated
• CSF studies
Factors Affecting approach to management

• The patient Age

• Onset and degree of the neurological deficits

• The most probable diagnosis
How to Approach

• Early diagnosis and treatment are essential to decrease the risk of permanent neurologic deficits

• Treatment include high-dose steroids, chemotherapy, emergent radiation, and surgical decompression via laminectomy
Spinal Cord Compression
Pearl

• The immediate start of chemotherapy is a valuable therapeutic option and should be the emergency treatment of choice in the absence of an experienced neurosurgeon
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Case 3
Take Home Message

- Anticipation
- Early recognition
- Institute management early
- Communication and Teamwork
Questions?
Thank You!