Renal Calculi: An Unusual Presentation of T-Cell Acute Lymphoblastic Leukemia

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Dr Daly participated in the initial workup, admission, and management of this patient in the pediatric emergency department; conceptualized the case report with Dr Thoreson; performed a literature search; wrote the initial manuscript; and made critical revisions after review by the other authors; Dr Barnard reviewed and revised the manuscript and provided further critical review; Dr Thoreson conceptualized the case report with Dr Daly and provided critical review; and all authors approved the final manuscript as submitted.

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Spontaneous tumor lysis syndrome is an oncologic emergency characterized by severe electrolyte disturbances, metabolic acidosis, and acute renal failure (ARF) before the initiation of chemotherapy. It is most commonly seen in adults with hematologic malignancies that have a high rate of cell turnover (eg, Burkitt’s lymphoma) and has only rarely been described in the pediatric literature.1,2 There is a single reported case of STLS secondary to T-cell acute lymphoblastic leukemia (ALL) in the under 6 years age group.3 However, our case is the first description of pediatric STLS presenting with gross hematuria and renal calculi.

CASE REPORT

A 5-year-old previously healthy Hispanic boy presented to the emergency department (ED) with a chief complaint of gross hematuria. His father reported that for 2 days before presentation, the child had decreased energy, reduced appetite, and several episodes of vomiting. The patient’s mother had recently been unwell with gastrointestinal symptoms, and therefore the family initially attributed the child’s symptoms to an infectious etiology.

On the day of presentation to the ED, the boy was no longer vomiting but had worsening lethargy and continued to complain of right-sided abdominal pain. When his father accompanied the child to the toilet, he noticed that the boy had grossly bloody urine and some discomfort with urination, which prompted an emergency medical consultation.

The child had no recent fevers or other illnesses, and there was no report of weight loss, cough, night sweats, pallor, or other recent episodes of abnormal bleeding or bruising.

Examination and Laboratory Results

On examination in the ED, his vital signs were as follows: temperature 98.9°F, heart rate 86 beats per minute,
respiratory rate 20 breaths per minute, and blood pressure 110/66 mm Hg. He was awake, alert, and nontoxic in appearance. Significant physical examination findings included diffuse lymphadenopathy; there were several enlarged lymph nodes in both the anterior and posterior cervical chains, as well as palpable bilateral supravacuclar nodes, each measuring approximately 1.2 cm × 1.2 cm. There were moderately enlarged inguinal lymph nodes bilaterally, and a diffusely nodular abdomen on palpation. Additionally, there was a palpable mass in the right flank just inferior to the costal margin and generalized tenderness of the abdomen that was most pronounced in the right lower quadrant. The chest was clear to auscultation, and there was no hepatomegaly or splenomegaly.

Initial laboratory testing demonstrated a complete blood count with differential that was within normal limits (Table 1). The comprehensive metabolic panel showed notable electrolyte abnormalities, including hyperkalemia, hyperphosphatemia, and hypermagnesemia. Additionally, serum urea nitrogen and creatinine were significantly elevated (74 mg/dL and 4.9 mg/dL, respectively), making it evident that the child had an anion gap metabolic acidosis with intrinsic ARF. After these laboratory results returned with such significantly elevated electrolyte levels, lactate dehydrogenase and uric acid were obtained; the uric acid level was markedly elevated, confirming suspicion for occult malignancy (Table 1).

**Initial Workup and Management**

Given the chief complaint of gross hematuria and right-sided abdominal pain, the differential diagnosis included urinary tract infection, renal trauma, nephrolithiasis, glomerular disease, and malignancy (Wilms tumor, transitional cell carcinoma of the bladder). Therefore, along with previously discussed laboratory studies, the initial workup included a renal/bladder ultrasound looking for evidence of renal calculi or trauma as well as anatomic abnormalities. This ultrasound showed bilateral hydronephrosis and a dilated right ureter with an echogenic focus in the hilum, consistent with a kidney stone. Additionally, a complete abdominal ultrasound was obtained due to concern for appendicitis because the child’s pain and tenderness on physical examination was located primarily in the right lower quadrant; this showed florid lymphadenopathy in the abdomen.

