TLS Masquerading as Dialysis Inadequacy: Our Experience

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Disclosures

• None
Outline

• Introduction
• Case Presentation
• Discussion
• Questions
Introduction

• Tumor Lysis Syndrome (TLS) is an oncological emergency caused by rapid release of intracellular potassium, phosphate and nucleic acids from tumor cell lysis.

• Commonly seen in hematologic malignancies:
  • Acute Lymphocytic or Lymphoblastic Leukemia
  • Acute Myeloid Leukemia
  • Burkitt lymphoma
  • After initiation of chemotherapy

• TLS in End Stage Renal Disease (ESRD) is uncommon and such cases have rarely been reported in literature.

1 F. Perry Wilson and Jeffrey S. Berns  Onco-Nephrology: Tumor Lysis Syndrome; CJASN October 2012, 7 (10) 1730-1739; DOI: https://doi.org/10.2215/CJN.03150312
Case Presentation

• A 35 year old Caucasian male with end-stage renal disease due to neurogenic bladder from spina bifida and congenitally absent right kidney status post failed deceased donor renal transplant from February 2000, now on home hemodialysis five times per week via AV fistula since 2010, was admitted when he was indecently found to have 25% blast in peripheral blood.

• He denies any fevers, infections, bleeding tendencies, weight loss, worsening fatigue.

• He is anuric and has no residual renal function.

• He is compliant to hemodialysis and mostly adheres to low phosphate, low potassium diet.

• He underwent bone marrow biopsy to confirm diagnosis of acute leukemia.
Physical Exam

**T:** 36.6 °C  **HR:** 88bpm  **RR:** 18/min  **BP:** 146/82mmHg  **SpO2:** 98% on room air
Awake, alert, in no distress.
**LUNGS:** Bilateral equal air entry.
**HEART:** Regular rate & rhythm, normal S1 and S2.
**ACCESS:** Left Upper Extremity AV fistula with pseudoaneurysm at the proximal end of about 4 cm, with palpable strong thrill and audible bruit.
**Laboratory Data:**

<table>
<thead>
<tr>
<th>Detail</th>
<th>Day 1</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>3.66 x10^9/L</td>
<td>3.50-10.50</td>
</tr>
<tr>
<td>HGB</td>
<td>11.5 g/dL</td>
<td>13.5-17.5</td>
</tr>
<tr>
<td>HCT</td>
<td>34.9 %</td>
<td>38.8-50.0</td>
</tr>
<tr>
<td>PLT</td>
<td>159 x10^9/L</td>
<td>150-450</td>
</tr>
<tr>
<td>Blasts Manual</td>
<td>25.0%</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes Manual</td>
<td>35.0 %</td>
<td></td>
</tr>
<tr>
<td>Abs Lymphocytes Manual</td>
<td>1.28 x10^9/L</td>
<td>0.90-2.90</td>
</tr>
<tr>
<td>Sodium</td>
<td>139 mmol/L</td>
<td>136-145</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.8 mmol/L</td>
<td>3.5-5.1</td>
</tr>
<tr>
<td>Chloride</td>
<td>96 mmol/L</td>
<td>98-107</td>
</tr>
<tr>
<td>CO2</td>
<td>26 mmol/L</td>
<td>22-29</td>
</tr>
<tr>
<td>Glucose</td>
<td>102 mg/dL</td>
<td>74-106</td>
</tr>
<tr>
<td>BUN</td>
<td>43 mg/dL</td>
<td>6-20</td>
</tr>
<tr>
<td>Creatinine, standard</td>
<td>9.52 mg/dL</td>
<td>0.70-1.20</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.5 mg/dL</td>
<td>8.6-10.2</td>
</tr>
<tr>
<td><strong>Phosphorus</strong></td>
<td><strong>6.1 mg/dL (H)</strong></td>
<td>2.7-4.5</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>6.4 mg/dL</td>
<td>3.4-7.0</td>
</tr>
<tr>
<td>LDH</td>
<td>167 U/L</td>
<td>135-225</td>
</tr>
</tbody>
</table>
Peripheral blood smear of acute lymphoblastic leukemia

Wright-Giemsa stain peripheral blood smear: small, uniform blasts with scant cytoplasm & inconspicuous nucleoli.
Bone marrow aspirate of acute lymphoblastic leukemia

Bone marrow aspirate shows lymphoblasts with variable sizes, scant cytoplasm with vacuolation in a few cells, and convoluted nucleus consistent with Acute B-lymphoblastic leukemia.
Management:

- Allopurinol 300 mg daily
- Induction protocol:
  - Prednisone 30 mg/m$^2$ 60 mg po bid Day 1 – Day 28
  - Vincristine 2 mg IV once per day on Day 1, Day 8, Day 15, Day 22.
  - Daunorubicin 25 mg/m$^2$ IV per day on Day 1, Day 8, Day 15, Day 22.
  - Pegaspargase 2500 IU/m$^2$ once on Day 4.
- Rasburicase 3mg iv on Day 2.
- CNS prophylaxis with Intrathecal Methotrexate administered. CNS fluid is negative for leukemia.
Hemodialysis

