Hyperuricemia and acute renal failure secondary to spontaneous tumor lysis syndrome in low risk myelodysplastic syndrome.

Yunlin Feng, M.D.¹, Tao Jiang²

¹ Correspondence: Yunlin Feng  fengyunlin@tsinghua.org.cn

¹ Division of Nephrology, Sichuan Academy of Medical Sciences & Sichuan Provincial People’s Hospital, Chengdu 610072, China

² Division of Hematology, Sichuan Academy of Medical Sciences & Sichuan Provincial People’s Hospital, Chengdu 610072, China
Abstract:

**Background:** This is a rare instance of acute renal failure caused by hyperuricemia due to spontaneous tumor lysis syndrome and the first case of spontaneous tumor lysis syndrome reported in myelodysplastic syndrome. **Case Presentation:** A 53-year-old man presented with abrupt oligouria. Laboratory findings on admission suggested hyperuricemia, hyperphosphatemia, hypocalcinemia, metabolic acidosis and rapidly elevated serum creatinine, which were consistent with acute tumor lysis syndrome in the absence of precipitating chemotherapy or radiotherapy. After hemodialysis and oral uric acid lowering therapy, the serum uric acid levels returned to normal range and the renal function rapidly recovered. The patient was diagnosed myelodysplastic syndrome eleven months later. **Conclusion:** Occult malignancy including solid tumors and hematological malignancies should be carefully evaluated in the case of unexplainable acute renal failure with hyperuricemia. Aggressive examinations should be thoroughly considered and repeated as necessary in this population.

**Key words:**

acute renal failure, hyperuricemia, myelodysplastic syndrome, spontaneous tumor lysis syndrome
**Background**

Acute tumor lysis syndrome (TLS) is a metabolic disorder manifesting as abrupt occurrence of acute renal failure (ARF), metabolic acidosis and electrolytes disturbances which include hyperuricemia, hyperphosphatemia, hyperkalemia and hypocalcemia. TLS most commonly results from treatment of malignancies, especially high turnover rate hematologic malignancies. Spontaneous tumor lysis syndrome (STLS) before chemotherapy is a rare event which has been mostly reported in Burkitt lymphoma and non-T-cell acute lymphoblastic leukemia. Here we report a rare case of STLS in myelodysplastic syndrome (MDS) which presented with marked hyperuricemia and ARF months before the diagnosis of MDS.

**Case Presentation:**

A 53-year-old man presented to Nephrology department with generalized malaise and decreased urine volume for 5 days. He denied nausea, vomiting or fever. The medical history included hypertension for 10 years and type 2 diabetes mellitus for 8 years, both of which had been well controlled. He had received laparoscopic cholecystectomy (LC) one week before the admission due to right upper quadrate abdominal pain, which had been diagnosed as cholithiasis and cholecystitis. The laboratory data pre- and post-op was summarized in Table 1.

At the current admission, physical examination showed a chronically ill-appearing man in no acute distress, with stable vital signs. The patient was awake, alert and oriented. There was no jugular venous distention. Pulmonary and cardiac examinations were unremarkable. Abdominal examination showed well cured small scars left by the LC. Mild bilateral pretibial pitting edema presented in both lower limbs. Neurological examination was unremarkable.

The results of electrocardiogram, chest/abdominal CT were unremarkable. An ultrasound showed relatively enlarged renal size (right side, 11.1x5.1cm; left side, 11.8x5.9cm). Further investigations including complete blood count (CBC), renal function, liver function, serum uric acid (UA), electrolytes and serum biomarkers were completed. Laboratory results summarized in Table 1 indicated elevated serum creatinine (SCr), hyperuricemia, hyperphosphatemia, hypocalcineemia as well as severe anemia and slightly decreased WBC count. The remainder of lab tests including serum tumor biomarkers was normal. The patient’s clinical manifestations of ARF and electrolytes disturbance were consistent with TLS.