The patient was admitted to the PICU for management of his ARF with obstructive uropathy, and the pediatric oncology, nephrology, and urology services were all consulted simultaneously. After admission, a chest radiograph was performed to rule out a mediastinal mass, which showed mediastinal lymphadenopathy. A peripheral smear revealed circulating lymphoblasts and a bone marrow aspirate showed 95% hypercellularity with immature lymphoblasts. Supravacuclar lymph node biopsy performed 4 hours after admission confirmed the diagnosis of T-cell ALL. Aggressive intravenous hydration and rasburicase therapy (a recombinant version of urate oxidase, used for the treatment of STLS) were initiated, and he was started on continuous venovenous hemofiltration and chemotherapy according to Children’s Oncology Group protocol AALL0434 within 24 hours of admission. He subsequently underwent placement of bilateral ureteral stents with removal of multiple uric acid nephroliths.

### TABLE 1 Initial Laboratory Results

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Result</th>
<th>Reference Rangea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.5</td>
<td>10.5–14.7</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>35.5</td>
<td>32–44</td>
</tr>
<tr>
<td>WBC, × 10^9/Lb</td>
<td>5.4</td>
<td>5.0–15.0</td>
</tr>
<tr>
<td>Platelets, × 10^9/L</td>
<td>156</td>
<td>150–450</td>
</tr>
<tr>
<td>Comprehensive metabolic panel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>136</td>
<td>131–145</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>6</td>
<td>↑ 3.2–5.7</td>
</tr>
<tr>
<td>Chloride, mmol/L</td>
<td>103</td>
<td>98–118</td>
</tr>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>15</td>
<td>15–30</td>
</tr>
<tr>
<td>SUN, mg/dLc</td>
<td>74</td>
<td>↑ 5–27</td>
</tr>
<tr>
<td>Creatinine, mg/dLc</td>
<td>4.9</td>
<td>↑ 0.3–1.0</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>80</td>
<td>56–120</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>18</td>
<td>↑ 4–12</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.3</td>
<td>8.5–10.5</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>9</td>
<td>↑ 2.9–5.9</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.8</td>
<td>2.4–4.8</td>
</tr>
<tr>
<td>TSP, g/dL</td>
<td>6.6</td>
<td>5.4–7.7</td>
</tr>
<tr>
<td>AP, IU/L</td>
<td>106</td>
<td>↓ 110–341</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>24</td>
<td>13–58</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>12</td>
<td>8–39</td>
</tr>
<tr>
<td>LDH, IU/L</td>
<td>294</td>
<td>140–304</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.6</td>
<td>0.6–2.0</td>
</tr>
<tr>
<td>Magnesium, mg/dL</td>
<td>3</td>
<td>↑ 1.7–2.8</td>
</tr>
<tr>
<td>Uric acid, mg/dL d</td>
<td>&gt;24</td>
<td>↑ 1.9–5.4</td>
</tr>
</tbody>
</table>

AP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; SUN, serum urea nitrogen; TSP, total serum protein. ↑, above reference range; ↓, below reference range.

a All reference ranges are those used at the laboratory for this patient at Dell Children’s Hospital in Austin, TX, at the time and age of presentation.

b WBC differential: neutrophils, 42%; lymphocytes, 49%; monocytes, 8%.

c Intrinsic ARF.

d Too high to measure.
The patient underwent continuous venovenous hemofiltration for 3 days, after which he was transferred from the PICU to the general hematology/oncology unit. His tumor lysis laboratory studies (comprehensive metabolic panel, magnesium, phosphorus, uric acid) normalized, and he was discharged on the 11th hospital day. He is currently undergoing chemotherapy according to Children's Oncology Group protocol AALL0434.

**DISCUSSION**

Tumor lysis syndrome (TLS) is an oncologic emergency that is characterized by classic laboratory findings of hyperkalemia, hyperphosphatemia, and hypocalcemia, along with hyperuricemia, metabolic acidosis, and ARF. Risk factors for the development of TLS include large tumor burden, high rate of cell turnover, and tumors that are highly sensitive to chemotherapy.  It is most commonly seen after the initiation of chemotherapy for high-grade lymphoproliferative malignancies such as lymphoblastic lymphoma, acute B-cell lymphoblastic leukemia, and Burkitt's lymphoma. The initiation of cytotoxic chemotherapeutic agents results in the rapid release of intracellular ions, such as phosphorus and potassium, as well as nucleic acids and other protein breakdown products into the circulation.