• Initially switched to thrice weekly: Monday Wednesday Friday dialysis schedule.
• Started chemotherapy 4 days after admission.
• From Day 2 onwards patient required daily dialysis due to persistent hyperkalemia.
• Due to concerns for access recirculation, Dialysis adequacy studies performed.
• Urea Reduction Ratio 60% and single pool Kt/V 1.2
• Patient received daily hemodialysis for 21 consecutive days.
Clinical Course

• 4\textsuperscript{th} dose of Induction chemotherapy held due to hyperbilirubinemia.

• After Day 22 of chemotherapy, potassium levels stabilize.

• No further episodes of hyperkalemia.

• Patient placed on thrice weekly hemodialysis.

• Discharged 2 weeks later.
Discussion
Metabolism of purine nucleic acids

![Diagram showing the metabolism of purine nucleic acids.]

Key Steps:
1. Adenosine Monophosphate → Inosine Monophosphate → Hypoxanthine (1.5 mg/dl) → Allopurinol → Oxypurinol
2. Guanosine → Guanine → Xanthine (0.13 mg/ml) → Xanthine Oxidase
3. Xanthine (0.13 mg/ml) → Urate (2.2 mg/ml) → Urate Oxidase (Absent in Humans) → Allantoin (5 mg/ml)
4. Allopurinol inhibition of xanthine oxidase

References:
Uric Acid

<table>
<thead>
<tr>
<th>Urine pH</th>
<th>Solubility of Uric Acid</th>
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<tbody>
<tr>
<td>5.0</td>
<td>15 mg/dL</td>
</tr>
<tr>
<td>7.0</td>
<td>200 mg/dL</td>
</tr>
</tbody>
</table>
Uric Acid

- Scavenges Nitric Oxide causing vasoconstriction
- Inhibits endothelial cell proliferation, prolongs duration of AKI
- Inflammatory Cytokines released
- Crystals precipitate, Crystallize, Tubular obstruction
Hyperkalemia

• Intracellular concentration of potassium is as high as 120 mEq/L.
• Cell lysis can cause severe hyperkalemia.
• Renal clearance of potassium is reduced in CKD and ESRD.
Phosphorus & Calcium

Secondary Hypocalcemia

Calcium Phosphate Crystals

Arrhythmias
Seizure
Tenancy
Death

Nephrocalcinosis
## Risk Factors

<table>
<thead>
<tr>
<th>Patient Related Factors:</th>
<th>Tumor Related Factors:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hydration status</td>
<td>• Tumor Size</td>
</tr>
<tr>
<td>• Advanced age</td>
<td>• Sensitivity of Cancer to chemotherapy</td>
</tr>
<tr>
<td>• Underlying kidney Disease</td>
<td>• Cancer stage or Extent of involvement</td>
</tr>
<tr>
<td>• Uric acid level</td>
<td>• Rate of proliferation rate</td>
</tr>
<tr>
<td>• Tumor Burden: LDH level</td>
<td></td>
</tr>
<tr>
<td>• WBC count</td>
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</table>

Therapy-Related Factors:

- Intensive polychemotherapy
- Corticosteroids
- Intrathecal chemotherapy
- Radiotherapy
- Interferon
Management of TLS in non-ESRD

• Aggressive volume repletion:
  • 24-48 hours before induction therapy
  • Maintain urine output of at 80-100 mL/m²/h in adults

• Therapy for hyperkalemia, hyperphosphatemia, and hypocalcemia.

• Hyperuricemia:
  • Allopurinol, Febuxostat, Rasburicase, Pegloticase
  • Use of Diuretics & Urinary Alkalinization generally not recommended.

• Exogenous Calcium.
Dialysis

• Uric acid and phosphate effectively removed by diffusive therapy and intermittent hemodialysis.

  Molecular size:
  Uric acid – 168 Da
  Phosphate Anion – 95 Da
  Potassium – 39 Da
TLS in ESRD

• Avoid volume expansion.
• Use of CRRT in hemodynamically unstable patients. ¹
• Hybrid therapies: sustained, low-efficiency dialysis and extended daily dialysis, in centers unequipped to perform CRRT. ¹
• Peritoneal dialysis is not a preferred modality.
• Daily HD. ²

Conclusion

• Tumor Lysis Syndrome in patients with end stage renal disease poses significant challenges.

• Need frequent monitoring of electrolytes and assessment of fluid status.

• Dialysis prescription needs to be assessed regularly: longer sessions or daily dialysis might be required.

• Use of Hypouricemic agents remains controversial.
Thank you!
Questions?