After admission, the patient was given transfusion and intermittent hemodialysis, after which SCr almost returned normal and the dialysis was stopped. Changes of serum biochemical parameters were shown in Figure 1. Since the anemia consisted and there were no signs of solid tumors, we highly suspected hematological malignancies and repeatedly performed bone marrow examinations. Bone marrow smears from the first two times had no signs of malignancies. There was mild dysphaematoipoiesis on the third time smear but was still inconclusive to make a diagnosis. The biopsy was normal and the molecular analysis returned negative.

The patient visited the clinic every 2-3 months after discharge. Investigations showed HGB was fluctuating in the range of 75-90g/L while SCr and UA kept normal. Chest/abdominal CT was done 3 months and 9 months later with unremarkable findings. However, the patient complained persistent malaise which had been progressively worsening. Eleven months later, he was admitted again because of refractory anemia. At this time, bone marrow smear indicated hyperplasia of erythroid and significant dysphaematoipoiesis of all three lineages. Major loss of D20S108 signal
suggesting 20q- along with minor gains of D8Z2 signal was discovered by fluorescence in situ hybridization (FISH), which was consistent with G banding karyotype. MDS was confirmed and the patient was classified as low-moderate risk group, hence no chemotherapy. He has been on regular clinic follow-up and the condition hasn’t deteriorated till now.

### Table 1. Laboratory investigation results.

<table>
<thead>
<tr>
<th>Date</th>
<th>WBCs (x10^9/L)</th>
<th>PLT (x10^9/L)</th>
<th>HGB (g/dL)</th>
<th>SCr (µEq/L)</th>
<th>UA (µEq/L)</th>
<th>CO₂ (mEq/L)</th>
<th>K (mEq/L)</th>
<th>cCa (mEq/L)</th>
<th>P (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before LC</td>
<td>2.13</td>
<td>218</td>
<td>79</td>
<td>111.9</td>
<td>866</td>
<td>22.6</td>
<td>3.88</td>
<td>2.15</td>
<td>1.34</td>
</tr>
<tr>
<td>5 days before admission /after LC</td>
<td>3.75</td>
<td>40</td>
<td>61</td>
<td>120.0</td>
<td>911</td>
<td>22.1</td>
<td>3.12</td>
<td>2.02</td>
<td>1.14</td>
</tr>
<tr>
<td>1 day before admission</td>
<td>4.50</td>
<td>134</td>
<td>58</td>
<td>839.0</td>
<td>2240</td>
<td>16.3</td>
<td>3.54</td>
<td>1.98</td>
<td>2.71</td>
</tr>
<tr>
<td>Admission</td>
<td>3.97</td>
<td>146</td>
<td>52</td>
<td>1032.1</td>
<td>2369.6</td>
<td>16.7</td>
<td>3.59</td>
<td>2.11</td>
<td>3.06</td>
</tr>
<tr>
<td>1 day after admission</td>
<td>4.12</td>
<td>130</td>
<td>62</td>
<td>905.9</td>
<td>1869.1</td>
<td>17.7</td>
<td>3.74</td>
<td>2.20</td>
<td>2.52</td>
</tr>
<tr>
<td>3 days after admission</td>
<td>2.31</td>
<td>165</td>
<td>70</td>
<td>752.4</td>
<td>1438.3</td>
<td>22.7</td>
<td>3.69</td>
<td>2.43</td>
<td>1.48</td>
</tr>
<tr>
<td>Discharge</td>
<td>5.20</td>
<td>156</td>
<td>77</td>
<td>100.1</td>
<td>368.6</td>
<td>23.6</td>
<td>4.42</td>
<td>2.31</td>
<td>1.56</td>
</tr>
</tbody>
</table>

Abbreviations: LC, laparoscopic cholecystectomy; WBCs, white blood cells; PLT, platelets; HGB, hemoglobin; SCr, serum creatinine; UA, uric acid; CO₂, bicarbonate; K, potassium; cCa, corrected calcium; P, phosphate.