STLS describes the same constellation of laboratory abnormalities before the initiation of chemotherapy, which has only rarely been described in the pediatric literature. The initial presentation of hyperphosphatemia, hyperkalemia, metabolic acidosis, hyperuricemia with concomitant renal calculi, ARF, and the subsequent diagnosis of T-cell ALL in our patient is consistent with STLS. STLS has been described more frequently in adult populations with hematologic malignancy (most commonly Burkitt lymphoma); our case is the second to be reported in this age group of ≤6 years. Kobayashi et al described a 5-year-old female patient with STLS and T-cell ALL who presented with acute azotemia in the setting of recurrent urinary tract infections. Our case is the first to describe gross hematuria and renal stones from STLS in the pediatric population.

Electrolyte abnormalities are the hallmark of TLS and are responsible for its significant morbidity and mortality. Hyperkalemia is the most serious complication of TLS and is caused by the rapid movement of intracellular potassium into the circulation after cell lysis. This can cause weakness, paresthesias, muscle cramps, nausea, vomiting, and, in severe cases, ventricular tachyarrhythmias. Treatment of hyperkalemia in the emergency setting includes administration of potassium-binding agents (eg, Kayexalate) and hemodialysis. Hyperphosphatemia is also commonly seen because malignant hematologic cells may contain up to 4 times more intracellular phosphate compared with normal mature lymphoid cells, and high cell turnover results in hyperphosphatemia as the serum concentration of phosphate exceeds the renal excretion threshold. Precipitation of calcium phosphate in the renal tubules subsequently results in hypocalcemia. Nephrocalcinosis can occur in this instance, which causes ARF in affected patients.

Because of their increased cellular activity, malignant cells have a high concentration of nucleic acid products; this high turnover leads to ongoing DNA catabolism. This results in an increased breakdown of purine nucleotides and high concentrations of hypoxanthine, which is converted to uric acid. Tumor lysis therefore results in hyperuricemia, which in turn leads to a rapid increase in both plasma and renal tubular concentrations. These elevated concentrations predispose patients to form uric acid stones. Treatment of hyperuricemia involves either allopurinol (a xanthine oxidase inhibitor, which prevents the formation of uric acid) or rasburicase, a compound that converts uric acid to allantoin, which is then easily excreted by the kidneys, and so is the preferred medication in the emergency setting.

The pathophysiology of ARF in STLS is multifactorial; the 2 major tenets of which are volume depletion and uric acid nephropathy. A low pH in the renal collecting ducts reduces the threshold at which precipitation of uric acid occurs; these crystals then obstruct the flow of urine through the tubules, leading to uric acid nephropathy, which is exacerbated in volume-depleted patients. Our patient (like many patients with hematologic malignancy) was volume depleted, secondary to decreased appetite and vomiting. Volume depletion in conjunction with our patient’s elevated uric acid concentration overwhelmed the nephrons’ ability to autoregulate and maintain intraglomerular flow, resulting in ARF.

Our case illustrates a rare initial presentation of T-cell ALL with uric acid nephrolithiasis and ARF in the setting of STLS. Pediatric physicians seeing patients in the ED should be aware that occult hematologic malignancy is a potential underlying etiology of gross hematuria with renal stones, and lactate dehydrogenase and uric acid level should be considered in these patients to rule out STLS. Although STLS is rare, the implications of missing such a diagnosis are large and could significantly affect a patient’s morbidity and mortality. As with our patient, an initial complete blood count may be normal and cannot be used to exclude hematologic...
malignancy. Early management of STLS includes aggressive hydration, timely administration of rasburicase therapy, and initiation of hemodialysis in an intensive care setting.9,10

**ABBREVIATIONS**

ALL: acute lymphoblastic leukemia
ARF: acute renal failure
ED: emergency department
STLS: spontaneous tumor lysis syndrome
TLS: tumor lysis syndrome

**REFERENCES**


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