**Figure 1.** Serial biochemical study of the patient.

**Note:** SCr, in mg/dL, where 1mg/dL=88.4µmol/L; UA, in mg/dL, where 1mg/dL=59.48µmol/L.

**Abbreviation:** HD, hemodialysis.

**Discussion**

The mostly used diagnostic criteria for TLS are the laboratory and clinical criteria proposed by Cairo and Bishop³. A clinical diagnosis of TLS includes one clinical symptom and two laboratory criteria, and at least two laboratory criteria must be present for three days before treatment or up to seven days after treatment. In our case, the patient fulfilled one clinical symptom (ARF) and two laboratory criteria (hyperphosphatemia, hyperuricemia), thus met the clinical diagnosis criteria of TLS. Since there was no prior chemotherapy or radiotherapy, we considered this was a STLS case.

Acute TLS is usually observed after the initiation of cytotoxic chemotherapy of malignancies, especially high turnover rate hematologic malignancies. The severity of TLS depends on tumor burden, tumor type, proliferation rate, baseline uric acid level and exquisite sensitivity to chemotherapeutic agents⁴. STLS prior to the initiation of chemotherapy is rare, especially in the absence of evidence for tumor, including hematological malignancies and solid tumor. According to previous studies, STLS most commonly occurred in Burkitt lymphoma and non T-cell acute lymphoblastic leukemia², and it had also been reported in acute lymphoblastic leukemia (ALL)⁴, acute myeloid leukemia (AML)⁵, myelofibrosis⁶, metastatic germ cell tumor⁷ and solid tumors⁸.

To the best of our knowledge, our case is the first STLS reported for MDS. The initial presentations of significant hyperuricemia, hyperphosphatemia, metabolic acidosis, ARF and relative hypocalcinemia were all consistent with STLS. In 2003, Yang et al⁹ reported a 32-year-old man who had been diagnosed as MDS with refractory anemia and excess blasts in transformation subtype and developed TLS after a single dose of methylprednisolone 1.0g. However, in our case,
the patient didn’t fulfill the diagnostic criteria for MDS at the onset of STLS. Instead, he was diagnosed as MDS almost one year after this episode of STLS. When the STLS happened, repeated bone marrow cytology and biopsy didn’t show evidence of large tumor burden or tumor types which had been reported to be associated with STLS. The etiology in our case is inconclusive. Potential causes for STLS include endogenous secretion of glucocorticoid with infection\textsuperscript{10} and fever\textsuperscript{8}. In Daisuke et al’s case of STLS in ALL\textsuperscript{4}, it was believed the STLS might be triggered by a febrile gastroenteritis-like illness one month prior to the first admission and accelerated by the concomitant urinary tract infection. In our case, the patient had experienced abdominal pain consistent with cholecystitis before the admission and it had been only two weeks after a surgery when the ARF developed. The endogenous secretion of glucocorticoid triggered by the infection and the stress of operation might be the cause of the STLS.

**Conclusion:**

In summary, here we reported an adult of MDS presented with ARF and laboratory features of ATLS, occurring months before diagnosis of MDS, in the absence of precipitating chemotherapy and radiotherapy. It has been suggested occult malignancy should be considered in the case of unexplainable ARF with hyperuricemia\textsuperscript{11} with which our experience in this patient is consistent. Aggressive examinations for malignancies, including solid tumors and hematological malignancies should be thoroughly considered and repeated as necessary in this population, and the patients without definite diagnosis should be more closely followed-up in the clinic.

**Consent:**

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

**Competing Interests:**

The authors declare that they have no competing interests.

**Authors Contributions:**

FYL participated in the collection of clinic information and drafted the manuscript. JT also participated in the collection of information and helped to draft the manuscript. All authors read and approved the final manuscript.

**References:**

Figure 1. Serial biochemical study of the patient.